

PERIPHERAL BIOMARKERS AND BRAIN BEHAVIOR, STRUCTURE, AND FUNCTION
IN HEALTHY, AGING ADULTS

BY

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DISSERTATION

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ABSTRACT

The current demographic landscape is shifting toward a population disproportionately comprised of adults over the age of 65-years-old. These changes are occurring at an unprecedented rate and challenging the healthcare system to meet the needs of aging-centered care for more people than ever before. As the brain ages it undergoes changes yielding deficits of varying severity, from cognitive deficits seen in normal aging to functional deficits experienced with pathological aging. Observational and interventional studies suggest peripheral factors could influence challenges arising from normal brain aging, though the results are variable. Two such peripheral factors are nutrition, evidenced by studies in nutritional epidemiology, and inflammation, evidenced by studies in psychoneuroimmunology. The unique and regulated barrier between the periphery and the brain, commonly referred to as the blood-brain barrier, determines which nutrients and inflammation factors gain access to the central nervous tissues. Some nutrients, such as xanthophyll carotenoids, can cross this barrier while markers of inflammation are more regulated, with greater access permitted as the integrity of the barrier declines with age. Because these peripheral biomarkers have access to brain tissue, it is possible that they impact changes in cognitive function associated with brain aging by influencing brain structure, network connectivity, and white matter integrity. As such, these biomarkers are potential targets for intervention studies and precision medicine approaches to ameliorate normal brain aging. The following dissertation expands on how xanthophyll carotenoids and inflammation factors moderate relationships that predict facets of intelligence across imaging modalities, providing converging evidence that these peripheral biomarkers impact human health, aging, and disease.

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CHAPTER 1: LITERATURE REVIEW

Currently, the United States is home to an aging population in which the number of individuals 65 years-old and over is expected to double by the year 2050 (Ortman & Guarneri, 2009). That same year the global population within this age group is projected to reach 1.5 billion, accounting for 25% of the population in North America and Europe and for 16% of the world's total population (United Nations, Department of Economic and Social Affairs, Population Division, 2019). This demographic group faces unique challenges because it is susceptible to cognitive decline regardless of individual health status due to the normal aging process. When combined with chronic health conditions the neurobiological changes associated with normal aging can require varying levels of care, such as daily medication or even assisted living. The cognitive decline seen in normal aging may increase the need for assistance to perform tasks such as maintaining a household, caring for a pet, or adhering to medication regimens. When compounded with the health care required for chronic conditions related to normal aging or poor overall health, the health care system is struggling to accommodate the immense costs for care attributed to the increased demand of a growing aging population.

In fact, it is expected that beginning as early as the year 2037 the US government will not be able to provide scheduled Social Security health care benefits for 24% of its people (Goss, 2010). Together, this presents a situational opportunity where research can be used to simultaneously improve quality of life years for the growing population of older individuals while attenuating the needs of this demographic, thereby alleviating tensivity faced by the healthcare system. The shifting demographic landscape and current cost of healthcare presents a critical need to identify modifiable factors that are potential targets for promoting healthy brain aging. Identifying targets that promote healthy brain aging could improve the quality-of-life

years and decrease the burden of care for the millions of individuals currently experiencing various stages of normal brain aging. Two modifiable factors that show promise as targets for promoting healthy brain aging are nutrition and peripheral inflammation.

An accumulating body of literature suggests that dietary nutrition may be a cost-effective target to promote healthy brain aging. For example, evidence supports positive relationships between fruit juice and memory function (Krikorian, et. al., 2010a; Krikorian et. al., 2010b) and between omega-3 polyunsaturated fatty acids and cognition in the elderly (Titova et. al., 2013), as well as a reduced risk of cognitive decline and dementia in aging individuals taking Vitamin E and Vitamin C supplements (Maxwell et. al., 2005). Characterizing relationships between dietary nutrients and facets of cognitive functioning is an important contribution to the growing body of literature seeking targets for promoting healthy brain aging, as these relationships will inform cost-effective methods for increasing quality-of-life years in the aging population.

Evidence also suggests ameliorating systemic inflammation as an avenue to promote healthy brain aging. Cognitive function decreases with healthy aging and there are many hypothesized mechanisms behind these deficits. One leading hypothesis is that an amplified inflammatory state within the body (*i.e.*, increased peripheral inflammatory markers) is related to cognitive decline in an aging population (Schram et. al., 2007; Simen et. al., 2011). This growing body of literature suggests a strong role for inflammation in both normal brain aging (Dik et. al., 2005; Schram et. al., 2007) and pathological brain states such as Alzheimer's Disease (AD; McGeer & McGeer, 2001; Heneka & O'Banion, 2007) and mild cognitive impairment (Magaki, Mueller, Dickson, & Kirsch, 2007; for a meta-analysis see Bradburn, Murgatroyd, & Ray, 2019). Expanding on the research within this field to characterize relationships between peripheral

inflammation markers and facets of cognitive functioning holds great potential for identifying targets that promote healthy brain aging.

The following literature review details the current understanding of brain aging and how facets of cognitive functioning relate to these modifiable factors. The review will first outline changes in brain behavior, grey matter structure, network function, and white matter microstructure that accompany aging and will close with introductions to the fields of nutritional cognitive neuroscience and inflamm-aging.

1.1 *The Aging Brain*

As the brain undergoes normal aging, it experiences changes in some facets of intelligence, grey matter volume, functional connectivity, and white matter structure. Below is a brief review of these changes that focuses on information most relevant to the studies conducted in this dissertation.

1.1.1 *Cognitive Changes*

As people age, they experience a linear decline in the performance of many cognitive processes including memory, reasoning, spatial visualization, and object manipulation (Salthouse, 2010). This decline is well established and is reported in numerous studies using different neuropsychological assessment methods such as the Wechsler Memory Scale (WMS – IV), derivations of the Trail Making test, and the Block Design test (Salthouse, 2009; Rhee, 1996). As learning capacity gradually declines, deficits are reflected in many facets of intelligence including episodic memory, fluid intelligence, working memory, and others

(Murman, 2015). Still, there are some facets of intelligence that resist age-related decline including semantic memory, crystallized intelligence, and procedural memory.

Episodic memory is the recall of information including the “who,” “what,” “where,” and “when” pertaining to personal experiences (Tulving, 1983) and is thought to be the facet of intelligence most sensitive to age-related decline (Nyberg and Tulving, 1996). Longitudinal studies indicate that episodic memory decline begins in late middle age (Kausler, 1994; Nyberg et. al., 2012) and then accelerates in older age (Singer et. al., 2003). A different pattern of decline is seen in fluid intelligence, the ability to reason and manipulate novel information. Fluid intelligence declines steadily throughout the aging process (Murman, 2015; Salthouse, 2010) and this pattern is shared by some similar facets of intelligence, such as working memory. Working memory requires the temporary storage of information while simultaneously receiving and processing new information (Salthouse & Pink, 2008), engaged by tasks such as learning complex skills and reading comprehension (Feldman Barrett, Tugade, & Engle, 2004). Similar to both episodic memory and fluid intelligence, working memory appears to begin a steady decline as early as 55 years old (Hultsch, et. al., 1992; Park et. al., 2002).

Conversely, some facets of intelligence are largely unaffected by aging or even resist age-related decline. These processes generally require knowledge obtained much earlier in life or semantic memory, which is the recall of objective information such as vocabulary, numbers, or concepts (Nyberg et. al., 2003; Salthouse, 2009). For example, the ability to apply knowledge acquired earlier in life to a present problem (termed crystalized intelligence) tends to increase through middle age and then remain stable until an individual reaches their 80’s (Kliegl, 2001; Salthouse, 2010). Procedural memory, required for tasks such as tying one’s shoes, also remains stable through the aging process (Churchill et. al., 2003).

As these cognitive changes occur, the neural mechanisms comprising cognitive systems decline (Lawton et. al., 1999) and prefrontal activation appears to increase (Park & Reuter-Lorenz, 2009). This apparent dichotomy can be explained by the scaffolding theory of aging and cognition, which asserts that increased activation is an adaptation to compensate for deteriorating cognitive function and underlying neural mechanisms (Park & Reuter-Lorenz, 2009). However, as degradation continues these compensatory mechanisms are no longer sufficient and cognitive decline worsens. Such cognitive changes are reliably associated with structural and functional changes throughout the brain that correspondingly occur during aging. Structural changes are reflected in cortical grey matter volume, while functional changes are reflected in properties of intrinsic connectivity networks (ICNs) captured with functional magnetic resonance imaging (fMRI). More recently, scientists have connected behavioral changes with changes in white matter microstructure that occur during aging as well.

1.1.2 Volumetric Changes

Changes to brain structure that accompany normal aging are associated with cognitive decline and may provide insight into mechanistic relationships involved in this process. Like other organs the human brain experiences progressive deterioration after 50 years, however decline is not uniform across regions within the brain (Mendonca et. al., 2017). Grey matter regions are predominately affected, with volume loss principally occurring in the prefrontal cortex (Rhee, 1996; Raz et. al., 2005) as well as in the parietal and temporal lobes (Resnick et. al., 2003; Peters, 2006). Other regions such as the occipital lobe and entorhinal cortex appear to resist age-related changes (Raz et. al., 2005), though there appears to be conflicting evidence for these areas.

In 2005 a seminal, longitudinal study of healthy adults found that the greatest cortical volume loss over the five-year study period occurred within the lateral prefrontal and orbitofrontal cortices and found no significant change within the entorhinal cortex (Raz et. al., 2005). Later, however, a study from the same group observed a significant volume loss in the entorhinal cortex over a 30-month period (Raz et. al., 2010). This study also identified individual differences in the rate of volume loss for the lateral prefrontal cortex and medial temporal areas but did not identify variability in atrophy rate for the orbitofrontal cortex. Individual variability in the rate of grey matter volume loss for some regions but not others suggests that while age uniformly deteriorates some areas, other cortical regions may vary in susceptibility to age-related decline due to variable factors such as genotype, diet, or stress exposure.

Grey matter volume loss correlates with cognitive changes during aging, and longitudinal studies indicate that grey matter volume can predict changes in cognitive performance. For example, in older adults studied over a six-year period, an increased atrophy rate in the medial temporal lobe predicted general cognitive decline (Rusinek et. al., 2003) and in another study baseline measures of frontal and temporal grey matter volume in healthy, middle-aged women predicted changes in episodic memory over 10 years (Aljondi et. al., 2019). The same 10-year study showed that smaller grey matter volume, regardless of atrophy rate, is associated with higher rates of cognitive decline (Aljondi et. al., 2019). Though this body of literature is still growing, these studies suggest that regional grey matter volume could serve as a neurological marker for late-life cognitive deficits in healthy individuals. However, understanding cortical volume as a neurological marker for cognitive decline still requires further exploration into relationships between specific regions and different facets of intelligence.

1.1.3 *Functional Changes*

The properties that describe connections between brain regions are also susceptible to aging effects. Resting state functional magnetic resonance imaging (rsfMRI) facilitates the characterization of functional brain networks by their intrinsic properties using blood-oxygen-level-dependent signaling while an individual is at rest (Van Dijk et. al., 2010). In short, this method of data collection detects real-time oxygen levels within the brain's blood supply, enabling the visual mapping of networks being used while the individual is not engaging with any task. Connections throughout the entire brain, or global connectivity, can be parcellated into intrinsic connectivity networks (ICN's) that feature a modular organization structure often described using graph theory metrics (Meunier, Achard, Morcom, & Bullmore, 2009). This community organization has an internal framework composed of nodes (indicative of brain regions) and edges (indicative of connections between those brain regions), which also form connections with other communities within the network (Guimerà & Amaral, 2005). The nodes and edges within a community form properties such as global efficiency (average path length), local efficiency (local node clustering), small-world propensity (optimal balance between global and local efficiency), and strength of ICN's (Muldoon, Bridgeford, & Bassett, 2016).

As individuals age general network efficiency declines, and networks including frontal and temporal regions experience decline disproportionate to networks comprised of other regions (Archard & Bullmore, 2007). Because ICN's are reproducible across subjects, the disproportionate decrease in efficiency across functional networks led to investigation of relationships between network properties and facets of intelligence (Damoiseaux et. al., 2006; Guo et. al., 2012).

The most extensively studied ICN is the default mode network (DMN). This network is active during processes that occur at rest but is suspended as soon as goal-directed behavior begins (Raichle et. al., 2001). It is well documented that during healthy brain aging functional connectivity within the DMN decreases (Andrews-Hanna et. al., 2007; Damoiseaux et. al., 2008; Esposito et. al., 2008; Song et. al., 2014; Tomasi & Volkow, 2012;). In fact some properties of the DMN are already distinguishably lower in middle-age when compared to young adults,

Particularly vulnerable are edges spanning anterior and posterior nodes within the DMN, where severe disruption results in disconnection that correlates with cognitive decline (Andrews-Hanna et. al., 2007; Damoiseaux et. al., 2008). Within the DMN intrinsic properties are changing as early as middle age, with the strength, local efficiency, and global efficiency being lower in middle-aged individuals than in young adults (Song et. al., 2014). Unfortunately, literature detailing age-related changes in other ICNs is limited. There have been studies relating aging to disruption within the dorsal attention network (DAN; Tomasi & Volkow, 2012), salience network (Onoda, Ishihara, & Yamaguchi, 2012), executive control network (Zhang et. al., 2014), frontoparietal network (Campbell, Grady, Ng, & Hasher, 2012), somatomotor network (SMN; Song et. al., 2014; Zonneveld et. al., 2019), and ventral attention network (VAN; Zonneveld et. al., 2019). Even fewer studies have investigated relationships between ICNs and facets of intelligence, but there is evidence connecting disruption within the salience network (Onoda, Ishihara, & Yamaguchi, 2012) and DMN to cognitive decline (Damoiseaux et. al., 2008). Understanding how ICNs relate to facets of intelligence during healthy aging will provide insight into possible neurological markers of decline, however there are many questions regarding this relationship that remain unanswered.

1.1.4 *White Matter Changes*

White matter architecture can be understood in terms of microstructural properties describing the diffusion of water molecules in each voxel measured by diffusion tensor imaging (DTI). These properties include diffusion along (axial diffusivity, AxD) and perpendicular to (radial diffusivity, RD) the major axis of each voxel within a white matter tract (Madden et. al., 2012). Water molecules able to diffuse freely will do so in all directions equally, as described by the principle of Brownian motion, which explains that molecules at thermal equilibrium will move without net directionality (Einstein, Fürth, and Cowper, 1956; Naismith et. al., 2010). However, within the brain water molecules preferentially diffuse axially due to its microstructural organization thus yielding directional movement characterized as anisotropic in a normal state (Weishmann et. al., 1999). Obstructed molecules in this system experience a shift in directionality and become more isotropic, and the degree of directionality in diffusion is measured by fractional anisotropy (FA). Measured on a scale of 0-1, an FA of “0” indicates isotropy, or directionally equal diffusion, and an FA of “1” indicates anisotropy, or diffusion preferential to one direction (Madden et. al., 2012).

Measuring the degree of directionality in water diffusion within white matter tracts provides information about the integrity of these structures, a characteristic more susceptible to age-related changes than cortical volumes (Guttmann et. al., 1998). Loss of white matter integrity is etiological to both pathological brain states and normal, healthy brain aging and is responsible for reorienting the diffusion of water molecules within the brain. In older adults, FA is lower in the majority of white matter tracts, and the relationship grows stronger with age (Burzynska et. al., 2010; Cox et. al., 2016; Zahr, Rohlfing, Pfefferbaum, & Sullivan, 2009). The relationship between age and FA appears strongest in anterior regions including the inferior

longitudinal fasciculus, superior longitudinal fasciculus, and uncinate fasciculus (association fibers) and thalamic radiation fibers, while FA in the cingulum and sensory fibers modestly relate to age (Cox et. al., 2016; Zahr, Rohlfsing, Pfefferbaum, & Sullivan, 2009). Interestingly RD appears to have an opposite relationship, increasing with age (Sullivan, Rohlfsing, & Pfefferbaum, 2010; Vernooj et. al., 2008). This has been shown in the genu of the corpus callosum, middle frontal gyrus, superior corona radiata, external capsule, and the anterior limb of the interior capsule (Burzynska et. al., 2010). Axial diffusivity is thought to reflect axonal damage and exhibits a more complex relationship with aging than do FA or RD (Barrick et. al., 2010). Not only are changes in AxD less robust than those observed in FA or RD, but whether AxD increases or decreases with age is inconsistent. Some studies report regional decreases in AxD associated with aging (Burzynska et. al., 2010), while others report increases in some of the same regions (Vernooj et. al., 2008).

Despite conflicting evidence in some diffusivity measures, deterioration of white matter integrity appears to be associated with decline in various facets of intelligence, including working memory, executive functioning, processing speed, reasoning, and episodic memory (Madden et. al., 2012; Bennett and Madden, 2014). Further, lower FA in the genu of the corpus callosum and in the fornix are correlated with lower cognitive scores (Sullivan, Rohlfsing, and Pfefferbaum, 2010; Zahr, Rohlfsing, Pfefferbaum, & Sullivan, 2009). These studies suggest that diffusivity measures for individual tracts are far from understood. Additionally, filling this gap in knowledge would characterize healthy brain aging and help to better understand the nature of cognitive decline.

1.2 *Nutritional Cognitive Neuroscience and Aging*

Nutritional cognitive neuroscience is an emerging field that aims to characterize and understand the relationships between nutrients derived from the diet and the structural, functional, and behavioral properties of brain health (Zamroziewicz and Barbey, 2016). Using diet to attenuate negative health outcomes is not a new idea. In the late 1990's, the DASH (Dietary Approaches to Stop Hypertension) trial made waves when it published randomized studies showing that a managed diet of fruits, vegetables, and low-fat dairy could lower blood pressure levels without increased exercise or cutting sodium intake (Svetkey et. al., 1999; Harsha et. al., 1999; Appel et. al., 1997). Around this same time, the MeDi (Mediterranean Diet) was characterized using a pyramidal framework that could be compared to the food guide published by the United States Department of Agriculture (USDA; Willett et. al., 1995). This diet is based on food patterns common in and around Greece and southern Italy during the 1960's when it was first contrived (Keys, Keys, and Mayer, 1975; Willett et. al., 1995). Most recently the Rush Memory and Aging Project developed MIND (Mediterranean-DASH Diet Intervention for Neurodegenerative Delay), a combination of DASH and MeDi shown to delay Alzheimer's and Parkinson's related pathologies as well as to slow cognitive decline during aging (Agarwal et. al., 2018; Morris et. al., 2015a, 2015b).

Literature within the field also explores nutrients outside of their dietary context to understand how this modifiable factor may facilitate healthy brain aging. Seminal to this advancement was Gene Bowman, the first to publish a principal component analysis to statistically derive nutrient biomarker patterns and capture their joint contribution to cognitive neuroscience measures of aging (Bowman et. al., 2012). Since, several studies have used similar

methods to show that nutrient patterns moderate relationships between regional grey matter volume and auditory memory (Key, Zwilling, Talukdar, & Barbey, 2019) and between functional brain connectivity and executive function (Talukdar, Zamroziewicz, Zwilling, & Barbey, 2018; Zwilling, Talukdar, Zamroziewicz, & Barbey, 2019) as well as general intelligence (Zamroziewicz, Talukdar, Zwilling, and Barbey, 2017). Some studies also seek to identify relationships between individual nutrients and brain health, however intervention studies of this nature are often unsuccessful. Interestingly, there have been successful intervention studies demonstrating that xanthophyll carotenoid supplementation improves cognitive performance in multiple domains including complex attention, cognitive flexibility, and episodic memory (Hammond Jr. et. al., 2017; Power et. al., 2018). This dissertation aims to better understand the relationships between xanthophyll carotenoids and brain health in aging.

Carotenoids are a group of phytonutrient pigments and are divided by structure into two classes: carotenes (polyunsaturated hydrocarbons) and xanthophylls (oxygenated pseudo-hydrocarbons). The electrophilic hydroxide groups on xanthophylls conjugate with the rest of the molecule and provide a structure capable of quenching free radicals, therefore acting as an antioxidant. There are hundreds of carotenoids currently known with about 50 present in the human diet (reviewed in Krinsky and Johnson, 2005) and of those, blood serum analysis commonly measures three xanthophylls: β -cryptoxanthin, lutein, and zeaxanthin (see Figure 1.1).

Xanthophyll carotenoids are well established as vitally important for vision, as lutein and zeaxanthin are two pigments that compose the macula within the retina (Bone, Landrum, & Tarsis, 1985; Handelman et. al., 1992). In the macula, xanthophylls are essential for combating damage caused by oxidative stress and inflammation (Bone, Landrum, and Tarsis, 1985; Widomska, Zareba, and Subczynski, 2016). Since lutein and zeaxanthin cannot be synthesized

by humans, they must cross the blood-retina interface to reach the macula after gastrointestinal absorption. Interestingly, similar transporters exist which allow lutein and zeaxanthin to cross the blood-brain interface as well (Johnson, 2012), and it is documented that carotenoids accumulate in brain tissues across occipital, temporal, and frontal lobes of deceased centenarians (Craft et. al., 2004; Johnson et. al., 2013). It has also been shown that increasing dietary carotenoids leads to increased carotenoid levels in blood serum and that serum carotenoid levels are related to levels within brain tissue (Johnson et. al., 2013; Tanprasertsuk et. al., 2019). This provides the opportunity to understand how these nutrients may relate to measures of brain behavior, structure, and function using minimally invasive methods to investigate their levels in blood serum. As nutrients with antioxidant and anti-inflammatory activity (Kaulmann and Bohn, 2014), it is likely that carotenoids can promote healthy brain aging in myriad ways.

In fact, studies indicate that xanthophyll levels are related to various facets of intelligence across the lifespan. Xanthophylls have been shown to positively impact neural processing speed and efficiency in young adults (Bovier, Renzi, and Hammond, 2014), to relate to relational memory in obese and overweight young adults (Cannavale et. al., 2019), and to crystallized intelligence in healthy, older adults (Zamroziewicz et. al., 2016). In a more recent, randomized study xanthophyll supplementation improved general outcomes for Alzheimer's Disease (AD) patients when compared to healthy controls (Nolan et. al., 2015). Further, when compared with placebo, supplementing with a mixture of xanthophylls and other antioxidants saw improved visual processing speed (Bovier and Hammond, 2015) and better outcomes in tasks measuring working memory, cognitive flexibility, and episodic and semantic memory (Kesse-Guyot et. al., 2014), respectively. More recently, early- to middle-aged individuals showed significant

improvements in episodic memory after receiving 12 months of mixed xanthophyll supplementation (lutein, zeaxanthin, meso-zeaxanthin; Power et. al., 2018).

Considering the rapidly growing body of research supporting the connection between xanthophyll carotenoids and cognitive function, it logically follows that understanding this relationship in the aging brain is an important opportunity to promote healthy brain aging. Even more, understanding how carotenoids affect the aging brain past behavior and into brain structure and function is critical for promoting brain health in this growing demographic.

1.3 *Inflamm-aging and the Brain*

Inflamm-aging is a pattern of low-level, chronic inflammation that accompanies aging and consists of both pro- and anti-inflammatory responses (Franceschi et. al., 2000). It is largely believed that this inflammatory response is a contributor to infirmity in aging with repercussions manifesting as chronic diseases and even at the behavioral level as cognitive impairment. As individuals enter older age, the innate immune system is activated as circulating levels of pro-inflammatory cytokines (e.g. IL-1 β , IL-6, TNF- α , IFN- α) rise resulting in increased levels of both acute phase protein release from the liver (e.g. CRP, complement components) and anti-inflammatory cytokines (e.g. IL-4, IL-6, IL-10, TGF- β ; Fagiolo et. al., 1992; Fagiolo et. al., 1993; Franceschi, Monti, Sansoni & Cossarizza, 1995).

Chronic stress exposure through the lifespan accumulates to produce tissue stress and cellular damage resulting in danger signals that activate the NF- κ B signaling pathways and macrophages, the effector cells of the innate immune response. These danger signals are activated by protein misfolding, DNA damage, and oxidative stress, among other stressors. Oxidative stress, in particular, is known to be associated with aging and to promote changes in

DNA, proteins, and lipids through the presence of reactive species (ROS: reactive oxygen species, RNS: reactive nitrogen species; Salminen et. al., 2008). Interestingly, oxidative stress is also a byproduct of many biological processes, including aerobic metabolism, lipid peroxidation, and phagocyte activation within innate immunity.

This is particularly important when thinking about brain health during aging because not only do neurons *in vitro* produce 1-2% ROS from all oxygen consumed (Boveris & Chance, 1973), but within the CNS energy consumption is substantial. In fact, the brain alone accounts for roughly 20% of the body's total mitochondrial oxygen metabolism (Hyder, Rothman, & Bennett, 2013). The potential for ROS production is compounded by the high lipid content of brain tissue, which is second only to adipose in the human body and accounts for approximately 50% of the brain's dry weight (Hamilton, Hillard, Spector, & Watkins, 2007). Brain lipid content is a majority constituted from polyunsaturated fatty acids (PUFAs), which are targets for free radicals, resulting in lipid peroxidation. This process contributes a substantial source of reactive species that damage neuronal membranes. Lipid peroxidation has been associated with modified proteins in mild cognitive impairment (MCI) and all stages of AD (Sultana, Perluigi, & Butterfield, 2013). Further, miscellaneous mechanisms of normal functioning within the CNS can also release ROS. For example, NMDA (*N*-methyl-D-aspartate) glutamate receptor activation, which is mechanistically crucial in synaptic plasticity and memory function, releases ROS (Lafon-Cazal, Pietri, Culcasi, & Bockaert, 1993). Microglia, the resident macrophages of the CNS, also release ROS and RNS upon stimulation via the NADPH oxidase complex. Reactive species released from this complex can interact with nitric oxide (NO) to form peroxynitrite, yet another radical species (Finkel & Holbrook, 2000). With the multitude of

sources exposing the CNS to oxidative stress, preventing excessive activation of these systems is imperative.

Although there exists a blood-brain barrier (BBB) to control the amount of activation and signaling by microglia, this interface begins breaking down early in the aging process (Montagne et. al., 2015). Comprised of endothelial cells and pericytes, the BBB limits interactions between the periphery and the CNS through the neurovascular unit, which controls permeability from the blood into brain interstitial fluid with a system of tight junctions and adherens junctions (Ohtsuki & Terasaki, 2007; Hawkins & Davis, 2005). Permeability of the BBB is regulated by inflammatory mediators normally (Abbott, 2000), but under pathological conditions tight junctions between brain endothelial cells within the neurovascular unit become compromised, disrupting regulation and BBB function (Petty & Lo, 2002). Further, it is believed that the approximate 20% decrease in resting cerebral blood flow experienced during normal aging and the accompanying decrease in protein synthesis contribute to weakened tight junctions and uncoupling of the neurovascular unit (Zlokovic, 2008). Interestingly, it is not only inflammation within the CNS that can disrupt BBB function, but so too can peripheral inflammation since communication between the brain and peripheral immune system is bidirectional (Teeling & Perry, 2009; Hernández-Romero et. al., 2012; Varatharaj & Galea, 2017).

The interactions between peripheral inflammation and oxidative stress present in normal aging appear to comprise a cycle of continuous signaling and disruption of the BBB. It is no surprise, then, that both oxidative stress and peripheral levels of inflammatory cytokines are often evaluated in association with cognitive decline. For example, a longitudinal study of healthy, older adults in France found that markers for oxidative stress are correlated with greater risk for cognitive decline toward dementia as measured by the Mini-Mental Status Examination

(MMSE; Berr et. al., 2000). More recently, a four-year study of mid-aged adults found one oxidative stress marker (glutathione level) to be correlated with decreased executive function performance but found other markers of oxidative stress and C-reactive protein (CRP) not to correlate with executive function performance (Hajjar et. al., 2018). Conversely, a longitudinal study spanning decades found that CRP and a composite inflammation score composed of fibrinogen, von-Willebrand factor, Factor VIII, and white blood cell count are each related to cognitive decline over time (Walker et. al., 2019). Over 20 years of assessment, both subjects with higher composite inflammation scores and with higher CRP scores experienced steeper declines in memory compared to baselines taken during middle age. For those with the greatest levels of inflammation biomarkers, composite inflammation scores are associated with an 8.9% steeper decline and CRP is associated with a 12.3% steeper decline (Walker et. al., 2019).

Another study found that in the elderly elevated levels of inflammation biomarkers such as IL-6, TNF- α , IFN- γ , and IL-1 β are correlated with increased oxidative stress, and that both inflammation biomarker levels and oxidative stress are associated with low cognitive performance on tasks of verbal fluency-related semantic memory and executive function (Baierle et. al., 2015). Horvat et. al. (2016) found support that an increased level of ROS metabolites inversely correlated with global cognition and verbal fluency in mid-to-late aged individuals both in a cross-sectional sample and 3-4 years after baseline. Two other measures of oxidative stress, however, were either inconsistently or non-significantly associated with cognitive function in this population. Inconsistencies in studies relating oxidative stress and cognition in aging paired with a lack of human-based studies presents a gap in knowledge critical to understanding healthy brain aging. Biomarkers related to inflammation and stress hold potential as modifiable lifestyle factors capable of attenuating cognitive changes that occur during normal brain aging.

Understanding how inflammation biomarkers relate not only to cognitive behavior, but to brain structure and function, can inform strategies to promote overall healthy brain aging in a non-invasive manner.

In light of the reviewed literature, the program of research detailed within this dissertation was proposed with the overall objective to better understand relationships between brain structure, connectivity, and microstructure and facets of intelligence in healthy, older adults through an interdisciplinary lens. Studies followed a framework of linear regression and moderation analyses in an effort to address the following fundamental questions:

1. Can relationships between peripheral xanthophyll carotenoids and markers of brain health be characterized using a systematic framework of moderation analyses?

My guiding hypothesis is that peripheral levels of xanthophyll carotenoids will influence relationships between brain structure, connectivity, and integrity and performance on measures of memory and intelligence.

2. Can relationships between inflammation biomarkers and markers of brain health be characterized using a systematic framework of moderation analyses?

My guiding hypothesis is that peripheral levels of inflammation biomarkers will influence relationships between brain structure, connectivity, and integrity and performance on measures of memory and intelligence.

Investigation into each aim follows a similar framework of research questions to advance our understanding of healthy brain aging using concepts and methods from both nutritional cognitive neuroscience and psychoneuroimmunology. Each question is accompanied by a series of *constituent hypotheses* that structure the exploratory studies therein. Research questions and their motivating hypotheses are detailed in the overview of their respective chapters.

1.4 *Figure*

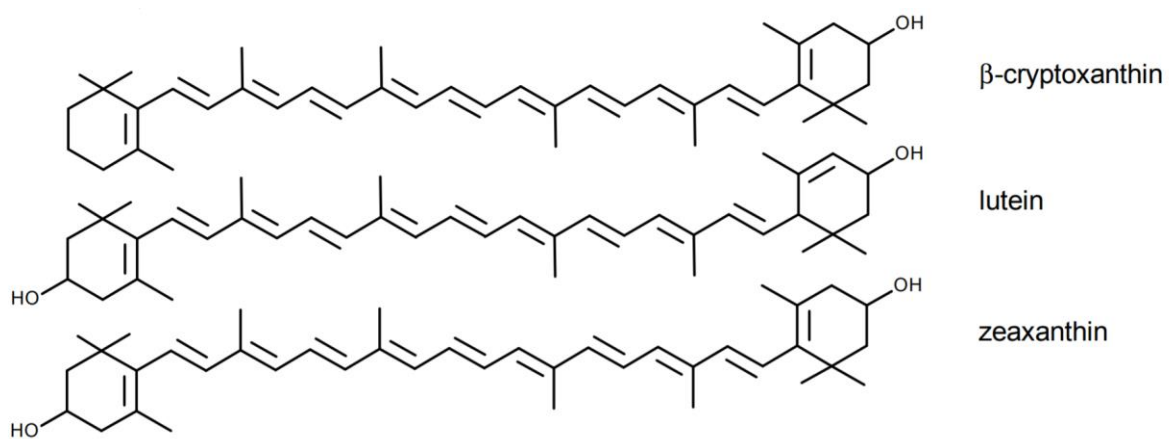


Figure 1.1 | Chemical structure of commonly studied xanthophyll carotenoids.
Adapted from Fiedor & Burda, 2014.

CHAPTER 2: XANTHOPHYLL CAROTENOIDS AND BRAIN BEHAVIOR, STRUCTURE, AND FUNCTION IN HEALTHY, AGING ADULTS

2.1 *Chapter Overview*

The fundamental question of this chapter asks whether xanthophyll carotenoids influence relationships between neurological markers of brain health and measures of memory and intelligence. I will address this fundamental question systematically using the following series of constituent hypotheses:

1. *Do individual xanthophyll carotenoids influence relationships between grey matter volume of regions bordering the parietal and occipital lobes and facets of intelligence?*
2. *Do individual xanthophyll carotenoids influence relationships between efficiency of intrinsic connectivity networks at the border of the parietal and occipital lobes and facets of intelligence?*
3. *Do individual xanthophyll carotenoids influence relationships between white matter microstructure and facets of intelligence?*

This program of questions advances the understanding of healthy brain aging through the lens of nutritional cognitive neuroscience by elucidating the nature of influence between individual xanthophyll carotenoids and markers of brain health in an observational, cross-sectional study of healthy elders.

2.2 *Introduction*

Nutritional cognitive neuroscience integrates nutritional epidemiology and cognitive neuroscience to understand how diet and nutrition impact brain health (Zamroziewicz and Barbey, 2016). Here, this approach is utilized to understand how xanthophyll carotenoids relate to brain health and cognitive function. A number of studies observe positive relationships between xanthophyll carotenoids and cognitive outcomes in various facets of intelligence including global cognition (Feeney et. al., 2018), visual processing speed (Bovier & Hammond, 2015; Bovier, Renzi, & Hammond, 2014; Mewborn et. al., 2018), working memory and cognitive flexibility (Hammond et. al., 2017; Kesse-Guyot et. al., 2014), episodic memory (Kesse-Guyot et. al., 2014; Power et. al., 2018), relational memory (Cannavale et. al., 2019), decision making (Mewborn et. al., 2018), and crystallized intelligence (Zamroziewicz et. al., 2016).

Less studied, however, are associations between xanthophylls and brain structure, network connectivity, or white matter integrity. One intervention study found that mixed xanthophyll supplementation did not change white matter microstructural or grey matter volumetric outcomes but did conclude that there may exist subgroups of individuals that benefit more from supplementation than others (Mewborn et. al., 2019). Another intervention study examined network efficiency after mixed xanthophyll supplementation and found changes in connectivity between the DMN and other networks but not within the DMN (Lindbergh et. al., 2019). Finally, one study comparing young, healthy adults to healthy, older adults found that serum xanthophyll levels associate with white matter integrity in fibers susceptible to age-related decline (Mewborn et. al., 2018).

Notably, these studies indicate that xanthophylls likely influence cognitive function throughout the lifespan and hold potential to be a modifiable lifestyle factor capable of attenuating cognitive changes that occur during normal brain aging. Understanding how xanthophylls relate not only to cognitive behavior, but to brain structure, network connectivity, and white matter microstructure will inform strategies to promote overall healthy brain aging in a non-invasive and relatively inexpensive manner. In this chapter, we seek to understand healthy brain aging using a systematic, multi-modal approach to characterize the nature of influence xanthophyll carotenoids have on healthy brain aging and to expand on the existing nutritional cognitive neuroscience literature.

2.3 *Methodology*

2.3.1 *Overall Design*

Data was collected from 128 consenting individuals between the ages of 65-75 years old over four sessions. All participants were void of cognitive impairment as measured by the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975), were neurologically healthy, deemed non-depressed by a subjective questionnaire, had normal or corrected-to-normal vision, and exhibited right handedness. Exclusion criteria were: cancer within the three years prior to enrollment, contraindications for MRI, dementia, inability to complete data collection activities, mild cognitive impairment diagnosis, ongoing chemotherapy or radiation therapy, prior participation in cognitive training or dietary intervention studies, psychiatric illness within the three years prior to enrollment, and stroke within the 12 months prior to enrollment.

Participants underwent two magnetic resonance imaging (MRI) sessions, one neuropsychological assessment, and one fasting blood draw for which they were compensated

monetarily by the hour. Following Institutional Review Board protocol for both the University of Illinois at Urbana-Champaign and Carle Foundation Hospital, informed consent was obtained from all participants to begin the first data collection session.

2.3.2 *Imaging*

Imaging was performed on a Siemens Magnetom 3T Trio (Erlangen, Germany) with a 12- channel head coil.

2.3.2.1 *Volumetric Magnetic Resonance Imaging (MRI)*

Structural MRI data were obtained with 3D high-resolution (0.9mm isotropic) T1-weighted scans with magnetization-prepared 180 degrees radio-frequency pulses and rapid gradient-echo acquisition (MPRAGE; Brant-Zawadzki, Gillan, & Nitz, 1992). Images were acquired with the following parameters: repetition time (TR) = 1900 ms, echo time (TE) = 2.32 ms, inversion time (TI) = 900 ms, acceleration factor of 2 with GRAPPA.

2.3.2.2 *Resting State Functional MRI*

Resting state fMRI data were obtained during using a blood-oxygen level-dependent (BOLD) accelerated gradient echoplanar imaging (EPI) sequence. Two, 7- minute EPI sequences were acquired with the following parameters: 2.5 x 2.5 x 3.0 mm voxel size, 2.5mm in-plane resolution, 3mm slice thickness, 38 slices with 10% gap, FOV = 230 mm, 90-degree flip angle, TE = 25 ms, and TR = 2000 ms were acquired. MRI data were processed using Freesurfer software (fmRIB Software Library, FSL: Oxford, UK).

Intrinsic connectivity networks (ICNs) were obtained using post-processing methods outlined in Yeo et. al. (2011) and Muldoon, Bridgeford, & Bassett (2016). Figure 2.1 depicts the seven ICNs for which graph theory metrics were computed. Graph theory metrics for each network include global efficiency (average pathlength), local efficiency (local node clustering), and small world propensity (optimal balance of local and global efficiency).

2.3.2.3 *Diffusion Tensor Imaging (DTI)*

Whole-brain DTI data was collected (FOV=240x240mm, 72 slices at 2mm, TE=98 ms, TR=10,000 ms, in-plane resolution = 1.875x1.875 mm, diffusion encoding direction $s = 30$, $b = 0$ s/mm² and 1000 s/mm²). Data were processed using the University of Oxford's Center for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL) diffusion toolbox (FDT). The eddy_correct tool was used for eddy current correction and the DTIFIT tool was used to generate fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD) values and create a diffusion tensor model for each voxel. The FSL tract-based statistics toolbox (TBSS) was used to further process the DTI images to represent the white-matter tracts common to all participants. Finally, mean values were calculated using the JHU ICBM DTI-81 atlas. Tracts relevant to this dissertation are listed in Table 2.1.

2.3.3 *Assessing Facets of Intelligence*

Participants attended two neuropsychological assessment sessions to complete several cognitive batteries used to measure facets of intelligence including task switching (Delis-Kaplan Executive Function System; DKEFS), general, fluid, and crystallized intelligence (Wechsler Abbreviated Scale of Intelligence – II; WASI), and immediate, delayed, auditory, visual, and

visual working memory (Wechsler Memory Scale – IV: Older Adult Battery; WMS). For simplicity, neuropsychological assessments are summarized in Table 2.2.

2.3.4 *Assessing Carotenoid Status*

To measure xanthophyll levels, 45mL of antecubital venous blood was drawn after a 10h fast. Blood was separated between EDTA-anticoagulated and Heparin tubes, treated according to the manufacturer's instructions, aliquoted into 1mL cryotubes, and stored at -80C. Xanthophyll measures (nmol/mL; β -cryptoxanthin, lutein, zeaxanthin) were obtained from EDTA treated plasma subjected to reversed-phase, high-performance liquid chromatography (HPLC) analysis using a diode array detector and fluorescence detection. Lutein is the summation of both -cis and -trans isomers, and xanthophyll status represents the summation of β -cryptoxanthin, lutein, and zeaxanthin levels.

2.3.5 *Statistical Analysis*

2.3.5.1 *Xanthophylls and Grey Matter Volume*

First, a correlation matrix conducted in R (version 3.4.4; RStudio Inc.: Boston, MA) identified significant Pearson correlations between total cortical volumes of brain regions at the border of the parietal and occipital lobes (cuneus, inferior parietal, lateral occipital, precuneus, and superior parietal) and facets of intelligence. Only significant correlations were followed by regression models.

Linear regression models were performed in SPSS 26 (IBM Corp.: Armonk, NY) to determine significant associations between total cortical volumes of brain regions at the border of the parietal and occipital lobes (cuneus, inferior parietal, lateral occipital, precuneus, and

superior parietal) and each facet of intelligence (Table 2.2). Total volume was represented by additive cortical volumes of the right and left hemispheres for each region of interest (ROI). All regression models used sex (F/M), education level (4 levels: some high school, high school degree, some college, college degree), income level (5 levels: >100,000, 75,000- 100,000, 50,000-75,000, 25,000-50,000, and 15,000-25,000 USD annually), body mass index (BMI, continuous), and age (continuous) as covariates.

Significant linear models ($p < .05$) were followed by moderation analyses conducted with the PROCESS macro v3.4 application in SPSS to evaluate the relationships between brain structure (independent variable, IV), serum carotenoid levels (moderator, M), and facets of intelligence derived from regression models (dependent variable, DV). Significant moderations were followed up with a Johnson-Neyman analysis (Johnson & Fay, 1950) at ± 1 standard deviation from the mean (SD). False discovery rate (FDR; Benjamini & Hochberg, 1995) was conducted to correct for multiple comparisons in all significant overall models. All moderation analyses used the same covariates as the regression models.

2.3.5.2 *Xanthophylls and Functional Connectivity*

Linear regression analyses were performed in SPSS 26 to determine relationships between network characteristics (local efficiency, global efficiency, and small world propensity) and the facets of intelligence used in the volumetric analyses (auditory memory, crystallized intelligence, general intelligence, and immediate memory). Functional networks were chosen based on the ROI used for volumetric moderation analyses. This included the default mode (DMN), frontoparietal (FPN), visual (VisN), dorsal attention (DAN), and ventral attention networks (VAN; Figure 2.1). All models included the five covariates used in volumetric models.

Significant linear models ($p < .05$) were explored with moderation analyses using the same covariates and protocol as for the volumetric moderation analyses, substituting individual network characteristics as the IV. Significant overall models were corrected for multiple comparisons using FDR.

2.3.5.3 *Xanthophylls and White Matter Structure*

Linear regression analyses were performed in SPSS 26 to determine relationships between axial diffusivity (AxD), radial diffusivity (RD), and fractional anisotropy (FA) of white matter tracts (listed in Table 2.1) and crystallized intelligence, general intelligence, and immediate memory. All models included the five covariates used in previous models. Significant linear models ($p < .05$) were followed up with moderation analyses using the same covariates and protocol as previous analyses, substituting individual diffusion characteristics as the IV. Significant overall models were corrected for with multiple comparisons using FDR.

2.4 **Results**

2.4.1 *Xanthophylls and Grey Matter Volume*

A correlation matrix was conducted in to divulge possible relationships between regional grey matter volume and various facets of intelligence. The cuneus, inferior parietal, lateral occipital, precuneus, and superior parietal were included as ROIs. Demographic, neuropsychological assessment, and volumetric MRI data are presented for xanthophyll carotenoids in Table 2.3. Of the facets of intelligence listed in Table 2.1, ROIs correlated with auditory memory, crystallized intelligence, delayed memory, general intelligence, immediate intelligence, task switching, and visual memory.

Linear regression models were conducted to reveal relationships between regional grey matter volume in these ROIs (IV) and the facets of intelligence (DV) identified in the correlation matrix while accounting for multiple covariates. At least one ROI significantly predicted ($p < .05$) each facet of intelligence except task switching and visual memory (Table 2.4).

A series of moderation analyses were conducted between cortical ROI volumes (IV), facets of intelligence (DV) from significant regression models, and xanthophyll carotenoid status (M) as conceptualized in Figure 2.2. Despite some significant overall models, moderations with auditory memory (see Appendix A, Table A.1a), crystallized intelligence (see Appendix A, Table A.1b), or delayed memory (see Appendix A, Table A.1c) as outcomes had non-significant interaction terms. Similarly, interactions were not significant in moderations with inferior parietal lobule (see Appendix A, Table A.1d), lateral occipital cortex (see Appendix A, Table A.1e), or superior parietal lobule (see Appendix A, Table A.1f) volume as the IV.

2.4.1.1 *Cuneus Volume*

Overall models including cuneus volume (IV) and general intelligence (DV) were significant when each xanthophyll carotenoid was included as the moderator, even after FDR correction (Table 2.5). Only zeaxanthin status demonstrated a significant interaction ($F(1, 98) = 4.262, p = 0.042, \Delta R^2 = 0.029$; Figure 2.3).

A simple slopes analysis indicated that this interaction was conditional such that zeaxanthin status moderated the relationship between cuneus volume and general intelligence when the cuneus was small ($b = 126.600, t(99) = 3.699, p = 0.000$; 95% CI = [58.682 – 194.518]) and moderately sized ($b = 85.783, t(99) = 3.574, p = 0.000$; 95% CI = [38.158 – 133.408]), but not when the cuneus was large ($b = 44.966, t(99) = 1.629, p = 0.107$; 95% CI = [-

9.827 – 99.759]). Johnson-Neyman analysis indicated 15.9% of the population in this dataset fell within the significance region.

Overall models including cuneus volume (IV) and immediate memory (DV) were significant when each xanthophyll carotenoid was included as the moderator, even after FDR correction (Table 2.6). Only lutein status demonstrated a significant interaction ($F(1, 99) = 4.033, p = .047, \Delta R^2 = 0.034$; Figure 2.4).

A simple slopes analysis indicated that this interaction was conditional such that lutein status moderated the relationship between cuneus volume and immediate memory when the cuneus was small ($-1 SD; b = 17.655, t(99) = 2.507, p = 0.014$; 95% CI = [3.682 – 31.628]) but not when the cuneus was moderately sized ($b = 8.310, t(99) = 1.473, p = 0.144$; 95% CI = [-2.882 – 19.501]) or large ($+1 SD; b = -1.036, t(99) = -0.137, p = 0.891$; 95% CI = [-16.061 – 13.989]). Johnson-Neyman analysis indicated 44.4% of the population in this dataset fell within the significance region.

2.4.1.2 *Precuneus Volume*

Overall models including precuneus volume (IV) and immediate memory (DV) were significant when each xanthophyll carotenoid was individually included as the moderator, even after FDR correction (Table 2.6). Only zeaxanthin status demonstrated a significant interaction ($F(1, 100) = 6.261, p = .014, \Delta R^2 = 0.048$; Figure 2.5).

A simple slopes analysis indicated that this interaction was conditional such that zeaxanthin status moderated the relationship between precuneus volume and immediate memory when the precuneus was small ($-1 SD; b = 143.996, t(100) = 3.141, p = 0.002$; 95% CI = [53.034 – 234.958]) and moderately sized ($b = 26.290, t(100) = 2.631, p = 0.010$; 95% CI = [17.019 –

121.337]), but not when the precuneus was large (+1 *SD*; $b = -5.640$, $t(100) = -0.172$, $p = 0.893$; 95% CI = [-70.487 – 59.208]). Johnson-Neyman analysis indicated 65.1% of the population in this dataset fell within the significance region.

2.4.2 *Xanthophylls and Functional Connectivity*

Linear regression models revealed relationships between efficiency in intrinsic connectivity networks (ICNs) of interest (IV) and the facets of intelligence (DV) identified in volumetric linear regression models (see section 2.4.1). Networks of interest ($p < .05$) included the default mode (DMN), frontoparietal (FPN), visual (VisN), dorsal attention (DAN), and ventral attention (VAN) networks. Demographic, neuropsychological assessment, and rsfMRI data are presented for xanthophyll carotenoids in Table 2.7. Across networks, efficiency significantly predicted crystallized intelligence and general intelligence (Table 2.8), and only efficiency in the DAN did not significantly predict immediate memory when accounting for multiple covariates (Table 2.9). Additionally, only efficiency in the VAN predicted delayed memory, and there were no network efficiency measures that predicted auditory memory (Table 2.9).

A series of moderation analyses were conducted between efficiency in ICNs of interest (IV), facets of intelligence (DV) from significant regression models, and xanthophyll carotenoid status (M) as conceptualized in Figure 2.2. Despite some significant overall models, moderations with efficiency in the VisN as IVs did not have significant interactions (see Appendix A, Table A.2a). In the remaining networks, there were not significant interactions between efficiency and individual xanthophyll status when general intelligence was the outcome (see Appendix A, Table A.2b).

2.4.2.1 Default Mode Network

A series of moderation analyses between efficiency in the DMN and individual xanthophyll carotenoids revealed significant overall models when crystallized intelligence or immediate memory was the outcome, even after FDR correction (Table 2.10).

When crystallized intelligence was the outcome, only global efficiency and zeaxanthin status had a significant interaction ($F(1, 82) = 7.048, p = .010, \Delta R^2 = 0.048$; Figure 2.6). A simple slopes analysis indicated a conditional interaction with zeaxanthin status when global efficiency was low ($-1 SD; b = 149.751, t(82) = 3.859, p = 0.000$; 95% CI = [72.558 – 226.944]) and moderate ($b = 71.981, t(82) = 2.792, p = 0.006$; 95% CI = [20.699 – 123.264]), but not when global efficiency was high ($+1 SD; b = -5.788, t(82) = -0.148, p = 0.883$; 95% CI = [-83.843 – 72.266]). Johnson-Neyman analysis indicated 64.8% of the population in this dataset fell within the significance region.

When immediate memory was the outcome, local efficiency independently interacted with lutein status ($F(1, 81) = 4.576, p = .035, \Delta R^2 = 0.047$; Figure 2.7) and zeaxanthin status ($F(1, 82) = 5.096, p = .037, \Delta R^2 = 0.050$; Figure 2.8) significantly. A simple slopes analysis indicated a conditional interaction with lutein status when local efficiency was high ($+1 SD; b = 22.398, t(81) = 2.472, p = 0.016$; 95% CI = [4.370 – 40.425]) but not moderate ($b = 11.406, t(81) = 1.786, p = 0.078$; 95% CI = [-1.304 – 24.116]) or low ($-1 SD; b = 7.234, t(81) = 0.057, p = 0.954$; 95% CI = [-13.979 – 14.808]). Johnson-Neyman analysis indicated 45.6% of the population in this dataset fell within the significance region. A simple slopes analysis indicated a conditional interaction with zeaxanthin status when local efficiency was high ($+1 SD; b = 74.764, t(82) = 2.313, p = 0.023$; 95% CI = [10.452 – 139.077]) but not moderate ($b = 21.627, t(82) = 0.801, p = 0.426$; 95% CI = [-32.102 – 75.356]) or low ($-1 SD; b = -31.510, t(82) =$

-0.808, $p = 0.422$; 95% CI = [-109.119– 46.098]). Johnson-Neyman analysis indicated 26.4% of the population in this dataset fell within the significance region.

2.4.2.2 *Frontoparietal Network*

A series of moderation analyses between efficiency in the FPN and individual xanthophyll carotenoids revealed significant overall models when crystallized intelligence or immediate memory was the outcome (Table 2.11). When crystallized intelligence was the outcome, only local efficiency and cryptoxanthin status had a significant interaction ($F(1, 81) = 6.631$, $p = .012$, $\Delta R^2 = 0.050$; Figure 2.9). Simple slopes analysis indicated that this interaction was conditional such that cryptoxanthin status was a moderator when local efficiency was high (+1 SD ; $b = 50.558$, $t(81) = 2.699$, $p = 0.008$; 95% CI = [13.282 – 87.835]) but not moderate ($b = 18.600$, $t(81) = 1.512$, $p = 0.134$; 95% CI = [-5.878 – 43.079]) or low (-1 SD ; $b = -13.357$, $t(81) = -0.829$, $p = 0.410$; 95% CI = [-45.426 – 18.711]). Johnson-Neyman analysis indicated 41.1% of the population in this dataset fell within the significance region.

When immediate memory is the outcome, only local efficiency and lutein status had a significant interaction ($F(1, 81) = 5.280$, $p = .024$, $\Delta R^2 = 0.053$; Figure 2.10). This interaction was also conditional such that lutein status was a moderator when local efficiency was high (+1 SD ; $b = 24.848$, $t(81) = 2.630$, $p = 0.010$; 95% CI = [6.046 – 43.651]) but not moderate ($b = 11.935$, $t(81) = 1.875$, $p = 0.064$; 95% CI = [-0.729 – 24.599]) or low (-1 SD ; $b = -0.978$, $t(81) = -0.132$, $p = 0.895$; 95% CI = [-15.719 – 13.762]). Johnson-Neyman analysis indicated 47.8% of the population in this dataset fell within the significance region.

2.4.2.3 Dorsal Attention Network

A series of moderation analyses between efficiency in the DAN and individual xanthophyll carotenoids revealed significant overall models when crystallized intelligence was the outcome (Table 2.12). Only small world propensity and lutein status had a significant interaction ($F(1, 80) = 4.833, p = .031, \Delta R^2 = 0.032$; Figure 2.11).

Simple slopes analysis indicated that this interaction was conditional such that lutein status was a moderator when small world propensity was high (+1 *SD*; $b = 29.305, t(80) = 3.717, p = 0.000$; 95% CI = [13.616 – 44.994]) or moderate ($b = 14.220, t(80) = 2.383, p = 0.020$; 95% CI = [2.343 – 26.096]), but not when small world propensity was low (-1 *SD*; $b = -0.866, t(80) = -0.085, p = 0.932$; 95% CI = [-21.087 – 19.356]). Johnson-Neyman analysis indicated 58.4% of the population in this dataset fell within the significance region.

2.4.2.4 Ventral Attention Network

A series of moderation analyses between efficiency in the VAN and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, delayed memory, or immediate memory was the outcome (Table 2.13). When delayed or immediate memory was the outcome, individual xanthophyll status and local efficiency did not interact significantly. When crystallized intelligence was the outcome, only global efficiency and zeaxanthin status had a significant interaction ($F(1, 82) = 4.007, p = .049, \Delta R^2 = 0.025$; Figure 2.12). Simple slopes analysis indicated that this interaction was conditional such that zeaxanthin status was a moderator when global efficiency was low (-1 *SD*; $b = 137.957, t(82) = 3.526, p = 0.001$; 95% CI = [60.134 – 215.780]) and moderate ($b = 84.314, t(82) = 3.329, p = 0.001$; 95%

CI = [33.928 – 134.700]), but not when global efficiency was high (+1 SD; $b = 30.671$, $t(82) = 0.890$, $p = 0.376$; 95% CI = [-37.925 – 99.267]). Johnson-Neyman analysis indicated 71.4% of the population in this dataset fell within the significance region.

2.4.3 *Xanthophylls and White Matter Structure*

Linear regression models revealed relationships between integrity of white matter tracts of interest and the facets of intelligence identified in significant network efficiency moderations (see section 2.4.2). White matter tracts of interest are listed in Table 2.1. Demographic, neuropsychological assessment, xanthophyll carotenoid, and white matter tract microstructure data are presented in Table 2.14. Across white matter tracts, integrity significantly predicted crystallized intelligence, general intelligence, and immediate memory when accounting for multiple covariates (Table 2.15).

A series of moderation analyses were conducted between integrity in white matter tracts of interest (IV), facets of intelligence (DV) from significant regression models, and individual xanthophyll carotenoid status (M) as conceptualized in Figure 2.2. Despite some significant overall models, moderations with fornix microstructure as IVs did not have any significant interactions (see Appendix A, Table A.3a).

2.4.3.1 *Global White Matter*

A series of moderation analyses between global white matter integrity and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome even after FDR correction (Table 2.16). When crystallized intelligence was the outcome, lutein status significantly interacted with

both AD ($F(1, 94) = 5.827, p = .018, \Delta R^2 = 0.036$; Figure 2.13) and RD ($F(1, 94) = 4.407, p = .038, \Delta R^2 = 0.029$; Figure 2.14). A simple slopes analysis indicated a conditional interaction with lutein status when AD was low ($-1 SD; b = 28.941, t(94) = 3.578, p = 0.001$; 95% CI = [12.878 – 45.005]) or moderate ($b = 14.286, t(94) = 2.656, p = 0.009$; 95% CI = [3.604 – 24.967]), but not when AD was high ($+1 SD; b = -0.370, t(94) = -0.046, p = 0.964$; 95% CI = [-16.519 – 15.778]). Johnson-Neyman analysis indicated 60.2% of the population in this dataset fell within the significance region. Lutein status is also a moderator when RD was low ($-1 SD; b = 24.852, t(94) = 3.322, p = 0.001$; 95% CI = [9.999 – 39.704]) or moderate ($b = 13.431, t(94) = 2.386, p = 0.019$; 95% CI = [2.253 – 24.608]), but not when RD was high ($+1 SD; b = 2.010, t(94) = 0.246, p = 0.806$; 95% CI = [-14.196 – 18.216]). Johnson-Neyman analysis indicated 62.1% of the population in this dataset fell within the significance region.

Similarly, lutein status significantly interacted with both AD ($F(1, 94) = 7.618, p = .007, \Delta R^2 = 0.056$; Figure 2.15) and RD ($F(1, 94) = 4.388, p = .039, \Delta R^2 = 0.033$; Figure 2.16) when general intelligence was the outcome. A simple slopes analysis indicated a conditional interaction with lutein status when AD was low ($-1 SD; b = 21.092, t(94) = 2.707, p = 0.008$; 95% CI = [5.620 – 36.565]), but not moderate ($b = 4.577, t(94) = 0.906, p = 0.367$; 95% CI = [-5.457 – 14.611]), or high ($+1 SD; b = -11.939, t(94) = -1.517, p = 0.133$; 95% CI = [-27.568 – 3.691]). Johnson-Neyman analysis indicated 28.2% of the population in this dataset fell within the significance region. When RD was low ($-1 SD; b = 14.592, t(94) = 1.986, p = 0.050$; 95% CI = [0.000 – 29.184]), but not moderate ($b = 2.696, t(94) = 0.521, p = 0.604$; 95% CI = [-7.577 – 27.594]) or high ($+1 SD; b = -8.243, t(94) = -1.076, p = 0.284$; 95% CI = [-23.449 – 6.963]) there was a significant interaction with lutein status. Johnson-Neyman analysis indicated 12.6% of the population in this dataset fell within the significance region.

When immediate memory was the outcome, lutein significantly interacted only with AD ($F(1, 97) = 4.220, p = .043, \Delta R^2 = 0.035$; Figure 2.17). A simple slopes analysis indicated this was also a conditional interaction, significant when AD was low ($-1 SD; b = 22.880, t(97) = 2.741, p = 0.007$; 95% CI = [6.315 – 39.445]), but not moderate ($b = 9.934, t(97) = 1.787, p = 0.077$; 95% CI = [-1.097 – 20.965]), or high ($+1 SD; b = -3.012, t(97) = -0.356, p = 0.723$; 95% CI = [-19.801 – 13.778]). Johnson-Neyman analysis indicated 39.6% of the population in this dataset fell within the significance region.

2.4.3.2 *Corpus Callosum*

A series of moderation analyses between corpus callosum integrity and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction. The genu and body of the corpus callosum were considered independently, and neither significantly interacted with individual xanthophyll carotenoids to predict crystallized intelligence (see Appendix A, Table A.3d).

When general intelligence was the outcome, the body of the corpus callosum did not significantly interact with individual xanthophyll carotenoids (see Appendix A, Table A.3e). Axial diffusion in the genu (Table 2.17) did significantly interact with cryptoxanthin ($F(1, 95) = 7.163, p = .009, \Delta R^2 = 0.055$; Figure 2.18), lutein ($F(1, 94) = 4.018, p = .048, \Delta R^2 = 0.031$; Figure 2.19), and zeaxanthin ($F(1, 97) = 4.713, p = .032, \Delta R^2 = 0.33$; Figure 2.20).

When cryptoxanthin status was the moderator, a simple slopes analysis indicated a conditional interaction when AD was low ($-1 SD; b = 18.832, t(95) = 2.233, p = 0.028$; 95% CI = [4.665 – 79.436]), but not moderate ($b = 7.187, t(95) = 0.617, p = 0.539$; 95% CI = [-15.929 –

30.304]), or high (+1 *SD*; $b = -27.676$, $t(95) = -1.730$, $p = 0.087$; 95% CI = [-59.435 – 4.082]).

Johnson-Neyman analysis indicated 16.3% of the population in this dataset fell within the significance region.

When lutein status was the moderator, a simple slopes analysis indicated a conditional interaction when AD was low (-1 *SD*; $b = 17.247$, $t(94) = 2.116$, $p = 0.037$; 95% CI = [1.061 – 33.433]), but not moderate ($b = 4.229$, $t(94) = 0.816$, $p = 0.416$; 95% CI = [-6.060 – 14.518]), or high (+1 *SD*; $b = -8.790$, $t(94) = -1.039$, $p = 0.302$; 95% CI = [-25.592 – 8.012]). Johnson-Neyman analysis indicated 15.5% of the population in this dataset fell within the significance region.

When zeaxanthin status was the moderator, a simple slopes analysis indicated a conditional interaction when AD was low (-1 *SD*; $b = 136.866$, $t(97) = 3.401$, $p = 0.001$; 95% CI = [56.992 – 216.740]) or moderate ($b = 63.840$, $t(97) = 2.760$, $p = 0.007$; 95% CI = [17.929 – 109.750]), but not when AD was high (+1 *SD*; $b = -9.186$, $t(97) = -0.222$, $p = 0.825$; 95% CI = [-91.350 – 72.977]). Johnson-Neyman analysis indicated 59.4% of the population in this dataset fell within the significance region.

When immediate memory was the outcome, only AD in the genu (Table 2.17) and body (Table 2.18) of the corpus callosum interacted significantly with individual xanthophylls, despite significant overall models for FA and RD in both white matter tracts. In the genu, the relationship between AD and immediate memory was moderated by zeaxanthin ($F(1, 99) = 6.773$, $p = .011$, $\Delta R^2 = 0.052$; Figure 2.21). A simple slopes analysis indicated a conditional interaction with zeaxanthin status when AD was low (-1 *SD*; $b = 144.437$, $t(99) = 3.366$, $p = 0.001$; 95% CI = [59.284 – 229.590]) or moderate ($b = 50.050$, $t(99) = 2.010$, $p = 0.047$; 95% CI = [0.649 – 99.450]), but not when AD was high (+1 *SD*; $b = -44.338$, $t(99) = -0.984$, $p =$

0.327; 95% CI = [-133.709 – 45.034]). Johnson-Neyman analysis indicated 51.8% of the population in this dataset fell within the significance region.

In the body of the corpus callosum, the relationship between AD and immediate memory was moderated by lutein ($F(1, 97) = 4.640, p = .034, \Delta R^2 = 0.038$; Figure 2.22) and zeaxanthin ($F(1, 99) = 7.511, p = .007, \Delta R^2 = 0.057$; Figure 2.23). A simple slopes analysis revealed that lutein was a conditional moderator such that the interaction was significant when AD was low ($-1 SD; b = 30.574, t(97) = 2.768, p = 0.007$; 95% CI = [8.654 – 52.495]) or moderate ($b = 12.400, t(97) = 2.196, p = 0.030$; 95% CI = [1.194 – 23.606]), but not when AD was high ($+1 SD; b = -5.774, t(97) = -0.630, p = 0.530$; 95% CI = [-23.981 – 12.432]). Johnson-Neyman analysis indicated 50.0% of the population in this dataset fell within the significance region. Similarly, zeaxanthin was a moderator when AD was low ($-1 SD; b = 167.056, t(99) = 3.501, p = 0.001$; 95% CI = [72.372 – 261.740]) or moderate ($b = 67.622, t(99) = 2.704, p = 0.008$; 95% CI = [18.005– 117.239]), but not when AD was high ($+1 SD; b = -31.813, t(99) = -0.794, p = 0.429$; 95% CI = [-111.337 – 47.712]). Johnson-Neyman analysis indicated 58.3% of the population in this dataset fell within the significance region.

2.4.3.3 *Uncinate Fasciculus*

A series of moderation analyses between uncinate fasciculus microstructure and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction (see Table 2.19). However, neither crystallized intelligence (see Appendix A, Table A.3d) nor immediate memory (see Appendix A, Table A.3f) were significantly predicted by an interaction between individual xanthophylls and microstructure.

Zeaxanthin status significantly moderated the relationship between FA and general intelligence ($F(1, 97) = 4.388, p = .039, \Delta R^2 = 0.030$; Figure 2.24). Simple slopes analysis revealed that this interaction was conditionally significant when FA was high (+1 *SD*; $b = 110.542, t(97) = 3.529, p = 0.001$; 95% CI = [48.374 – 172.711] or moderate ($b = 50.857, t(97) = 2.112, p = 0.037$; 95% CI = [3.068 – 98.645]), but not when FA was low (-1 *SD*; $b = -8.829, t(97) = -0.208, p = 0.836$; 95% CI = [-93.083 – 75.426]). Johnson-Neyman analysis indicated 54.7% of the population in this dataset fell within the significance region.

Additionally, both cryptoxanthin ($F(1, 95) = 4.375, p = .039, \Delta R^2 = 0.034$; Figure 2.25) and zeaxanthin ($F(1, 97) = 3.980, p = .049, \Delta R^2 = 0.028$; Figure 2.26) status independently interacted with RD to predict general intelligence. Cryptoxanthin status was a moderator when its levels were above the group average ($b = -31,779.213, t(95) = -2.479, p = 0.015$; 95% CI = [-57,230.094 – -6328.332]). Johnson-Neyman analysis indicated 41.3% of the population in this dataset fell within the significance region. Zeaxanthin was a moderator when RD was low (-1 *SD*; $b = 128.900, t(97) = 3.206, p = 0.001$; 95% CI = [51.506 – 206.295]), but not moderate ($b = 46.565, t(97) = 1.853, p = 0.067$; 95% CI = [-3.312 – 96.442]), or high (+1 *SD*; $b = -35.771, t(97) = -0.638, p = 0.525$; 95% CI = [-147.143 – 75.601]). Johnson-Neyman analysis indicated 54.7% of the population in this dataset fell within the significance region.

2.4.3.4 *Corticospinal Tract*

A series of moderation analyses between corticospinal tract microstructure and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction (see Table 2.20).

Cryptoxanthin status moderated relationships between FA ($F(1, 95) = 7.421, p = .008, \Delta R^2 = 0.047$; Figure 2.27) and RD ($F(1, 95) = 5.078, p = .026, \Delta R^2 = 0.032$; Figure 2.28) in the corticospinal tract and crystallized intelligence. The interaction with FA was conditionally significant when FA was low ($-1 SD; b = 46.445, t(95) = 2.974, p = 0.004$; 95% CI = [15.439 – 77.451]) but not moderate ($b = 15.049, t(95) = 1.300, p = 0.197$; 95% CI = [-7.933 – 38.0341]) or high ($+1 SD; b = -16.347, t(95) = -0.960, p = 0.339$; 95% CI = [-50.140 – 17.445]). Johnson-Neyman analysis indicated 38.5% of the population in this dataset fell within the significance region. The interaction with RD was also conditional, significant when RD was high ($+1 SD; b = 38.452, t(95) = 2.599, p = 0.011$; 95% CI = [9.084 – 67.821]) but not moderate ($b = 14.662, t(95) = 1.274, p = 0.206$; 95% CI = [-8.192 – 37.517]) or low ($-1 SD; b = -9.127, t(95) = -0.556, p = 0.579$; 95% CI = [-41.696 – 23.441]). For this moderation, 36.5% of the population in this dataset fell within the significance region.

Additionally, zeaxanthin was a moderator when AD was the IV ($F(1, 97) = 11.108, p = .001, \Delta R^2 = 0.061$; Figure 2.29). Simple slopes analysis revealed that this interaction was conditionally significant when AD was low ($-1 SD; b = 193.042, t(97) = 4.305, p = 0.000$; 95% CI = [104.038 – 282.045]) or moderate ($b = 88.057, t(97) = 3.545, p = 0.001$; 95% CI = [38.757 – 137.357]), but not when AD was high ($+1 SD; b = -16.928, t(97) = -0.487, p = 0.627$; 95% CI = [-85.896 – 52.041]). Johnson-Neyman analysis indicated 62.3% of the population in this dataset fell within the significance region.

When general intelligence was the outcome, Zeaxanthin significantly interacted with AD ($F(1, 97) = 7.290, p = .008, \Delta R^2 = 0.048$; Figure 2.30). This interaction was conditionally significant when AD was low ($-1 SD; b = 166.687, t(97) = 3.897, p = 0.000$; 95% CI = [81.791 – 251.583]) or moderate ($b = 83.489, t(97) = 3.627, p = 0.000$; 95% CI = [37.799 – 129.179]), but

not when AD was high (+1 *SD*; $b = 0.291$, $t(97) = -0.009$, $p = 0.993$; 95% CI = [-66.406 – 66.988]). For this moderation, 65.1% of the population in this dataset fell within the significance region.

When immediate memory was the outcome, lutein status ($F(1, 97) = 4.806$, $p = .031$, $\Delta R^2 = 0.040$; Figure 2.31) and zeaxanthin status ($F(1, 99) = 5.312$, $p = .023$, $\Delta R^2 = 0.042$; Figure 2.32) independently interacted with AD. Lutein was a moderator when AD was low (-1 *SD*; $b = 21.376$, $t(97) = 2.773$, $p = 0.007$; 95% CI = [6.074 – 36.678]) but not moderate ($b = 9.011$, $t(97) = 1.609$, $p = 0.111$; 95% CI = [-2.107 – 20.128]), or high (+1 *SD*; $b = -3.355$, $t(97) = -0.410$, $p = 0.683$; 95% CI = [-19.595 – 12.885]). For this moderation, 41.5% of the population in this dataset fell within the significance region. Zeaxanthin was a moderator when AD was low (-1 *SD*; $b = 144.702$, $t(99) = 3.076$, $p = 0.003$; 95% CI = [51.375 – 238.023]) or moderate ($b = 67.466$, $t(99) = 2.626$, $p = 0.010$; 95% CI = [16.494 – 118.438]), but not when AD was high (+1 *SD*; $b = -9.769$, $t(99) = -0.266$, $p = 0.791$; 95% CI = [-82.772 – 63.233]). For this moderation, 56.4% of the population in this dataset fell within the significance region.

2.4.3.5 *Corona Radiata*

A series of moderation analyses between corona radiata integrity and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction. The anterior, posterior, and superior tracts were considered independently, and none of the three significantly interacted with individual xanthophyll carotenoids to predict immediate memory (see Appendix A, Table A.3f).

When crystallized intelligence is the outcome, the posterior corona radiata did not significantly interact with individual xanthophyll carotenoids (see Appendix A, Table A3d), but the anterior (Table 2.21) and superior (Table 2.22) corona radiata did. Axial diffusion in the anterior corona radiata interacted with cryptoxanthin ($F(1, 95) = 4.114, p = .045, \Delta R^2 = 0.027$; Figure 2.33) and zeaxanthin ($F(1, 97) = 4.295, p = .041, \Delta R^2 = 0.026$; Figure 2.34) to predict crystallized intelligence. Lutein status interacted with RD in the anterior corona radiata ($F(1, 94) = 4.248, p = .042, \Delta R^2 = 0.028$; Figure 2.35).

Cryptoxanthin was a conditional moderator when AD was low ($-1\ SD; b = 45.789, t(95) = 2.568, p = 0.012$; 95% CI = [10.392 – 81.186]) but not moderate ($b = 21.348, t(95) = 1.813, p = 0.073$; 95% CI = [-2.023 – 44.718]) or high ($+1\ SD; b = -3.094, t(95) = -0.196, p = 0.845$; 95% CI = [-34.464 – 28.276]) and 46.% of the population in this dataset fell within the significance region. The interaction between AD in the anterior corona radiata and zeaxanthin status was conditionally significant when AD was low ($-1\ SD; b = 119.400, t(97) = 3.356, p = 0.001$; 95% CI = [48.839 – 189.962]) or moderate ($b = 70.854, t(97) = 2.780, p = 0.006$; 95% CI = [20.262 – 121.446]), but not when AD was high ($+1\ SD; b = 22.308, t(97) = 0.663, p = 0.509$; 95% CI = [-44.499 – 89.114]). Johnson-Neyman analysis indicated 60.4% of the population in this dataset fell within the significance region. Similarly, the interaction between RD in the anterior corona radiata and lutein status was conditionally significant when RD was low ($-1\ SD; b = 25.547, t(94) = 3.288, p = 0.001$; 95% CI = [10.118 – 40.976]) or moderate ($b = 14.204, t(94) = 2.545, p = 0.012$; 95% CI = [3.124 – 25.284]), but not when RD was high ($-1\ SD; b = 2.860, t(94) = 0.362, p = 0.718$; 95% CI = [-12.834 – 18.554]). In this population, 70.9% of the dataset fell within the significance region.

Lutein also moderated the relationship between RD in the superior corona radiata and crystallized intelligence ($F(1, 94) = 4.521, p = .036, \Delta R^2 = 0.030$; Figure 2.36). This was a conditional interaction such that lutein status was a moderator when RD was low ($-1 SD; b = 26.504, t(94) = 3.304, p = 0.001; 95\% CI = [10.578 - 42.430]$) or moderate ($b = 13.364, t(94) = 2.3885, p = 0.019; 95\% CI = [2.255 - 24.474]$), but not when RD was high ($+1 SD; b = 0.225, t(94) = 0.026, p = 0.979; 95\% CI = [-16.932 - 17.381]$). In this population, 60.2% of the dataset fell within the significance region.

When general intelligence is the outcome, the superior corona radiata did not significantly interact with individual xanthophyll carotenoids (see Appendix A, Table A3e), but the anterior (Table 2.21) and posterior (Table 2.23) corona radiata did. Cryptoxanthin ($F(1, 95) = 7.925, p = .006, \Delta R^2 = 0.061$; Figure 2.37) and zeaxanthin ($F(1, 97) = 4.579, p = .035, \Delta R^2 = 0.032$; Figure 2.38) moderated the relationship between AD in the anterior corona radiata and general intelligence. Lutein status moderated the relationship between AD in the posterior corona radiata and general intelligence ($F(1, 94) = 4.683, p = .033, \Delta R^2 = 0.035$; Figure 2.39). Simple slopes analyses indicated that all three moderations were conditional, and Johnson-Neyman analyses revealed that each moderation was significant in at least 10% of this population.

Cryptoxanthin was a moderator when AD in the anterior corona radiata was low ($-1 SD; b = 43.359, t(95) = 2.363, p = 0.020; 95\% CI = [6.925 - 79.793]$) but not when it was moderate ($b = 8.634, t(95) = 0.742, p = 0.460; 95\% CI = [-14.374 - 31.730]$) or high ($+1 SD; b = -26.090, t(95) = -1.690, p = 0.094; 95\% CI = [-56.730 - 4.549]$). In this population, 30.8% of the dataset fell within the significance region. Zeaxanthin was a moderator when AD in the anterior corona radiata was low ($-1 SD; b = 114.087, t(97) = 3.604, p = 0.000; 95\% CI = [51.257 - 176.916]$) and moderate ($b = 67.536, t(97) = 2.934, p = 0.004; 95\% CI = [21.851 - 113.221]$), but not when AD

was high (+1 *SD*; $b = 20.986$, $t(97) = 0.662$, $p = 0.509$; 95% CI = [-41.901 – 83.873]). In this population, 59.4% of the dataset fell within the significance region.

Lutein status was a moderator when AD in the posterior corona radiata was low (-1 *SD*; $b = 14.693$, $t(94) = 2.052$, $p = 0.043$; 95% CI = [0.473 – 28.913]) but not when it was moderate ($b = 4.232$, $t(94) = 0.827$, $p = 0.410$; 95% CI = [-5.924 – 14.389]) or high (+1 *SD*; $b = -6.228$, $t(94) = -0.901$, $p = 0.370$; 95% CI = [-19.952 – 7.496]). In this population, 10.7% of the dataset fell within the significance region.

2.4.3.6 *Posterior Thalamic Radiation*

A series of moderation analyses between posterior thalamic radiation microstructure and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction. Neither crystallized intelligence (see Appendix A, Table A.3d) nor immediate memory (see Appendix A, Table A.3f) were significantly predicted by interactions between individual xanthophyll carotenoids and microstructure in this tract (see Appendix A, Table A.3f).

Lutein status was a significant moderator the relationship between AD in the posterior thalamic radiation and general intelligence ($F(1, 94) = 4.737$, $p = .032$, $\Delta R^2 = 0.036$; Table 2.24; Figure 2.40). A simple slopes analysis indicated that this interaction was conditional such that lutein status was a moderator when AD was low (-1 *SD*; $b = 149.256$, $t(94) = 2.080$, $p = 0.040$; 95% CI = [0.646 – 27.866]) but not when AD was moderate ($b = 4.297$, $t(94) = 0.833$, $p = 0.407$; 95% CI = [-5.944 – 14.539]), or high (+1 *SD*; $b = -5.662$, $t(94) = -0.816$, $p = 0.416$; 95% CI = [-19.432 – 8.109]). Johnson-Neyman analysis indicated 21.4% of the population in this dataset fell within the significance region.

2.4.3.7 Superior Longitudinal Fasciculus

A series of moderation analyses between superior longitudinal fasciculus integrity and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction. Immediate memory was not significantly predicted by interactions between individual xanthophyll carotenoids and integrity of this tract (see Appendix A, Table A.3f), but crystallized and general intelligence were (Table 2.25).

When crystallized intelligence was the outcome, lutein status significantly interacted with RD ($F(1, 94) = 4.249, p = .042, \Delta R^2 = 0.028$; Figure 2.41). A simple slopes analysis indicated that this interaction was conditionally significant when RD was low ($-1 SD; b = 24.881, t(94) = 3.252, p = 0.002$; 95% CI = [9.692 – 40.071]) or moderate ($b = 14.004, t(94) = 2.489, p = 0.015$; 95% CI = [2.831 – 25.176]), but not when RD was high ($+1 SD; b = -12.317, t(94) = 0.402, p = 0.689$; 95% CI = [-12.3169 – 18.569]). Johnson-Neyman analysis indicated 64.1% of the population in this dataset fell within the significance region.

The relationship between AD and general intelligence was moderated by lutein status ($F(1, 94) = 5.644, p = .020, \Delta R^2 = 0.043$; Figure 2.42) and zeaxanthin status ($F(1, 97) = 6.933, p = .010, \Delta R^2 = 0.047$; Figure 2.43). Simple slopes analyses revealed that both moderations were conditional. Lutein status was a moderator when AD was low ($-1 SD; b = 15.632, t(94) = 2.270, p = 0.026$; 95% CI = [1.960 – 29.303]) but not moderate ($b = 3.839, t(94) = 0.736, p = 0.464$; 95% CI = [-6.524 – 14.201]) or high ($+1 SD; b = -7.954, t(94) = -1.060, p = 0.292$; 95% CI = [-22.859 – 6.950]). In this dataset, 25.2% of the population fell within the significance region. Zeaxanthin status was a moderator when AD was low ($-1 SD; b = 145.761, t(97) = 3.894, p = 0.000$; 95% CI = [71.469 – 220.053]) or moderate ($b = 68.765, t(97) = 3.008, p = 0.003$; 95%

CI = [23.393 – 114.137]) but not when AD was high (+1 *SD*; $b = -8.231$, $t(97) = -0.824$, $p = 0.824$; 95% CI = [-81.272 – 64.810]). In this dataset, 60.4% of the population fell within the significant region.

2.4.3.8 *Cingulum*

A series of moderation analyses between white matter integrity of the cingulum and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction. The cingulum – cingulate and cingulum – hippocampus tracts were considered separately and the cingulum – cingulate tract had no significant interactions with individual xanthophyll carotenoids for any of the facets of intelligence explored (see Appendix A, Table A.3b). For the cingulum – hippocampus tract, general intelligence was not significantly predicted by an interaction between microstructure and xanthophyll carotenoids (see Appendix A, Table A.3e), but crystallized intelligence and immediate memory were (Table 2.26).

When crystallized intelligence was the outcome, zeaxanthin status significantly interacted with AD ($F(1, 97) = 9.980$, $p = .002$, $\Delta R^2 = 0.057$; Figure 2.44). This interaction was conditional such that zeaxanthin status moderated the relationship between AD and crystallized intelligence when AD was low (1 *SD*; $b = 162.497$, $t(97) = 4.148$, $p = 0.000$; 95% CI = [84.756 – 240.238]) or moderate ($b = 71.716$, $t(97) = 2.903$, $p = 0.005$; 95% CI = [22.691 – 120.740]), but not when AD was high (+1 *SD*; $b = -19.066$, $t(97) = -0.521$, $p = 0.603$; 95% CI = [-91.651 – 53.519]). In this population, 61.3% of subjects fell within the significance region.

When immediate memory was the outcome, zeaxanthin status interacted with both FA ($F(1, 99) = 7.478$, $p = .007$, $\Delta R^2 = 0.058$; Figure 2.45) and RD ($F(1, 99) = 4.859$, $p = .030$, $\Delta R^2 =$

0.038; Figure 2.46). Simple slopes analyses revealed that both interactions were conditional. Zeaxanthin was a moderator when FA was moderate ($b = 61.619$, $t(99) = 2.472$, $p = 0.015$; 95% CI = [12.150 – 111.088]) or high (+1 SD ; $b = 120.957$, $t(99) = 3.440$, $p = 0.001$; 95% CI = [51.191 – 190.722]), but not when FA was low (-1 SD ; $b = 2.282$, $t(99) = 0.074$, $p = 0.941$; 95% CI = [-58.828 – 63.391]). In this population, 58.3% of subjects fell within the significance region. Zeaxanthin was also a moderator when RD was low (-1 SD ; $b = 103.570$, $t(99) = 3.055$, $p = 0.003$; 95% CI = [36.306 – 170.833]) or moderate ($b = 55.487$, $t(99) = 2.215$, $p = 0.029$; 95% CI = [5.788 – 105.185]), but not when RD was high (+1 SD ; $b = 7.403$, $t(99) = 0.228$, $p = 0.820$; 95% CI = [-57.110 – 71.917]). In this population, 52.8% of subjects fell within the significance region.

Additionally, lutein status moderated the relationship between AD ($F(1, 97) = 6.187$, $p = .015$, $\Delta R^2 = 0.050$; Figure 2.47) and RD ($F(1, 97) = 5.148$, $p = .026$, $\Delta R^2 = 0.042$; Figure 2.48) in the cingulum – hippocampus tract and immediate memory. Lutein status was a moderator when AD was low (-1 SD ; $b = 24.380$, $t(97) = 3.037$, $p = 0.003$; 95% CI = [8.447 – 40.313]) but not when AD was moderate ($b = 9.302$, $t(97) = 1.688$, $p = 0.094$; 95% CI = [-1.632 – 20.236]) or high (+1 SD ; $b = -5.776$, $t(97) = -0.692$, $p = 0.491$; 95% CI = [-22.351 – 10.799]). In this population, 36.8% of subjects fell within the significance region. Lutein status was also a moderator when RD was low (-1 SD ; $b = 20.695$, $t(97) = 2.840$, $p = 0.006$; 95% CI = [6.234 – 35.156]) but not when RD was moderate ($b = 8.957$, $t(97) = 1.602$, $p = 0.112$; 95% CI = [-2.140 – 20.055]) or high (+1 SD ; $b = -2.781$, $t(97) = -0.350$, $p = 0.727$; 95% CI = [-18.530 – 12.968]). In this population, 42.5% of subjects fell within the significance region.

2.4.3.9 *External Capsule*

A series of moderation analyses between white matter integrity of the external capsule and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction. Neither crystallized intelligence (see Appendix A, Table A.3d) nor immediate memory (see Appendix A, Table A.3f) were predicted by an interaction between integrity and xanthophyll carotenoids. General intelligence was predicted by an interaction between integrity and zeaxanthin status (Table 2.27).

When general intelligence was the outcome, zeaxanthin status significantly interacted with AD ($F(1, 97) = 6.045, p = .016, \Delta R^2 = 0.041$; Figure 2.49). A simple slopes analysis indicated that the moderation was conditional, such that zeaxanthin was a significant moderator when AD was low ($-1\ SD; b = 140.818, t(97) = 3.816, p = 0.000; 95\% \text{ CI} = [67.581 - 214.054]$) or moderate ($b = 71.567, t(97) = 3.134, p = 0.002; 95\% \text{ CI} = [26.242 - 116.892]$), but not when AD was high ($+1\ SD; b = 2.316, t(97) = 0.948, p = 0.948; 95\% \text{ CI} = [-68.364 - 72.996]$). Johnson-Neyman analysis indicated 71.7% of the population in this dataset fell within the significance region.

2.4.3.10 *Internal Capsule*

A series of moderation analyses between white matter integrity of the internal capsule and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory was the outcome after FDR correction. The anterior and posterior limbs were considered separately and neither the anterior

limb of the internal capsule nor the posterior limb of the internal capsule interacted significantly with xanthophyll carotenoids to predict immediate memory (see Appendix A, Table A.3f). Axial diffusion in both the anterior (Table 2.28) and posterior (Table 2.29) limbs interacted with xanthophylls to predict crystallized and general intelligence.

In the anterior limb, zeaxanthin status significantly moderated the relationship between AD and both crystallized ($F(1, 97) = 5.367, p = .023, \Delta R^2 = 0.031$; Figure 2.50) and general ($F(1, 97) = 7.147, p = .009, \Delta R^2 = 0.047$; Figure 2.51) intelligence. Cryptoxanthin also interacted with AD to predict general intelligence ($F(1, 95) = 4.611, p = .034, \Delta R^2 = 0.036$; Figure 2.52).

A simple slopes analysis indicated that the zeaxanthin moderated the relationship with crystallized intelligence when AD was low ($-1 SD; b = 134.802, t(97) = 3.567, p = 0.001$; 95% CI = [59.788 – 209.816]) and moderate ($b = 76.042, t(97) = 3.063, p = 0.003$; 95% CI = [26.776 – 125.307]), but not when AD was high ($+1 SD; b = 17.281, t(97) = 0.523, p = 0.602$; 95% CI = [-48.259 – 82.821]). Johnson-Neyman analysis indicated 67.0% of the population in this dataset fell within the significance region. Similarly, zeaxanthin status moderated the relationship with general intelligence when AD was low ($-1 SD; b = 137.534, t(97) = 4.005, p = 0.000$; 95% CI = [69.380 – 205.688]) or moderate ($b = 74.973, t(97) = 3.333, p = 0.001$; 95% CI = [30.331 – 119.615]), but not when AD was high ($+1 SD; b = 12.412, t(97) = 0.408, p = 0.685$; 95% CI = [-48.045 – 72.868]). In this population, 67.9% of subjects fell within the significance region. Cryptoxanthin status moderated the relationship with general intelligence when its levels were above the group average ($b = -79,642.036, t(95) = -2.645, p = 0.010$; 95% CI = [-139,410.69 – -19,873.38]). Johnson-Neyman analysis indicated 39.4% of the population in this dataset fell within the significance region.

In the posterior limb, zeaxanthin status moderated the relationship between AD and both crystallized ($F(1, 97) = 10.716, p = .002, \Delta R^2 = 0.061$; Figure 2.53) and general ($F(1, 97) = 6.925, p = .010, \Delta R^2 = 0.046$; Figure 2.54) intelligence. When crystallized intelligence was the outcome, zeaxanthin status was a moderator when AD was low ($-1\text{ SD}; b = 167.077, t(97) = 4.430, p = 0.000$; 95% CI = [92.218 – 241.936]) or moderate ($b = 88.214, t(97) = 3.512, p = 0.001$; 95% CI = [38.361 – 138.068]), but not when AD was high ($-1\text{ SD}; b = 9.352, t(97) = 0.296, p = 0.768$; 95% CI = [-53.413 – 72.117]). In this population, 67.0% of the subjects fell within the significance region. When general intelligence was the outcome, zeaxanthin status was a moderator when AD was low ($-1\text{ SD}; b = 143.422, t(97) = 4.068, p = 0.000$; 95% CI = [73.453 – 213.391]) or moderate ($b = 84.080, t(97) = 3.627, p = 0.000$; 95% CI = [38.069 – 130.091]), but not when AD was high ($+1\text{ SD}; b = 24.737, t(97) = 0.849, p = 0.398$; 95% CI = [-33.098 – 82.573]). In this population, 74.5% of subjects fell within the significance region.

2.4.3.11 *Cerebellar Peduncles*

A series of moderation analyses between white matter integrity of the cerebellar peduncles and individual xanthophyll carotenoids revealed some significant overall models when crystallized intelligence, general intelligence, or immediate memory is the outcome. The inferior, middle, and superior cerebellar peduncles were considered separately and only the inferior cerebellar peduncle had no significant interactions with individual xanthophyll carotenoids for any of the facets of intelligence explored (see Appendix A, Table A.3c). When immediate memory was the outcome, neither integrity of the middle cerebellar peduncle nor the superior cerebellar peduncle significantly interacted with xanthophylls (see Appendix A, Table A.3f).

Both the middle (Table 2.30) and superior (Table 2.31) peduncles significantly interacted with individual xanthophylls.

Zeaxanthin moderated the relationships between AD in the middle ($F(1, 97) = 9.336, p = .003, \Delta R^2 = 0.054$; Figure 2.55) and superior ($F(1, 97) = 5.008, p = .028, \Delta R^2 = 0.037$; Figure 2.56) cerebellar peduncles and crystallized intelligence. Simple slopes analyses revealed that both moderations were conditional. In the middle cerebellar peduncle, zeaxanthin status was a moderator when AD was low ($-1\ SD; b = 164.652, t(97) = 3.982, p = 0.000; 95\% \text{ CI} = [82.575 - 246.730]$) or moderate ($b = 76.572, t(97) = 3.056, p = 0.003; 95\% \text{ CI} = [26.842 - 126.302]$), but not when AD was high ($+1\ SD; b = -11.508, t(97) = -0.331, p = 0.741; 95\% \text{ CI} = [-80.470 - 57.454]$). In the superior cerebellar peduncle, zeaxanthin status was a moderator when AD was low ($-1\ SD; b = 171.502, t(97) = 3.172, p = 0.002; 95\% \text{ CI} = [64.193 - 278.811]$) or moderate ($b = 85.510, t(97) = 3.154, p = 0.002; 95\% \text{ CI} = [31.699 - 139.322]$), but not when AD was high ($+1\ SD; b = -0.481, t(97) = -0.012, p = 0.990; 95\% \text{ CI} = [-77.345 - 76.383]$). Johnson-Neyman analyses indicated 62.3% and 70.8% of the subjects in this population fell within the significance region, respectively. Zeaxanthin also moderated the relationship between RD in the middle cerebellar peduncle and crystallized intelligence ($F(1, 97) = 5.626, p = .020, \Delta R^2 = 0.035$; Figure 2.57). This moderation was significant when RD was low ($-1\ SD; b = 131.885, t(97) = 3.452, p = 0.001; 95\% \text{ CI} = [56.049 - 207.721]$) but not moderate ($b = 41.376, t(97) = 1.500, p = 0.137; 95\% \text{ CI} = [-13.376 - 96.128]$) or high ($+1\ SD; b = -49.134, t(97) = -0.901, p = 0.367; 95\% \text{ CI} = [-157.378 - 59.111]$). This moderation was significant in 47.2% of subjects.

In the middle cerebellar peduncle, lutein status moderated the relationship between FA and crystallized intelligence ($F(1, 94) = 4.321, p = .040, \Delta R^2 = 0.029$; Figure 2.58). This interaction was conditionally significant when FA was moderate ($b = 12.700, t(94) = 2.247, p =$

0.027; 95% CI = [1.478 – 23.921]) and high (+1 SD; $b = 26.936$, $t(94) = 3.234$, $p = 0.001$; 95% CI = [10.845 – 43.028]), but not when FA was low (-1 SD; $b = -1.537$, $t(94) = -0.160$, $p = 0.873$; 95% CI = [-20.584 – 17.509]). This moderation was significant in 59.2% of subjects.

Additionally, lutein moderated the relationship between RD and both crystallized ($F(1, 94) = 5.608$, $p = .020$, $\Delta R^2 = 0.037$; Figure 2.59) and general ($F(1, 94) = 4.595$, $p = .035$, $\Delta R^2 = 0.035$; Figure 2.60) intelligence. When crystallized intelligence was the outcome, lutein status was a significant moderator when RD was low (-1 SD; $b = 26.361$, $t(94) = 3.549$, $p = 0.001$; 95% CI = [11.613 – 41.110]) or moderate ($b = 11.561$, $t(94) = 2.034$, $p = 0.045$; 95% CI = [0.274 – 22.848]), but not when RD was high (+1 SD; $b = -3.239$, $t(94) = -0.346$, $p = 0.730$; 95% CI = [-21.820 – 15.342]). When general intelligence was the outcome, lutein status only moderated the relationship when RD was low (-1 SD; $b = 14.913$, $t(94) = 2.144$, $p = 0.035$; 95% CI = [1.106 – 28.721]), not when RD was moderate ($b = 2.113$, $t(94) = 0.400$, $p = 0.690$; 95% CI = [-8.368 – 12.593]) or high (+1 SD; $b = -10.688$, $t(94) = -1.205$, $p = 0.231$; 95% CI = [-28.300 – 6.924]). These moderations were significant in 56.3% and 19.4% of this population, respectively.

In the superior cerebellar peduncle, zeaxanthin status moderated the relationship between FA and general intelligence ($F(1, 97) = 4.360$, $p = .039$, $\Delta R^2 = 0.030$; Figure 2.61). A simple slopes analysis revealed that this moderation was conditionally significant when FA was high (+1 SD; $b = 93.476$, $t(97) = 3.472$, $p = 0.001$; 95% CI = [40.039 – 146.912]), but not when FA was moderate ($b = 37.314$, $t(97) = 1.358$, $p = 0.178$; 95% CI = [-17.224 – 91.851]) or low (-1 SD; $b = -18.849$, $t(97) = -0.399$, $p = 0.691$; 95% CI = [-112.620 – 74.923]). A Johnson-Neyman analysis indicated 46.2% of the population in this dataset falls within the significance region.

2.5 **Discussion**

2.5.1 *Summary of Findings*

This series of studies was performed to advance the understanding of healthy brain aging by investigating the following fundamental question and constituent hypotheses:

Can relationships between peripheral xanthophyll carotenoids and markers of brain health be characterized using a systematic framework of moderation analyses?

1. *Do individual xanthophyll carotenoids influence relationships between grey matter volume of regions bordering the parietal and occipital lobes and facets of intelligence?*
2. *Do individual xanthophyll carotenoids influence relationships between efficiency of intrinsic connectivity networks at the border of the parietal and occipital lobes and facets of intelligence?*
3. *Do individual xanthophyll carotenoids influence relationships between white matter integrity and facets of intelligence?*

A series of cross-sectional studies in a population of healthy, older adults revealed that individual xanthophyll carotenoids did indeed moderate relationships between markers of brain health and facets of intelligence at the structural, functional, and microstructural level.

2.5.2 *Do individual xanthophyll carotenoids influence relationships between grey matter volume of cortical regions at the border of the parietal and occipital lobes and facets of intelligence?*

Yes, in this population of healthy, older adults lutein and zeaxanthin status independently moderated the relationship between cuneus volume and immediate memory and general intelligence, respectively. Additionally, zeaxanthin status moderated the relationship between precuneus volume and immediate memory.

First, to determine relationships between markers of brain health in our population of healthy, older adults a correlation matrix revealed which facets of intelligence may associate with the grey matter ROIs chosen a priori – the cuneus, inferior parietal lobule, lateral occipital cortex, precuneus, and superior parietal lobule. Linear regression models performed with each ROI (IV), correlated facets of intelligence (DVs; auditory memory, crystallized intelligence, delayed memory, general intelligence, immediate memory, task switching, and visual memory), and five covariates (age, BMI, education, income, sex) revealed significant relationships between ROIs and auditory memory, crystallized intelligence, delayed memory, general intelligence, and immediate memory (Table 2.4).

Second, significant regression models were followed by a series of moderation analyses repeated with each individual xanthophyll carotenoid as a moderator (cryptoxanthin, lutein, zeaxanthin). To predict two facets of intelligence (general intelligence and immediate memory), lutein (Figure 2.4) and zeaxanthin (Figure 2.3) status independently interacted with cuneus volume. To predict immediate memory, zeaxanthin status also interacted with precuneus volume (Figure 2.5). In all three moderations, interactions were most significant when cortical volumes

were small. When zeaxanthin was the moderator interactions were also most significant when volumes were moderate.

The observed correlations between cortical volume and facets of intelligence are somewhat supported by the cognitive neuroscience literature. To my knowledge, cuneus (Brodmann area 17) volume has not been linked to general intelligence in healthy adults, however occipital lobe grey matter volume has been associated with working memory performance, of which immediate memory is a component (Bettcher et. al., 2016; Christophel, Cichy, Hebart, & Haynes, 2015). Additionally, activity in this region is influenced by attention and reward (Bayer et. al., 2017) and is generally suppressed to maintain attention on non-visually stimulating tasks. In older adults, however, engagement is not inhibited normally (Kuchinsky et. al., 2012) and this is believed to contribute to increased distractibility with aging. Because some components of the FSIQ are timed, distractibility could contribute to general intelligence score. The precuneus (Brodmann area 7) plays an important role in highly integrated functions and is believed to be important for higher-order cognitive function due to its size and complex columnar organization specific to humans (Cavanna & Trimble, 2006). In fact, the precuneus has a notable relationship with episodic memory (Nyberg, 2017; Wagner et. al., 2005) and loss of connectivity between the precuneus and medial prefrontal lobe predicts episodic memory in aging individuals (Salami, Pudas, & Nyberg, 2014). Interestingly, patients with early-onset AD exhibit disproportional grey matter atrophy in the precuneus, indicating a role for precuneus volume retention in cognitive performance (Karas et. al., 2007).

Lutein and zeaxanthin are present throughout the brain tissue, but preferentially accumulate within the occipital lobe (Craft et. al., 2004; Johnson et. al., 2013; Vishwanathan, Schalch, & Johnson, 2016). The levels of these nutrients within brain tissue correlate with blood

serum measures (Johnson et. al., 2013; Tanprasertsuk, et. al., 2019), allowing the use of peripheral xanthophyll levels to investigate relationships with brain health. Mixed xanthophyll supplements have been linked to improved visual processing speed (Bovier & Hammond, 2015) and better performance on tasks utilizing working memory, cognitive flexibility, episodic memory, and semantic memory when compared to placebo Kesse-Guyot et. al., 2014; Power et. al., 2008). In observational studies, lutein has been associated with relational memory (Cannavale et. al., 2019) and crystallized intelligence (Zamroziewicz et. al., 2016). This body of literature indicates that xanthophylls likely influence cognitive function and hold potential as a modifiable lifestyle factor capable of attenuating cognitive changes present during normal brain aging. The studies in this dissertation support that conclusion by demonstrating that lutein and zeaxanthin influence the relationship between grey matter volume and cognitive performance in older adults. Lutein and zeaxanthin independently moderate the cuneus's effect on immediate memory and general intelligence, respectively, and zeaxanthin moderates the precuneus's effect on immediate memory as well.

It is important to note that precuneus and cuneus grey matter volume are differentially impacted by aging. Precuneus volume decreases with age, however cuneus volume remains fairly consistent through adulthood (Raz et. al., 2005). Considering both xanthophylls were most influential when regional volume was small, there are a few possible conclusions that can be drawn about the reported observations.

In the cuneus it is reasonable to conclude that size variance is attributable to factors other than aging, such as differences in genotype, since its volume does not tend to shrink with age. Here, xanthophyll status may have an “ameliorating effect,” where moderation of the relationship between cortical volume and cognitive performance reflects some underlying

compensatory mechanism. In this scenario, xanthophyll status mitigates behavioral outcomes associated with small cortical volume. Conversely, size variance in the precuneus is more likely resultant from a combination of aging and other factors. One possible interpretation is that volume represents an aging trajectory, where those with larger volumes are earlier in the aging process compared with those who have smaller volumes. However, this perspective is less likely in this context given the cross-sectional nature of this study, that participation was limited to individuals between ages 65-75, and that statistical analyses controlled for age. Another possibility is that those with larger volumes could be perceived as being resistant to age-related atrophy and those with smaller volumes as susceptible to age-related atrophy. This perspective lends to an interesting interpretation of the observed results. First, it suggests that xanthophyll status influences the relationship between cortical volume and cognitive performance more significantly in those with a greater susceptibility to aging. Second, it suggests that zeaxanthin status may exhibit a “fostering effect,” where moderation of the relationship between cortical volume and cognitive performance reflects some underlying auxiliary mechanism. In this scenario, zeaxanthin status attenuates behavioral outcomes associated with age-related cortical atrophy.

Importantly, these are observations from cross-sectional data and inferences regarding causality or mechanisms of action cannot be made. Although there exists a vast body of literature that supports a relationship between cortical volume and cognition, the nature of moderation analyses and observational data do not permit claims of causal relationships between any of the variables studied. The interpretations provided are speculative and require further research to evaluate directionality and genetic influence on the observed associations. These findings do, however, demonstrate that xanthophyll carotenoids independently moderate relationships

between structure and function in the aging brain and that lutein and zeaxanthin exhibit differentiable influences in the aging brain.

2.5.3 *Do individual xanthophyll carotenoids influence relationships between efficiency of intrinsic connectivity networks at the border of the parietal and occipital lobes and facets of intelligence?*

Yes, in this population of healthy, older adults individual xanthophyll carotenoids independently moderated relationships between efficiency in the DMN, FPN, DAN, and VAN and crystallized intelligence. Zeaxanthin status also moderated the relationship between efficiency in the DMN and immediate memory. Further, lutein status moderated relationships between efficiency in the DMN or FPN and immediate memory.

First, to determine relationships between efficiency and facets of intelligence linear regression models were performed with efficiency measures in each ICN (IV; DMN, FPN, VisN, DAN, VAN), correlated facets of intelligence (DVs; auditory memory, crystallized intelligence, delayed memory, general intelligence, immediate memory), and five covariates (age, BMI, education, income, sex). Models revealed significant relationships between efficiency and crystallized intelligence, delayed memory, general intelligence, and immediate memory (Table 2.8 and Table 2.9). Then, significant regression models were followed by a series of moderation analyses repeated with each individual xanthophyll carotenoid as a moderator (cryptoxanthin, lutein, zeaxanthin). All reported moderations remained significant after correcting for multiple comparisons.

Accumulating evidence in the field of network neuroscience indicates that signaling efficiency among brain regions relates to cognitive performance (Gott-Fredson, 1997) and that

activity in ICNs captured by rsfMRI indicates processing ability (Damoiseaux et. al., 2006; Raichle et. al., 2001). Efficient signaling is characterized by high clustering (local efficiency) and short path length (global efficiency) which comprise a small-world topology directly linked to general intelligence (Barbey, 2018; Muldoon, Bridgeford, & Bassett, 2016). During aging efficiency decreases and long path lengths are preferentially disrupted within the DMN, and such disruptions are associated with cognitive decline (Andrews-Hanna et. al., 2007; Damoiseaux et. al., 2008; Koch et. al., 2010). Compared to the DMN, other ICNs are less studied in the context of brain aging resulting in a large gap in knowledge.

Although sparse, there does exist some evidence suggesting interplay between carotenoids and network efficiency. In our lab, studies revealed that lycopene status moderates the relationship between small world propensity in the DAN and executive function (Zwilling, Talukdar, Zamroziewicz, & Barbey, 2019) and that parahippocampal cortex volume, a region located within the DMN (Yeo et. al., 2011), mediates the relationship between lutein status and crystallized intelligence (Zamroziewicz, et. al., 2016). Most notably, an intervention study published last year found that mixed supplementation of lutein and zeaxanthin increased connectivity between the DMN and other networks but did not detect connectivity changes within the DMN in healthy, older adults (Lindbergh et. al., 2019). This group proposes that lutein and zeaxanthin may enhance network integration to compensate for brain aging, and to my knowledge it is the only intervention study on the subject.

Interestingly, the observation that zeaxanthin moderates the relationship between global efficiency and crystallized intelligence within the DMN (Figure 2.6) fits well within this narrative. Here, zeaxanthin status moderated the relationship when global efficiency was low or moderate. When considering the Scaffolding Theory of Aging and Cognition (See Section 1.1.1;

Park and Reuter-Lorenz, 2009) used to explain the increased connectivity between networks after xanthophyll supplementation (Lindbergh et. al., 2019), the present observation fits within the “ameliorating effect” interpretation described in section 2.5.3. Taken together, zeaxanthin may mitigate behavioral changes in the aging brain through a compensatory mechanism whereby zeaxanthin enhances network integration when global efficiency is below the mean to facilitate compensational reorganization. Additionally, in the present study both lutein and zeaxanthin status independently moderated the relationship between local efficiency in the DMN and immediate memory performance (Figures 2.7 and 2.8, respectively). These observations suggest that xanthophyll status influences immediate memory via interaction with local efficiency in the DMN, most notably when local efficiency is high. Importantly, local efficiency tends to decrease with age (Achard and Bullmore, 2007; Song et. al., 2014) rendering networks more susceptible to connectivity disruption (Geerligs et. al., 2015). Greater local efficiency, then, indicates minimal disruption and better behavioral outcome (Damoiseaux et. al., 2008; Koch et. al., 2010; Stanley et. al., 2015). Taken together, these observations fit within the “fostering effect” interpretation described in section 2.5.3. Here, xanthophylls may attenuate behavioral changes through an auxiliary mechanism whereby xanthophyll status preserves local efficiency to foster cognitive performance. It should be recognized that given the cross-sectional and observational nature of these data the interpretations provided are speculative and require further exploration to identify causal relationships.

To my knowledge the other networks explored within this chapter have not been studied in conjunction with xanthophyll carotenoids. Combined with the cross-sectional and observational nature of these data, the absence of literary context within nutritional cognitive

neuroscience makes it difficult to interpret results. The remaining findings, then, will be discussed only briefly.

The relationship between local efficiency and immediate memory was moderated by lutein status within the FPN (Figure 2.10). Local efficiency in this network also interacted with cryptoxanthin to predict crystallized intelligence (Figure 2.9). In both instances, xanthophyll influence was most significant when local efficiency was high. Notably, both intra- and inter-network connectivity of the FPN plays a seminal role in intelligence (Hearne, Mattingley, & Cocchi, 2016). These observations suggest the possibility that xanthophylls attenuate cognitive changes in the aging brain by preserving local efficiency within networks critical to intelligence.

The only other interaction observed with global efficiency occurred within the VAN (Figure 2.12). Similar to the previously described observation, zeaxanthin status moderated the relationship between global efficiency and crystallized intelligence when global efficiency was low. The VAN is involved in recognizing important stimuli and knowing what they are used for (Corbetta & Shulman, 2002), so it logically follows that efficiency in this network could predict crystallized intelligence. As for zeaxanthin's role, it is possible that zeaxanthin influences crystallized intelligence when global efficiency is low to enhance network integration with the VAN.

Finally, lutein status moderated the relationship between small world propensity in the DAN and crystallized intelligence (Figure 2.11). Interestingly, there is evidence that carotenoids interact with small world propensity in the DAN (Zwilling et. al., 2019). In that study of older adults, lycopene moderated the relationship between small world propensity in the DAN and executive function. The present investigations did not include executive function as an outcome nor was lycopene evaluated as a moderator. However, it is possible that these studies are

capturing the same relationship, where carotenoids generally influence facets of intelligence via small-world topography within the DAN. Future investigations should explore whether these moderating relationships are specific to carotenoid type and facet of intelligence or influence is convergent across either variable.

Importantly, the reported findings are observations from cross-sectional data and inferences regarding causality or mechanisms of action cannot be made. The interpretations provided are speculative and require further research to evaluate directionality and mechanistic explanations. The relationship between functional connectivity, cognitive performance, and xanthophyll carotenoids is not well understood, but the present study addresses that gap in knowledge by providing insight into the nature of influence these factors have in the aging brain. In all, the reported observations demonstrate converging evidence that xanthophyll carotenoids moderate relationships between network connectivity and facets of intelligence within the aging brain. Consistently, xanthophylls interact most significantly with low global efficiency and high local efficiency regardless of ICN, providing evidence that xanthophyll carotenoids contribute to neural efficiency in the aging brain.

2.5.4 Do individual xanthophyll carotenoids influence relationships between white matter microstructure and facets of intelligence?

Yes, in this population of healthy, older adults lutein moderated independent relationships between both AD and RD of global white matter and crystallized or general intelligence. Lutein also moderated the relationship between AD of global white matter and immediate memory. Further, independent xanthophyll status moderated relationships between

the microstructure of many white matter tracts and crystallized intelligence, general intelligence, and/or immediate memory.

First, to determine relationships between white matter integrity and facets of intelligence linear regression models were performed with measures in each of several white matter tracts (IV; Table 2.1), correlated facets of intelligence (DVs; crystallized intelligence, general intelligence, immediate memory), and five covariates (age, BMI, education, income, sex). Models revealed significant relationships between white matter microstructure and crystallized intelligence, general intelligence, and immediate memory (Table 2.14). Then, significant regression models were followed by a series of moderation analyses repeated with each individual xanthophyll carotenoid as a moderator (cryptoxanthin, lutein, zeaxanthin). All reported moderations remained significant after correcting for multiple comparisons.

This study was largely motivated by work published by the Hammond group that related serum xanthophyll levels to better white matter integrity in the uncinate fasciculus, cingulum, superior and posterior corona radiata, posterior thalamic radiation, and corticospinal tract (Mewborn et. al., 2018). To my knowledge, that is the first study to investigate relationships between xanthophyll carotenoids and white matter microstructure in healthy, older adults. The present study sought to expand upon Mewborn et. al. (2018) in three ways: (1) by exploring serum lutein and zeaxanthin status independently, (2) by expanding the white matter regions of interest, and (3) by including cognitive performance as the outcome and BMI, age, income, and sex as covariates. Importantly, these changes shifted the goal from identifying relationships between serum xanthophyll status and white matter integrity (Mewborn et. al., 2018) to the goal of the present study, which was to characterize the nature of relationships between independent

xanthophyll carotenoids, white matter microstructure, and facets of intelligence. The following discussion will focus primarily on overlap between these studies.

The present study evaluated the cingulum as two ROIs: the cingulum – cingulate tract and the cingulum – hippocampus tract. While integrity of the cingulum – cingulate tract did not interact with xanthophyll carotenoids (see Appendix A, Table A.3b), integrity of the cingulum – hippocampus tract significantly interacted with xanthophylls in multiple moderation analyses. Zeaxanthin status moderated the relationships between FA (Figure 2.45) and RD (Figure 2.46) in the cingulum – hippocampus tract and immediate memory, and lutein moderated the relationship between RD in the cingulum – hippocampus tract and immediate memory (Figure 2.48). Interactions were most significant when FA was high and when RD was low. These findings are supported by Mewborn et. al. (2018), which reported that serum xanthophyll level positively correlated with FA and negatively correlated with RD in the cingulum. When considered together, these observations suggest that lutein and zeaxanthin influence the relationship between neural integrity and cognitive performance, particularly in tracts vulnerable to aging.

We also observed associations with xanthophylls and AD in the cingulum – hippocampus tract and observed associations with integrity in the genu of the corpus callosum as well. In this population of healthy, older adults zeaxanthin status moderated the relationship between AD in the cingulum – hippocampus tract and crystallized intelligence (Figure 2.44) and lutein status moderated the relationship between AD in the cingulum – hippocampus tract and immediate memory (Figure 2.47). When considering the genu, cryptoxanthin (Figure 2.18), lutein (Figure 2.19), and zeaxanthin (Figure 2.20) each moderated the relationship between AD and general intelligence. Zeaxanthin also moderated the relationship between AD and immediate memory (Figure 2.21) in this region. An exploratory finding from the literature implicated a negative

correlation between AD and serum xanthophyll status and found no relationship between genu integrity and serum xanthophylls (Mewborn et. al., 2018). Since the moderation framework captures interactions between xanthophyll status and white matter integrity, it is possible that xanthophyll status and AD are not correlated in the same way that xanthophyll status is with FA and RD. Instead, the two could be influencing cognitive performance by a similar mechanism as opposed to influencing one another directly. However, further investigation is necessary to better understand the nuances of this relationship.

In the corticospinal tract, zeaxanthin moderated relationships between AD and crystallized intelligence (Figure 2.29), general intelligence (Figure 2.30), and immediate memory (Figure 2.32). Lutein moderated the relationship between AD and immediate memory as well (Figure 2.31). Under all conditions, the interaction was most significant when AD was low. Supporting evidence indicates a negative correlation between serum xanthophylls and AD in the corticospinal tract (Mewborn et. al., 2018). Although the relationship between AD and aging is unclear (Burzynska et. al., 2010; Vernooj et. al., 2008), these observations provide converging evidence that xanthophyll status influences cognitive performance across facets of intelligence by interacting with AD in the corticospinal tract. Additionally, cryptoxanthin moderated the relationships between FA (Figure 2.27) and RD (Figure 2.28) in the corticospinal tract and crystallized intelligence. Even though correlations between xanthophyll status and FA or RD in this tract were not detected previously, this discrepancy in findings could result from Mewborn et. al. (2018) only taking lutein and zeaxanthin into account. Since the present study did not detect interactions with lutein or zeaxanthin and FA or RD in this tract, it is possible that cryptoxanthin preferentially interacts with those measures of integrity over AD in this ROI.

These observations highlight the nuanced relationships between xanthophyll carotenoids and brain health, emphasizing the need for further research to unravel these complex interactions.

Mewborn et. al. (2018) also detected correlations between serum xanthophyll status and integrity within the superior and posterior corona radiata (FA and RD, FA, respectively), posterior thalamic radiation (RD), and uncinate fasciculus (AD). The present investigation found significant moderations in each of these ROIs, but for almost all different measures of integrity. In the superior corona radiata, lutein status moderated the relationship between RD and crystallized intelligence (Figure 2.36). In both the posterior corona radiata (Figure 2.39) and posterior thalamic radiation (Figure 2.40), lutein moderated the relationship between AD and general intelligence. In the uncinate fasciculus, zeaxanthin moderated the relationships between FA (Figure 2.24) and RD (Figure 2.26) and general intelligence. Cryptoxanthin also moderated the relationship between RD and general intelligence (Figure 2.25).

Despite implicating different measures of integrity, these observations combined with those reported in the literature provide converging evidence that xanthophyll status influences brain health at the microstructural level in regions most susceptible to age-related decline (Brickman et. al., 20123; Kochunov et. al., 2012). Age-related decline in white matter integrity disrupts cortical connections and has been associated with cognitive deficits related to aging such as decreased processing speed, executive function, reasoning ability, and episodic and working memory capacity (Bartzokis, 2004; Bennett and Madden, 2014; Madden et. al., 2012). These results emphasize the importance for xanthophyll carotenoids in neural functioning during brain aging (Lindbergh et. al., 2017; 2019) and provide evidence to motivate controlled designs able to elucidate causality.

Finally, the results of this study imply wide-reaching influence of xanthophyll carotenoids on white matter microstructure in the aging brain. Fractional anisotropy is considered a robust measure of age-related changes in brain structure (Guttmann et. al., 1998), and we observed interactions between zeaxanthin and FA in the superior cerebellar peduncle to predict general intelligence (Figure 2.61), and between lutein and FA in the middle cerebellar peduncle to predict crystallized intelligence (Figure 2.58). In the cerebellar peduncles, though, FA is only modestly related to age (Cox et. al., 2016; Zahr, Rohlfing, Pfefferbaum, & Sullivan). This observation suggests an influence of xanthophyll status on neural integrity independent of aging effects. As mentioned previously, AD exhibits a complex relationship with aging (Barrick et. al., 2010) making it difficult to interpret moderated relationships between AD and facets of intelligence. This study detected interactions between xanthophylls and AD in anterior regions (e.g., anterior corona radiata), medial regions (e.g., superior longitudinal fasciculus), and posterior regions (e.g. cerebellar peduncles) and all three facets of intelligence analyzed, indicating a widespread role for xanthophyll carotenoids in neural integrity. Although complex, this collection of observations provides a significant contribution to the field of nutritional cognitive neuroscience because it informs the nature of influence that xanthophyll carotenoids have on brain health.

2.6 *Strengths, Limitations, and Conclusions*

The collection of studies within this chapter contribute to the field of nutritional cognitive neuroscience by providing evidence that individual xanthophylls influence brain health via interactions with cortical structure, network efficiency, and neural integrity. Observations demonstrating an association between xanthophylls, cortical volume, and facets of intelligence

expand on the existing literature demonstrating similar associations (Zamroziewicz et. al., 2016), and observations demonstrating interactions with network efficiency and neural integrity contribute substantially to this undeveloped field of study. Together, observations in this dissertation provide converging evidence that individual xanthophyll carotenoids moderate relationships between multiple measures of brain health and cognitive performance, further supporting their potential as a target in addressing age-related changes in the brain.

Importantly, these studies are limited by the observational and cross-sectional nature of the data and do not allow inferences to be drawn regarding causality, directionality, or mechanisms of action. Additionally, the participants in these studies were Caucasian and mostly educated, which does not provide a representative sample and therefore limits the generalizability of these observations to other populations. Finally, genetic data and prescription records were not available for participants, which limit our understanding of these results since these factors could also influence the variables and relationships considered within these studies. Future studies that address these limitations will be important to understand how xanthophyll carotenoids influence brain health during aging.

This collection of studies sought to fill some of the gaps of knowledge that exist within the field of nutritional cognitive neuroscience by characterizing relationships between xanthophyll carotenoids and different measures of brain health. The data suggest that xanthophyll carotenoids independently moderate relationships between cortical volume, network efficiency, and neural integrity and facets of intelligence in healthy, older adults. The most significant contributions of this are threefold: (1) xanthophyll carotenoids do not influence brain health uniformly, but instead act in a nuanced way independently from one another, (2) there exists converging evidence across individual xanthophylls, facets of intelligence, and measures

of brain health supporting a role for xanthophyll carotenoids in brain aging, and (3) the nature of xanthophyll influence suggests a possible benefit to considering volume, efficiency, or integrity in the brain when developing intervention studies to isolate potential effects, as in a precision-medicine approach.

2.7 *Figures and Tables*

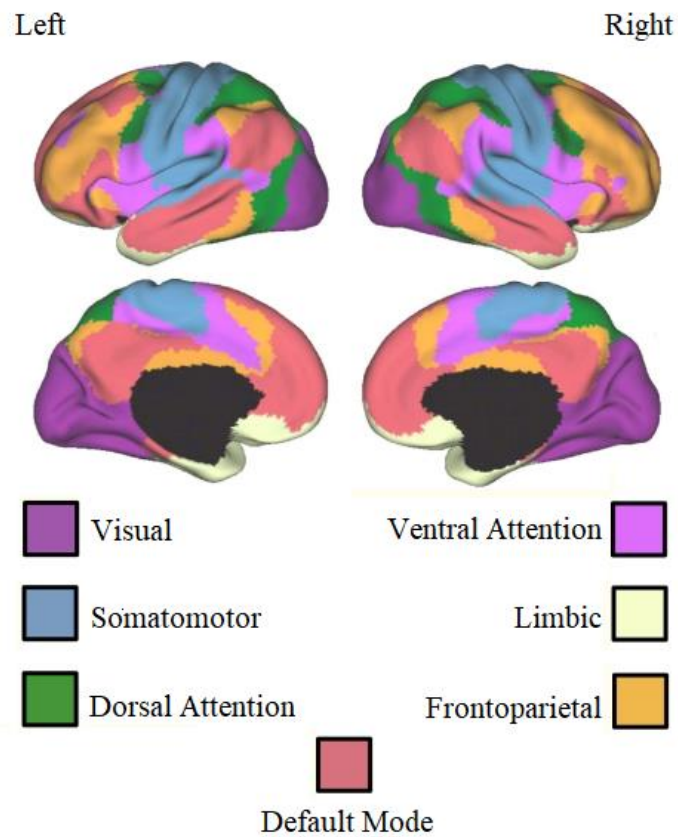


Figure 2.1 | Intrinsic connectivity networks for which graph theory metrics were computed. Adapted from Yeo et. al., 2011.

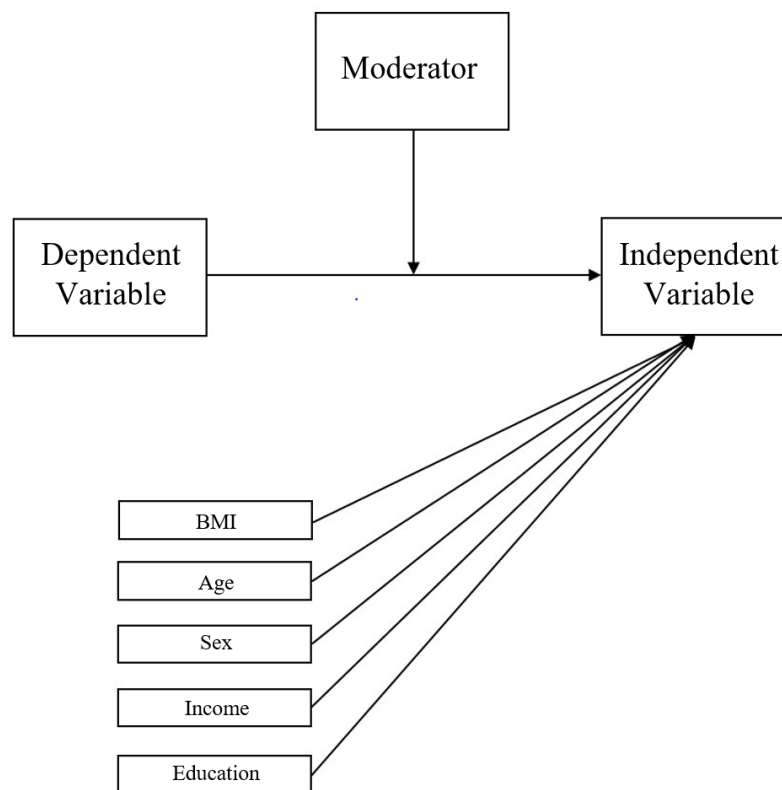


Figure 2.2 | Conceptual framework for moderation analyses including multiple covariates.

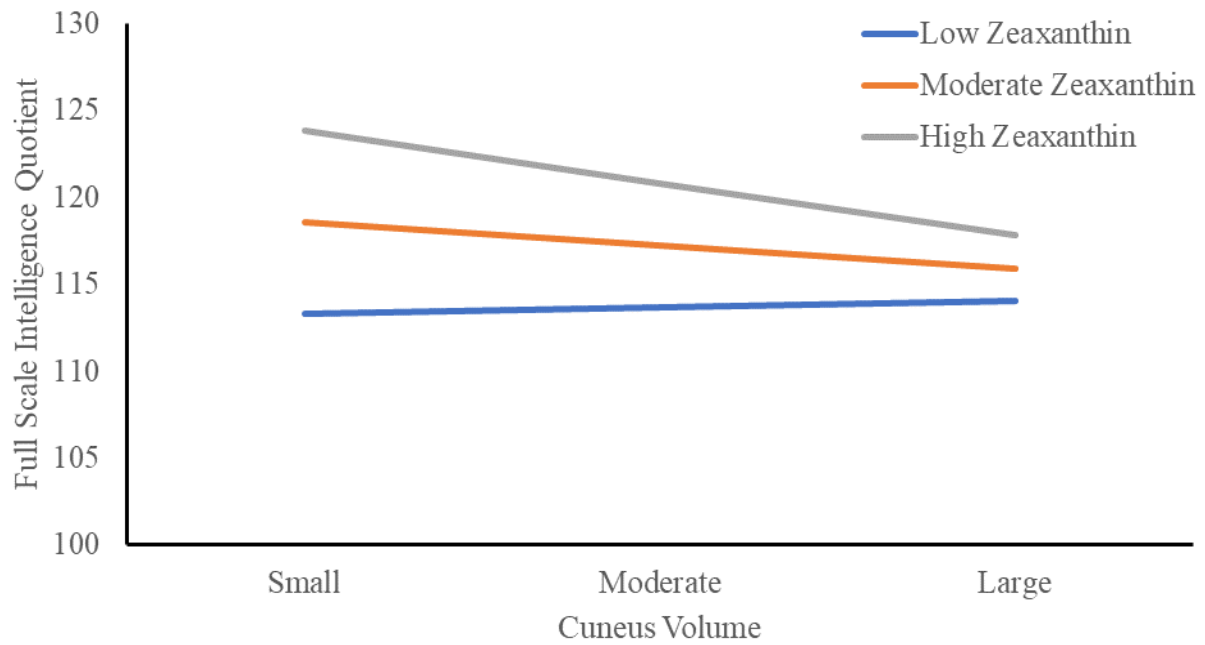


Figure 2.3 | Zeaxanthin status conditionally moderates the relationship between cuneus volume and general intelligence. When cuneus volume is small or moderate, zeaxanthin status significantly influences general intelligence score. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

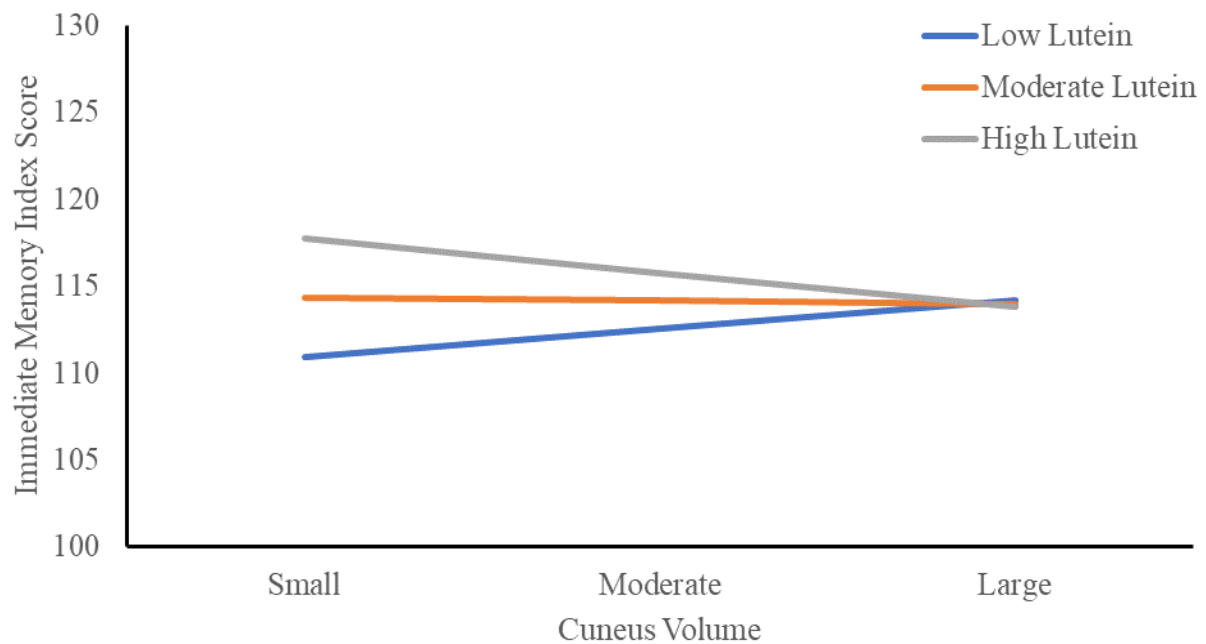


Figure 2.4 | Lutein status conditionally moderates the relationship between cuneus volume and immediate memory. When cuneus volume is small, lutein status significantly influences immediate memory score. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

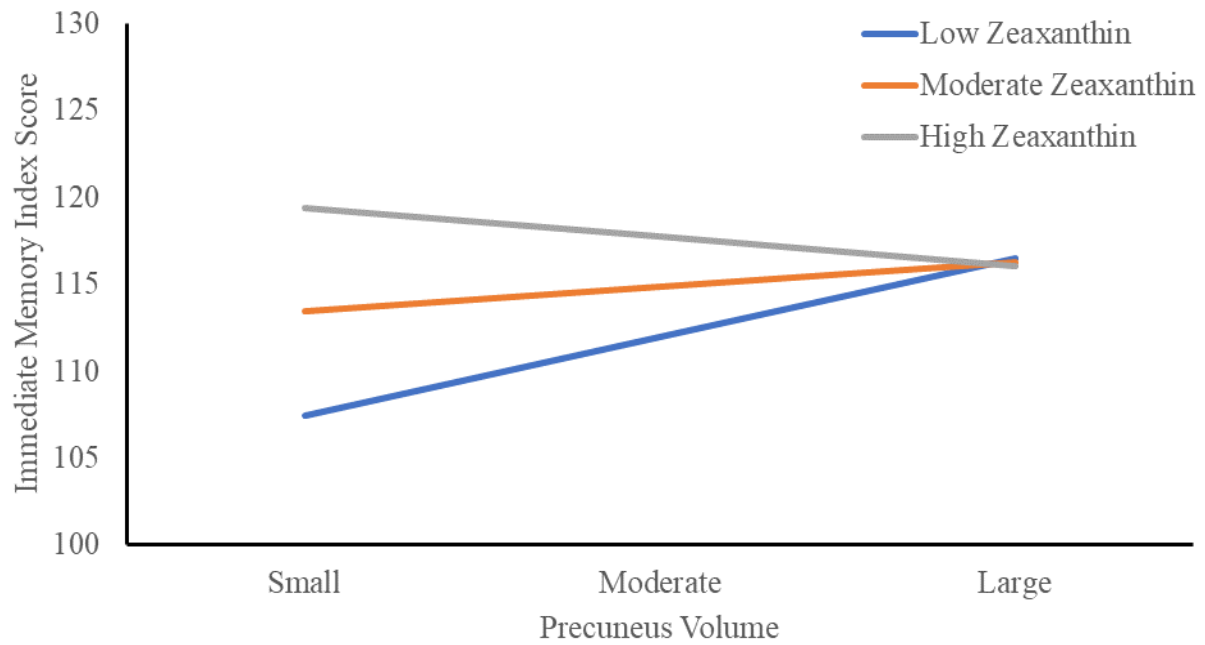


Figure 2.5 | Zeaxanthin status conditionally moderates the relationship between precuneus volume and immediate memory. When precuneus volume is small or moderate, zeaxanthin status significantly influences immediate memory score. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

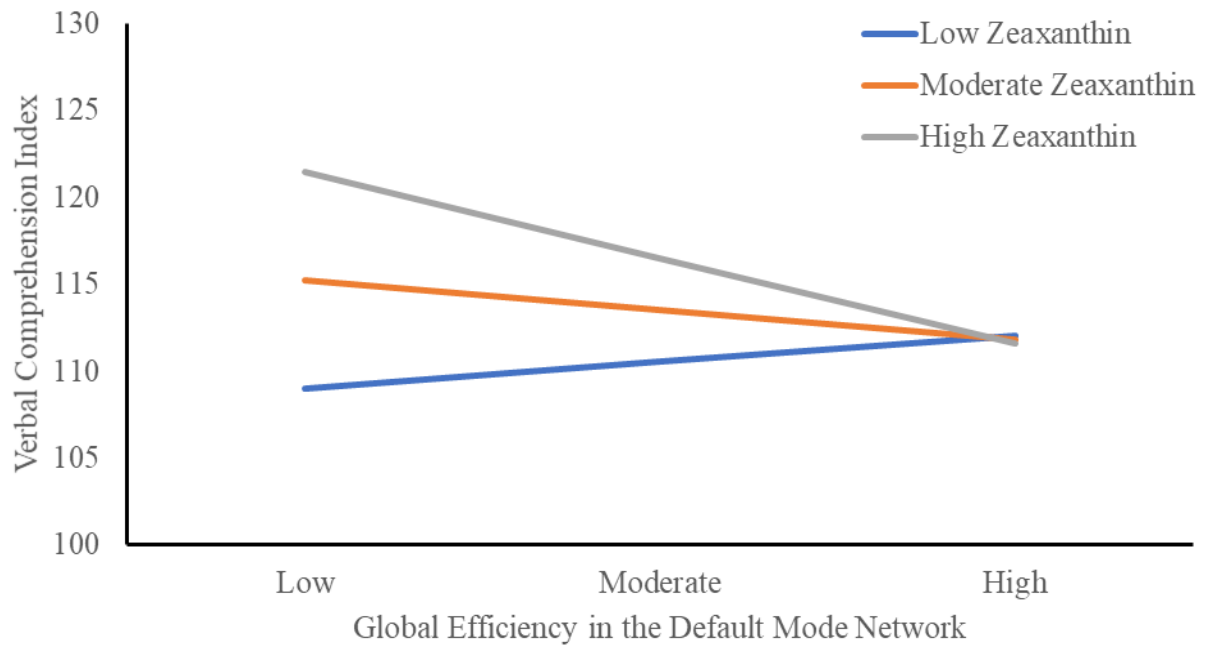


Figure 2.6 | Zeaxanthin status conditionally moderates the relationship between global efficiency in the DMN and crystallized intelligence. When global efficiency is low or moderate, zeaxanthin status significantly influences crystallized intelligence score. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

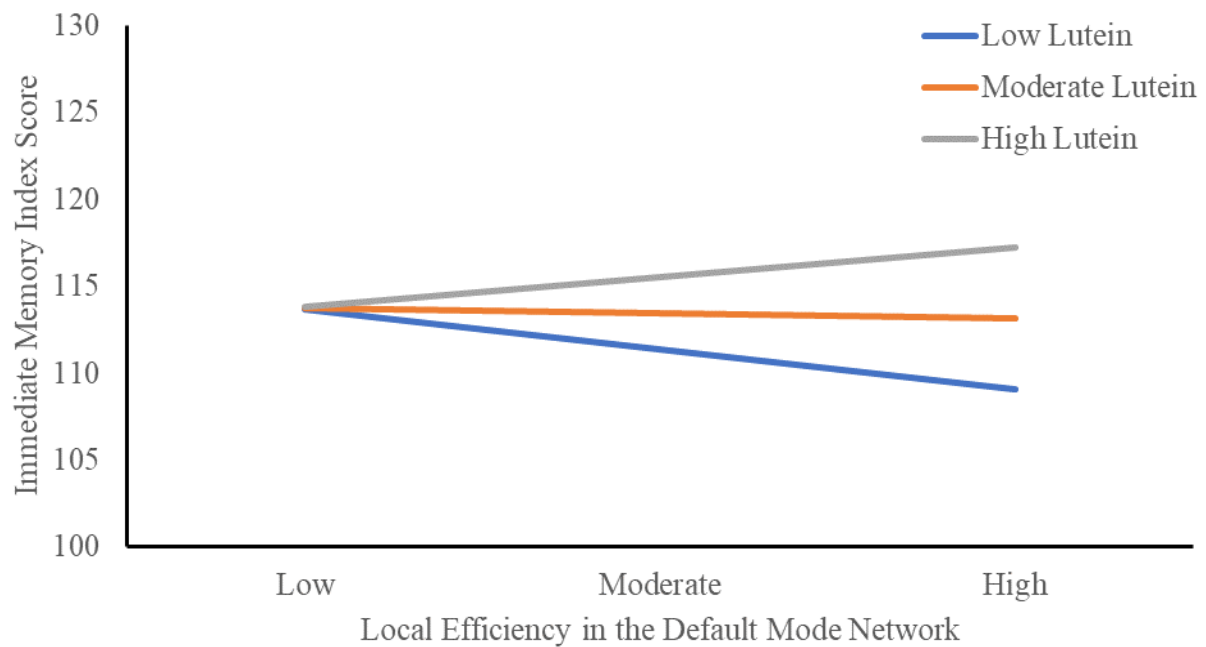


Figure 2.7 | Lutein status conditionally moderates the relationship between local efficiency in the DMN and immediate memory. When local efficiency is high, lutein status significantly influences immediate memory score. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

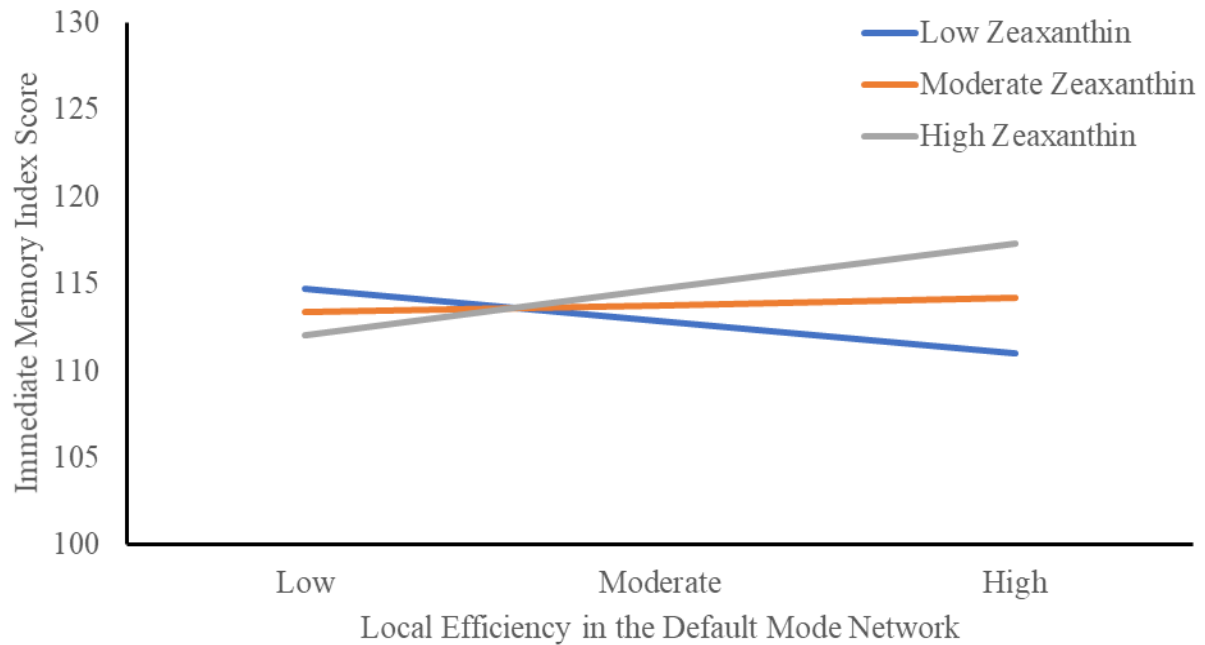


Figure 2.8 | Zeaxanthin status conditionally moderates the relationship between local efficiency in the DMN and immediate memory. When local efficiency is high, zeaxanthin status significantly influences immediate memory score. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

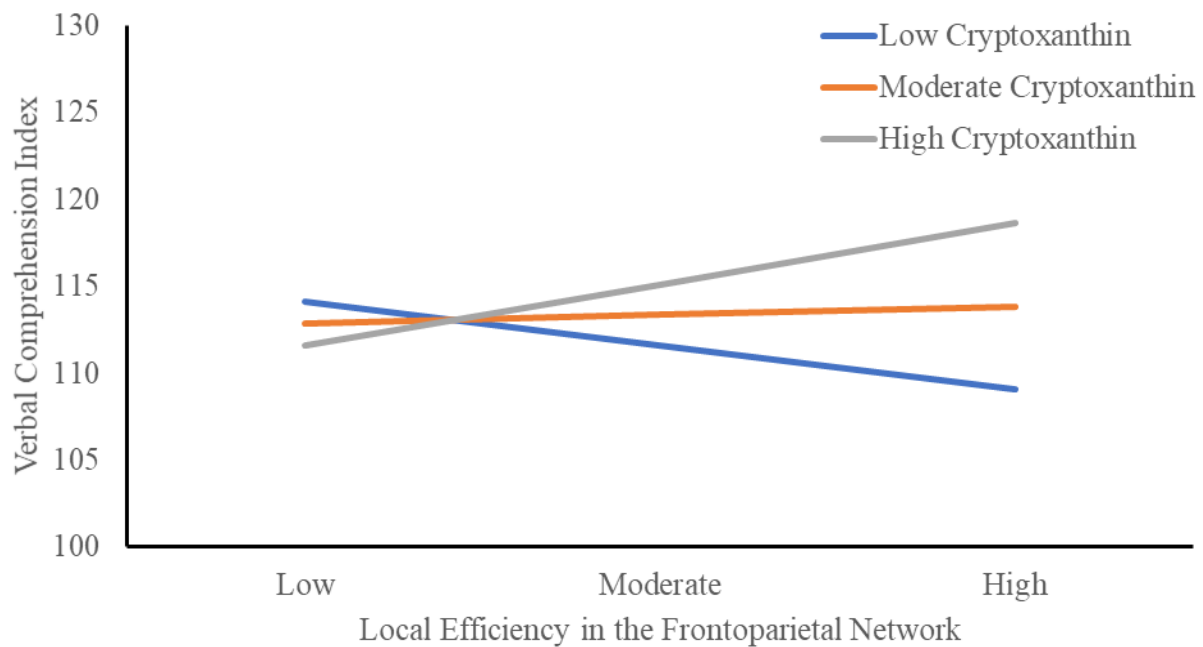


Figure 2.9 | Cryptoxanthin status conditionally moderates the relationship between local efficiency in the FPN and crystallized intelligence. When local efficiency is high, cryptoxanthin status significantly influences crystallized intelligence score. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

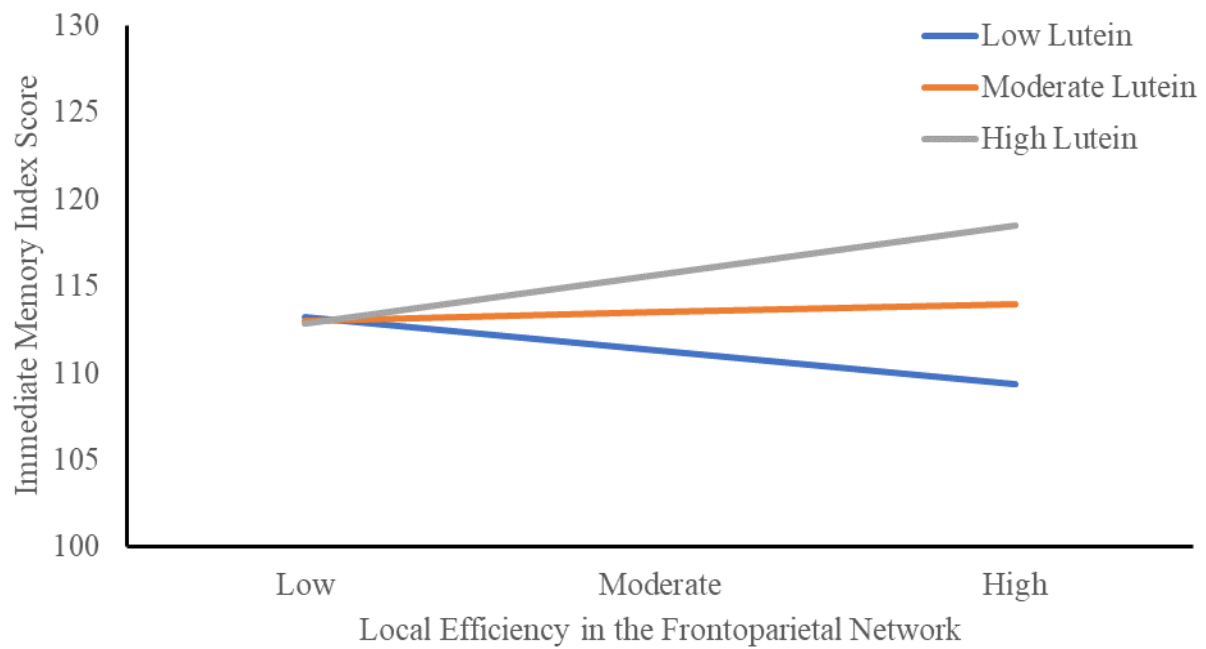


Figure 2.10 | Lutein status conditionally moderates the relationship between local efficiency in the FPN and immediate memory. When local efficiency is high, lutein status significantly influences immediate memory score. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

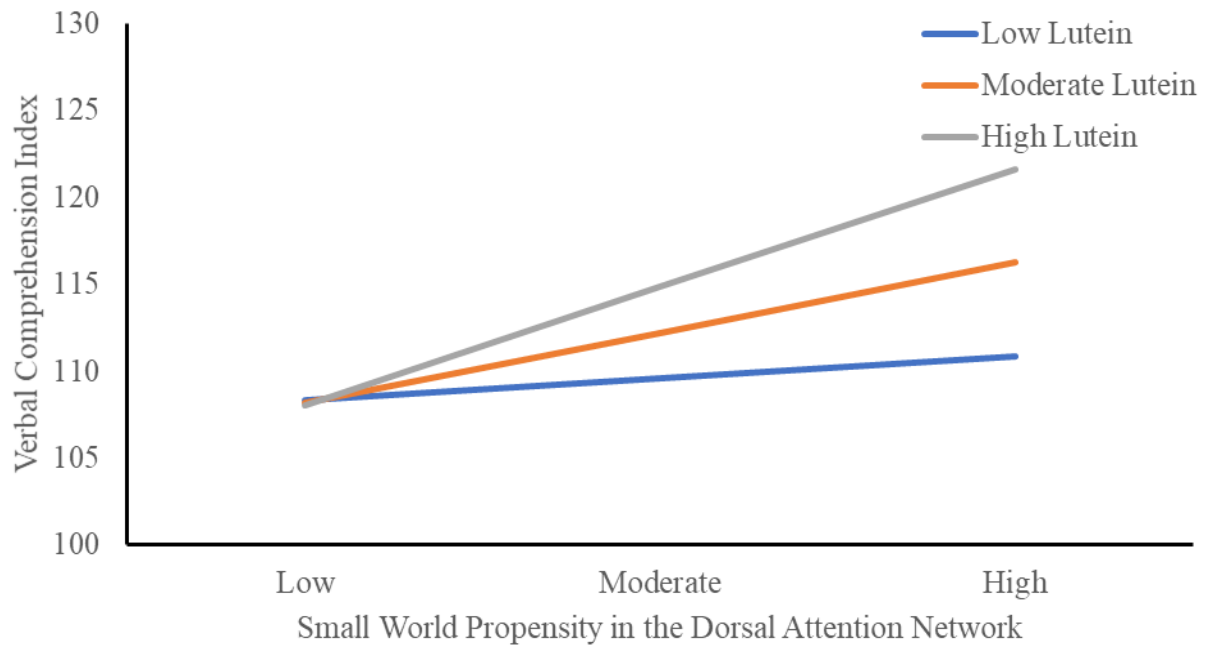


Figure 2.11 | Lutein status conditionally moderates the relationship between small world propensity in the DAN and crystalized intelligence. When small world propensity is high, lutein status significantly influences crystallized intelligence score. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

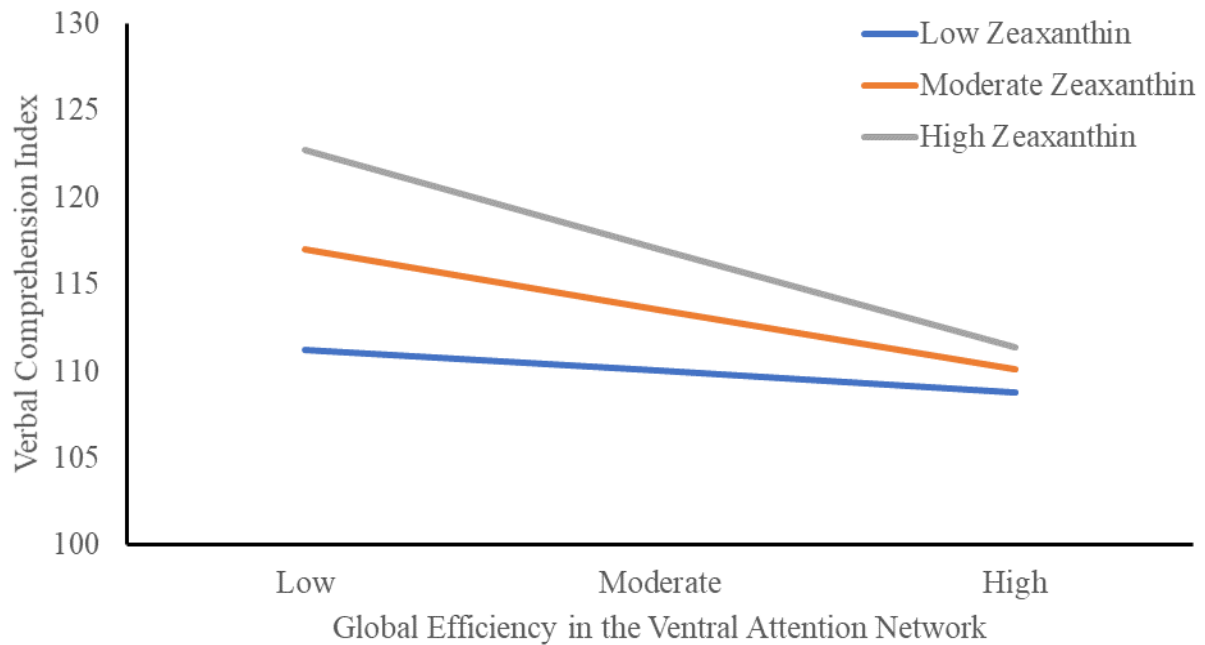


Figure 2.12 | Zeaxanthin status conditionally moderates the relationship between global efficiency in the VAN and crystallized intelligence. When global efficiency is high, zeaxanthin status significantly influences crystallized intelligence score. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

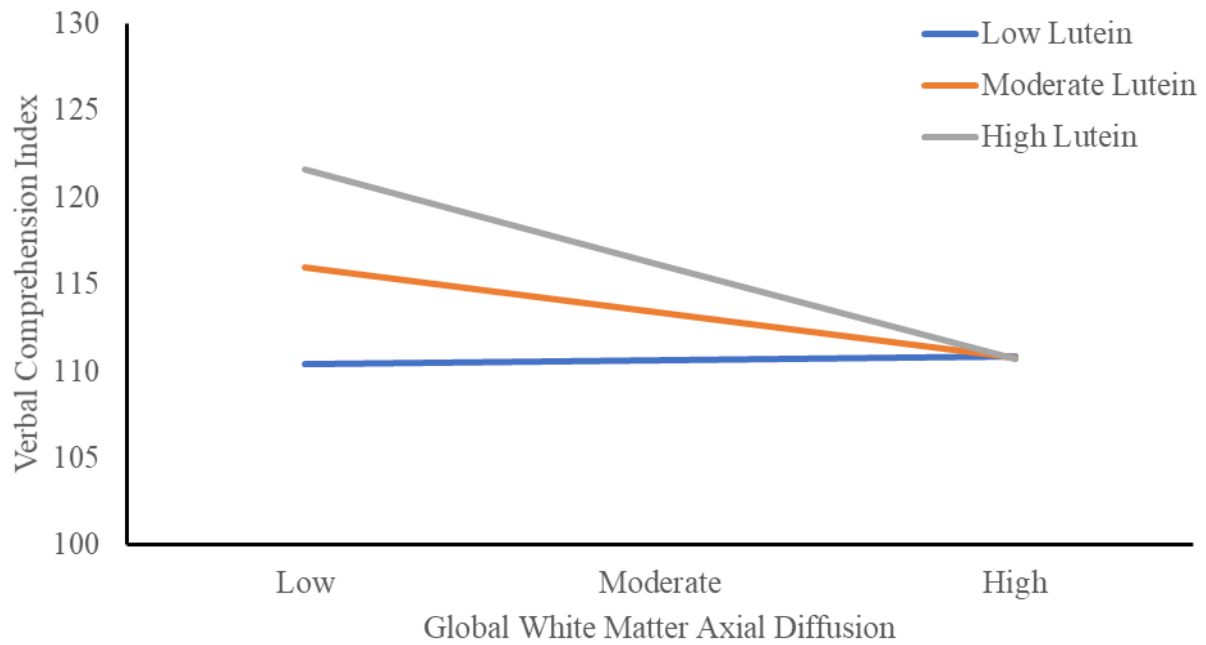


Figure 2.13 | Lutein status conditionally moderates the relationship between global white matter axial diffusion and crystallized intelligence. When local efficiency is low or moderate, lutein status significantly influences crystallized intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

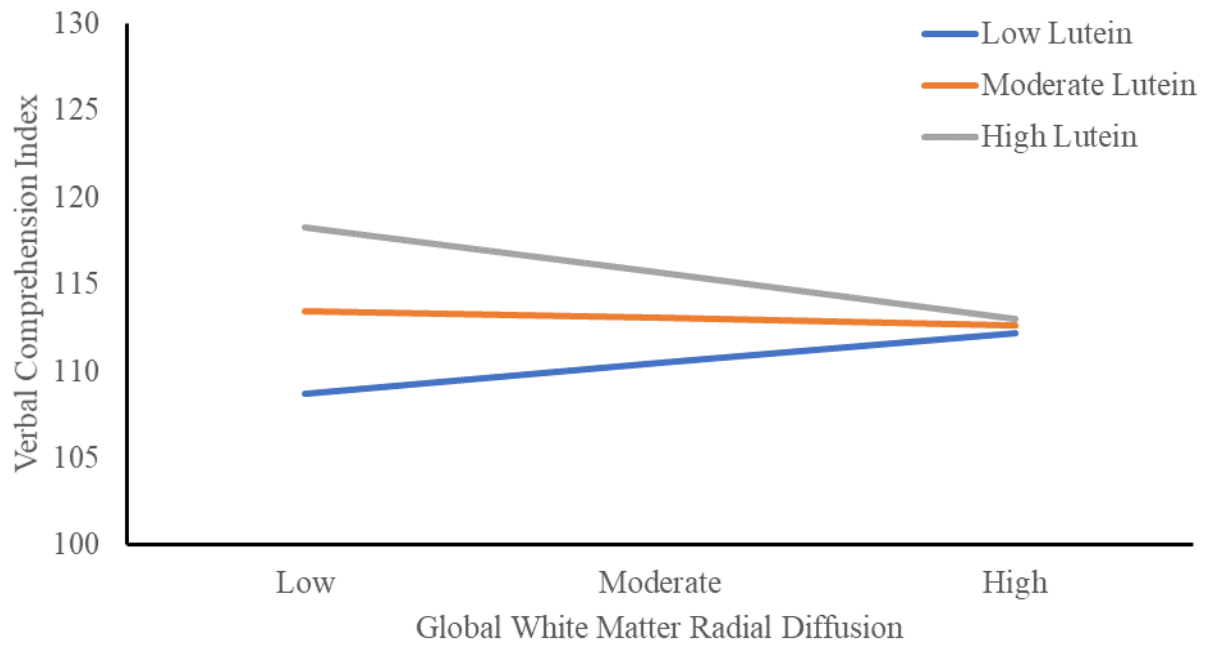


Figure 2.14 | Lutein status conditionally moderates the relationship between global white matter radial diffusion and crystallized intelligence. When RD is low or moderate, lutein status significantly influences crystallized intelligence score. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

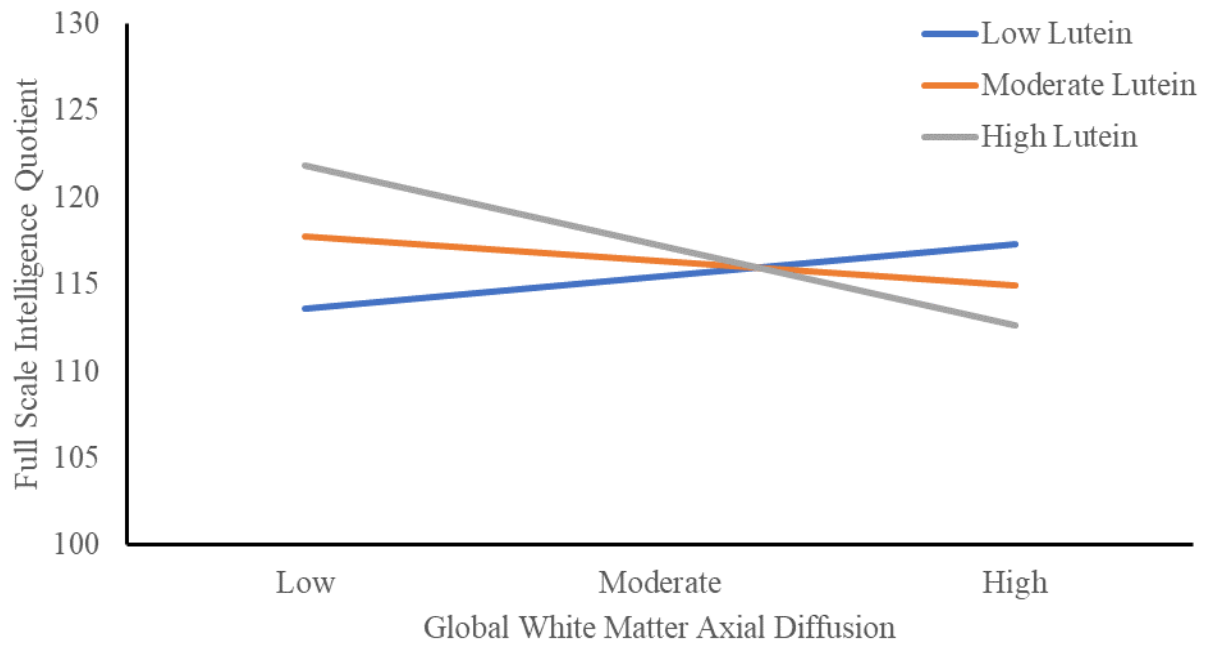


Figure 2.15 | Lutein status conditionally moderates the relationship between global white matter axial diffusion and general intelligence. When AD is low, lutein status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

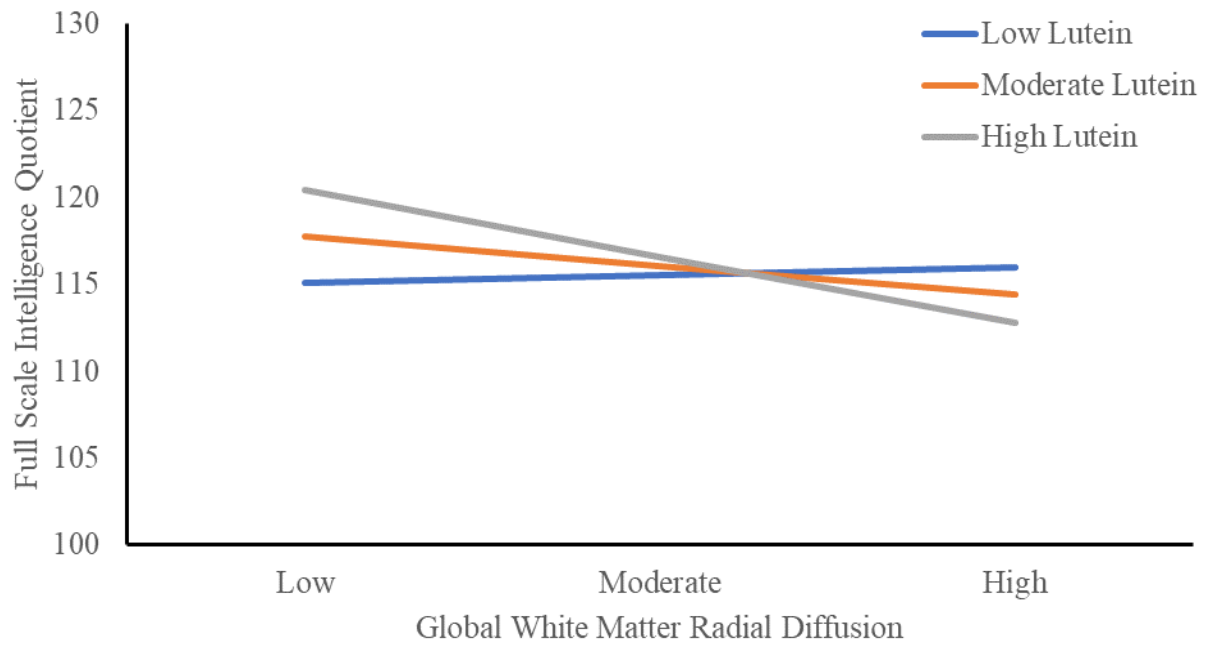


Figure 2.16 | Lutein status conditionally moderates the relationship between global white matter radial diffusion and general intelligence. When RD is low, lutein status significantly influences general intelligence score. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

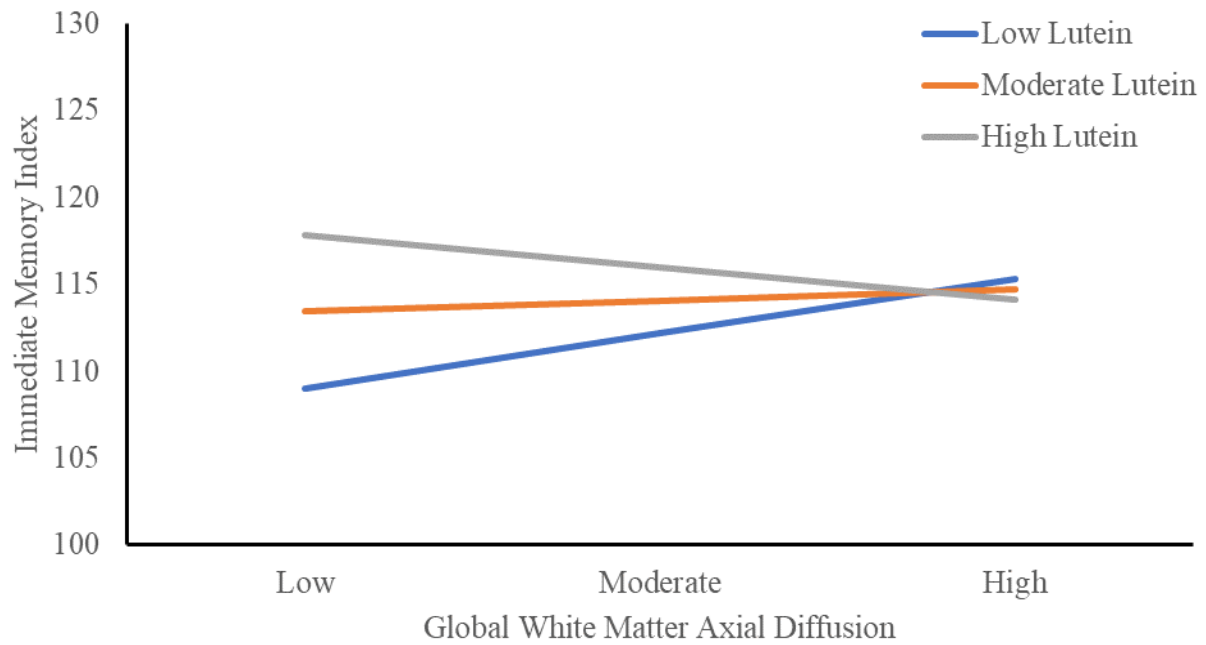


Figure 2.17 | Lutein status conditionally moderates the relationship between global white matter axial diffusion and immediate memory. When AD is low, lutein status significantly influences immediate memory score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

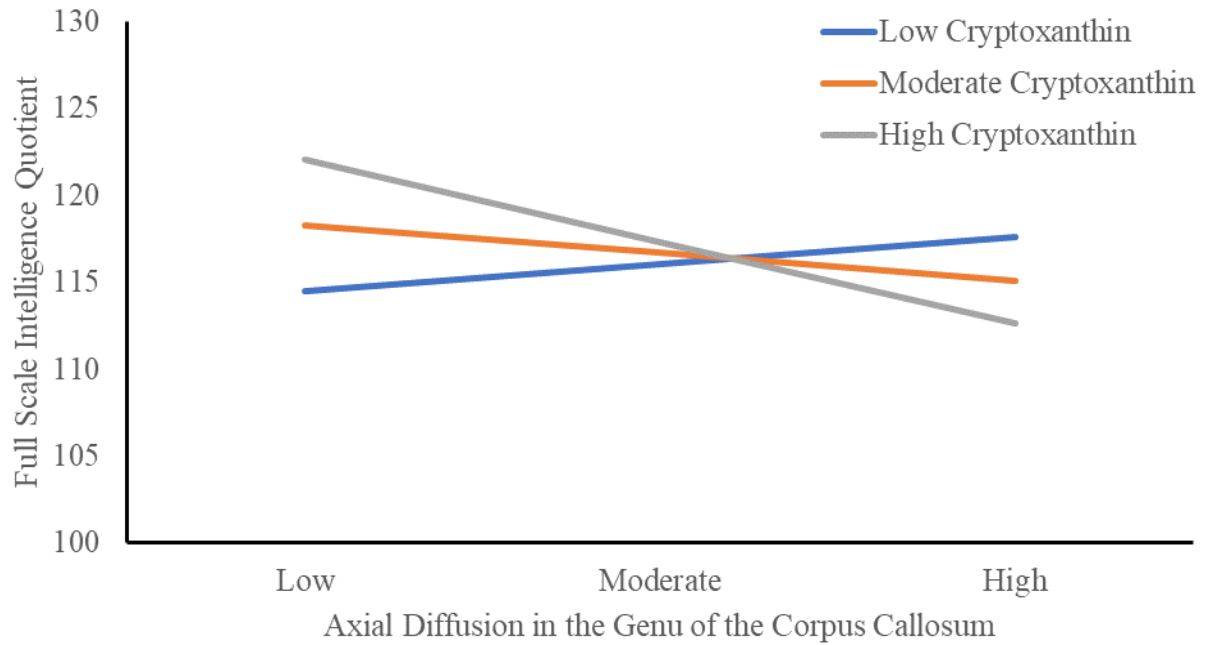


Figure 2.18 | Cryptoxanthin status conditionally moderates the relationship between axial diffusion in the genu of the corpus callosum and general intelligence. When AD is low, cryptoxanthin status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

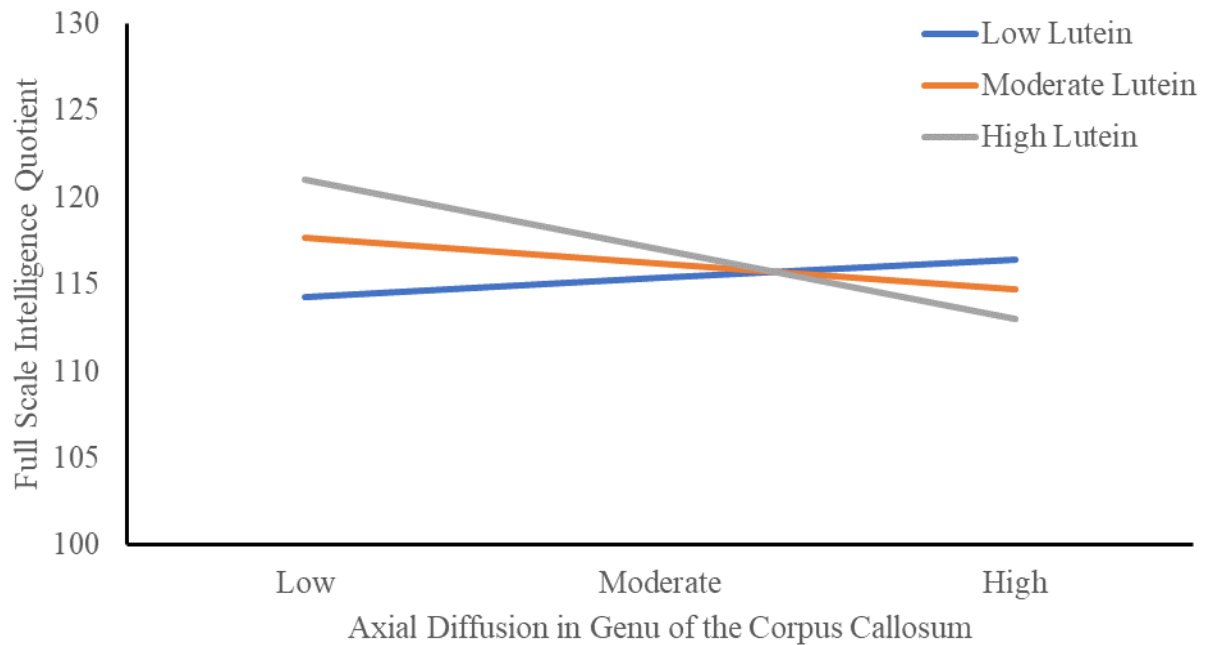


Figure 2.19 | Lutein status conditionally moderates the relationship between axial diffusion in the genu of the corpus callosum and general intelligence. When AD is low, lutein status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

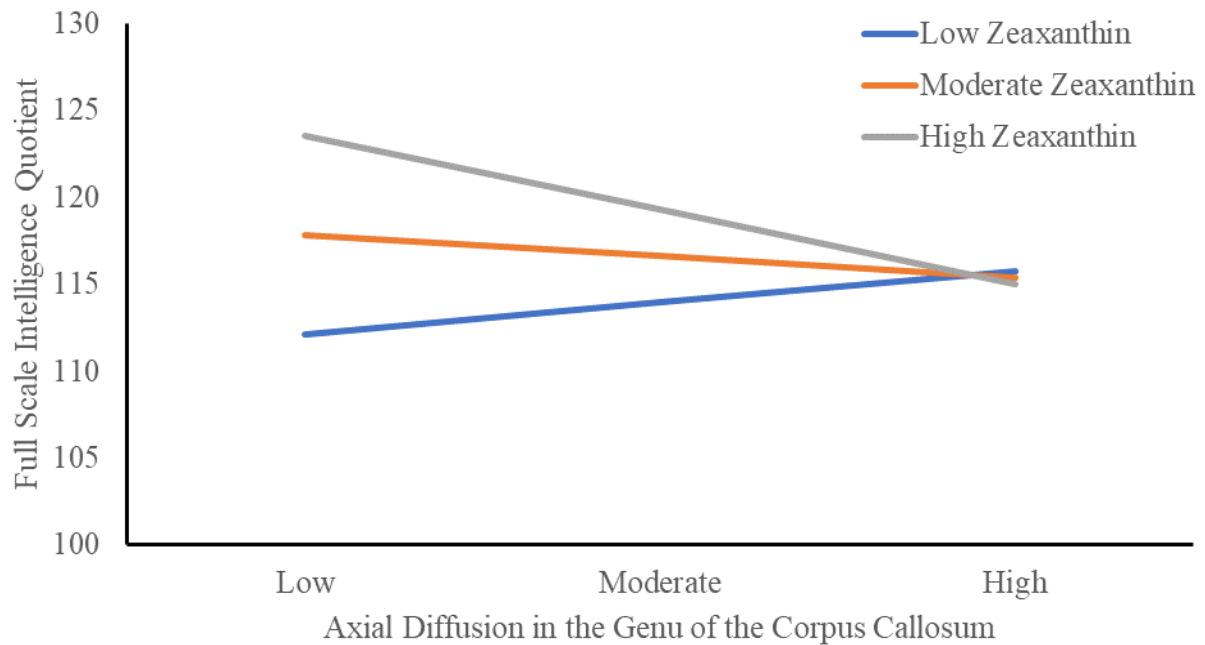


Figure 2.20 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the genu of the corpus callosum and general intelligence. When AD is low or moderate, zeaxanthin status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

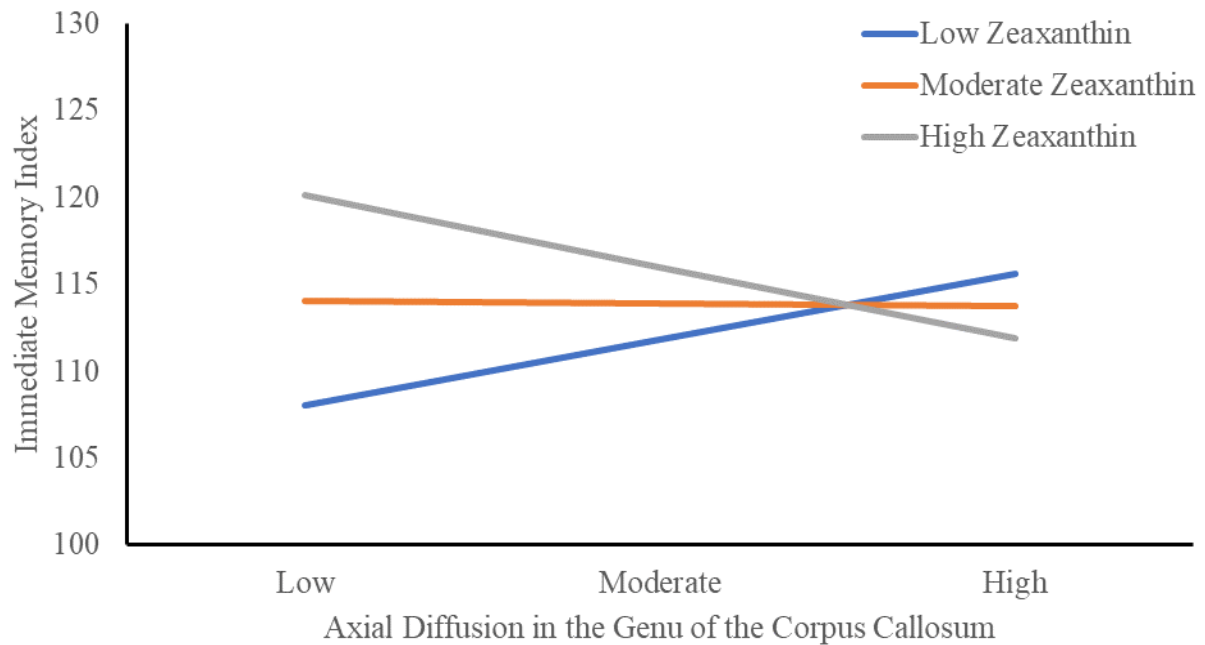


Figure 2.21 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the genu of the corpus callosum and immediate memory. When AD is low or moderate, zeaxanthin status significantly influences immediate memory score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

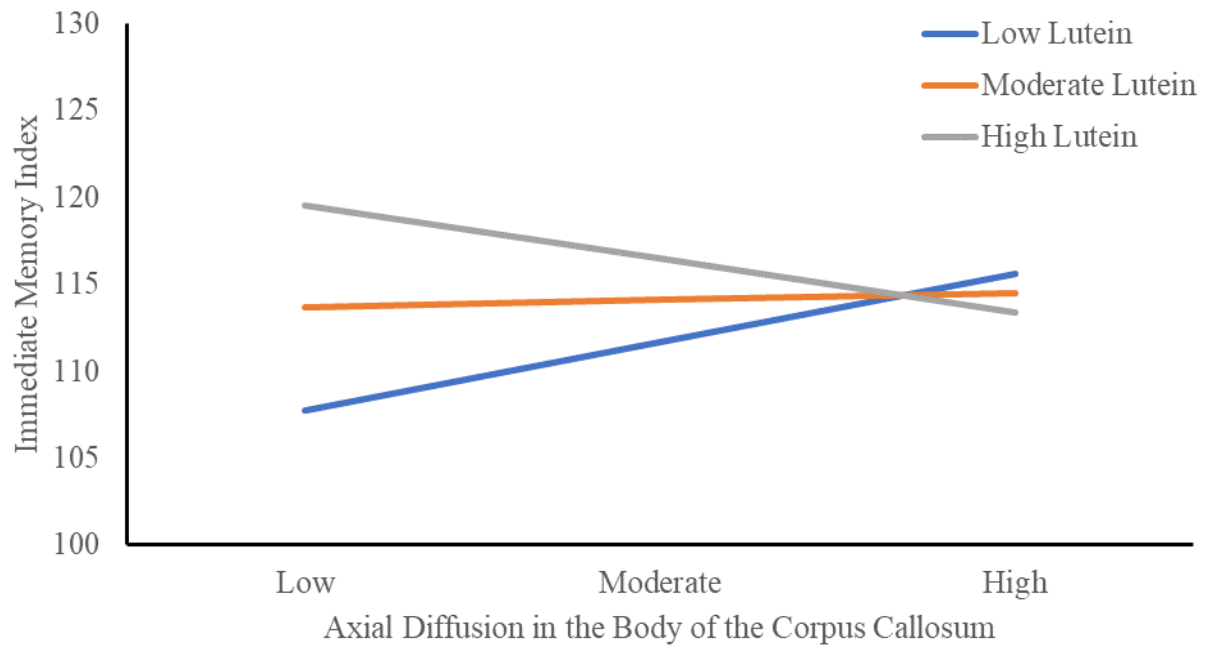


Figure 2.22 | Lutein status conditionally moderates the relationship between axial diffusion in the body of the corpus callosum and immediate memory. When AD low or moderate, lutein status significantly influences immediate memory score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

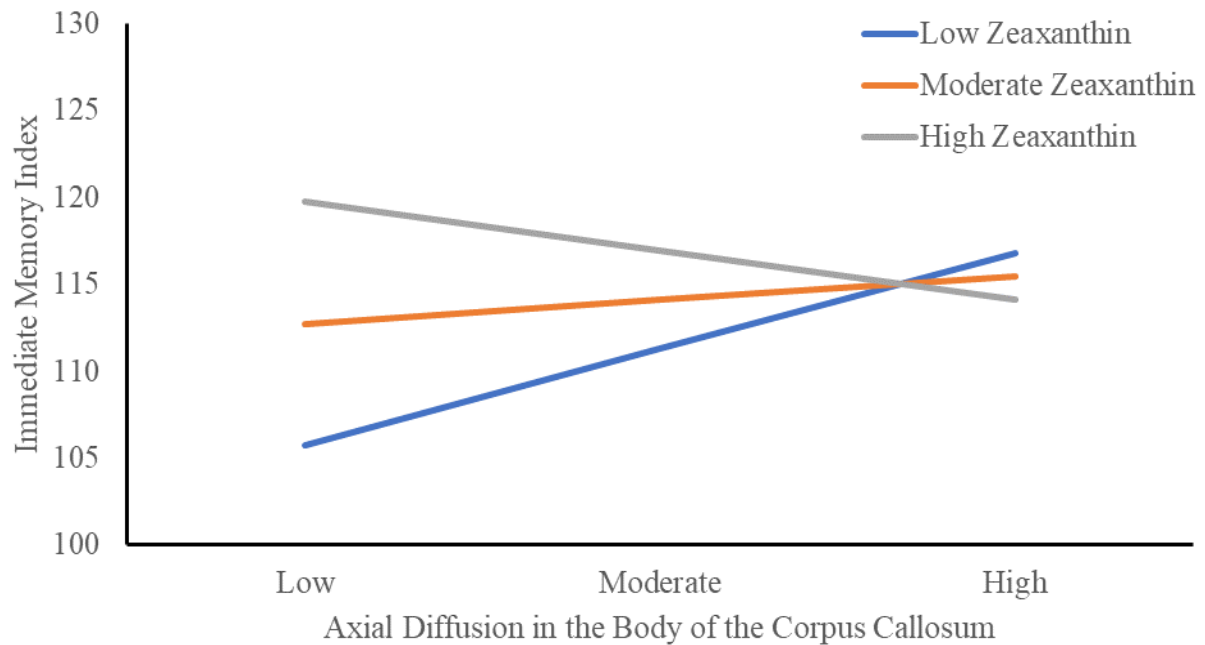


Figure 2.23 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the body of the corpus callosum and immediate memory. When AD is low or moderate, zeaxanthin status significantly influences immediate memory score. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

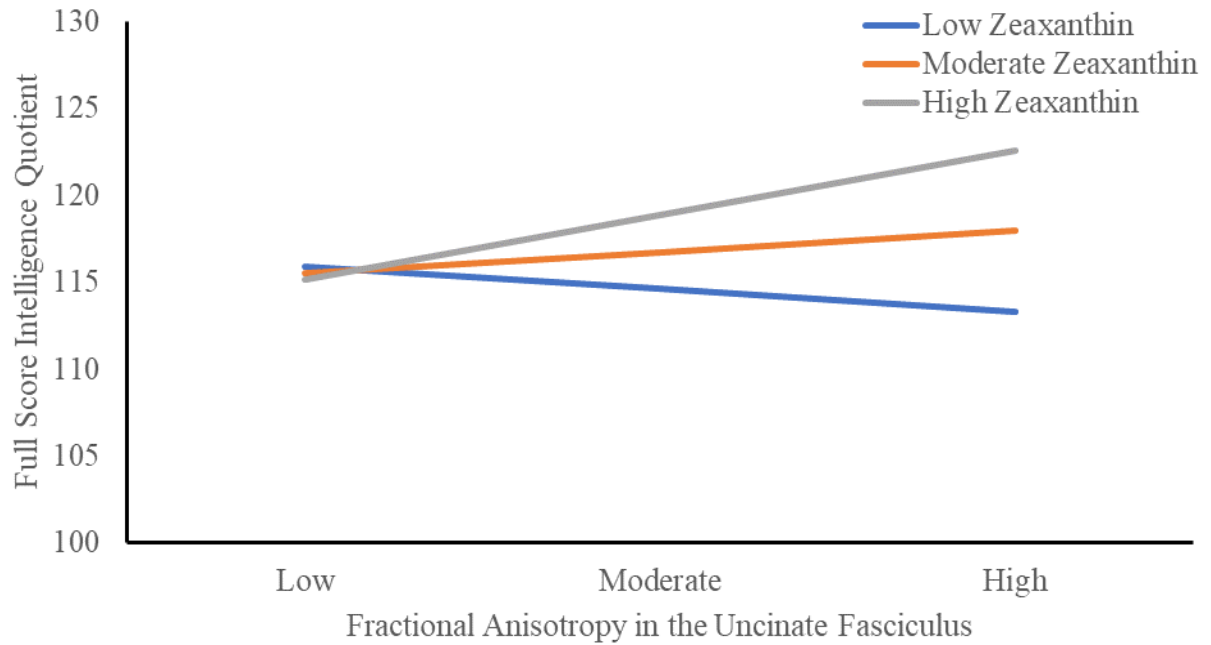


Figure 2.24 | Zeaxanthin status conditionally moderates the relationship between fractional anisotropy in the uncinate fasciculus and general intelligence. When FA is high or moderate, zeaxanthin status significantly influences general intelligence score. Low status and FA are defined as one *SD* below the mean; high status and FA are defined as one *SD* above the mean.

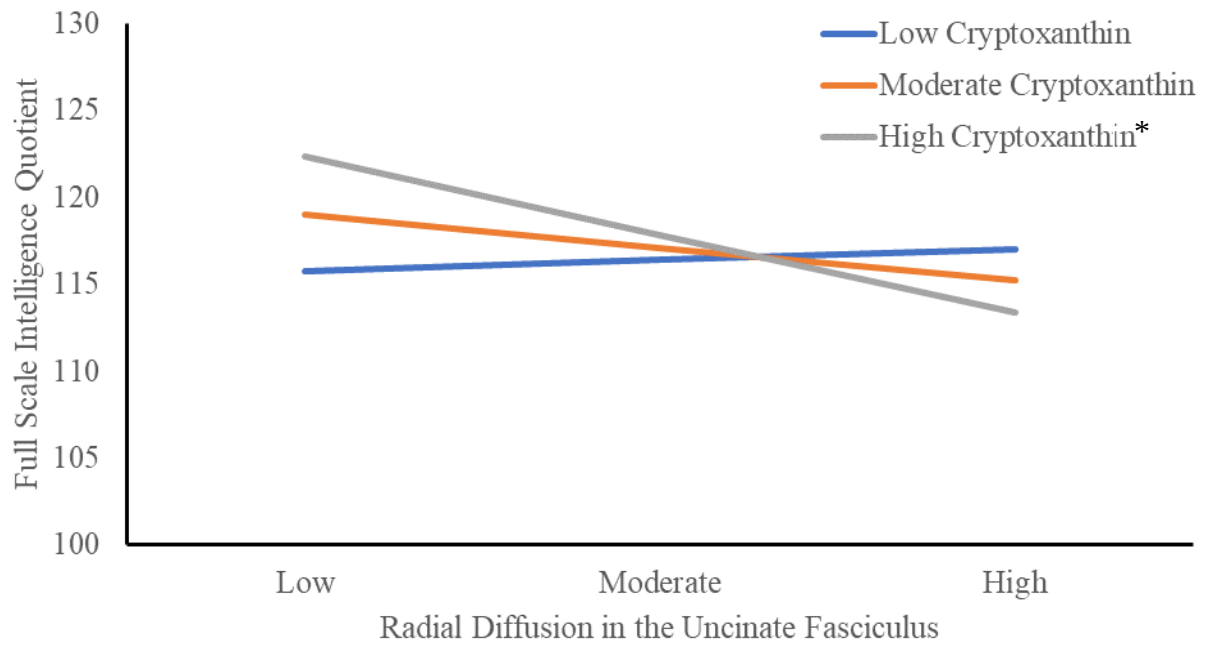


Figure 2.25 | Cryptoxanthin status conditionally moderates the relationship between radial diffusion in the uncinate fasciculus and general intelligence. When cryptoxanthin status is high, it significantly moderates the relationship between RD and general intelligence. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean. $*p < .05$

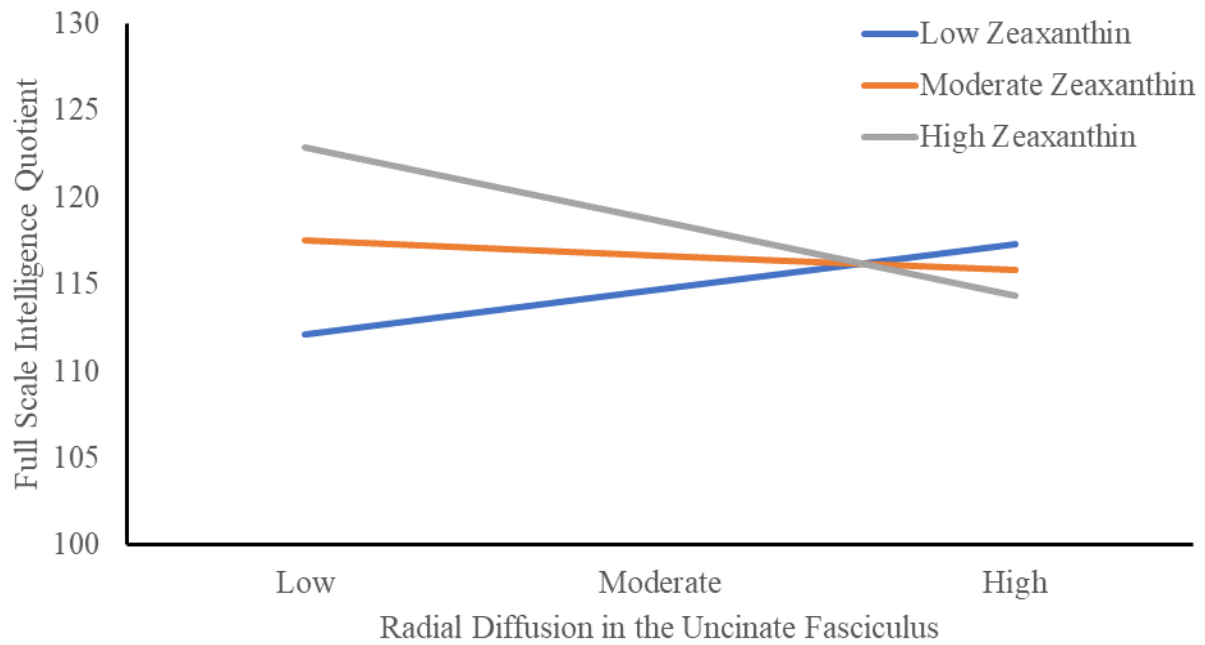


Figure 2.26 | Zeaxanthin status conditionally moderates the relationship between radial diffusion in the uncinate fasciculus and general intelligence. When RD is low, zeaxanthin status significantly influences general intelligence score. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

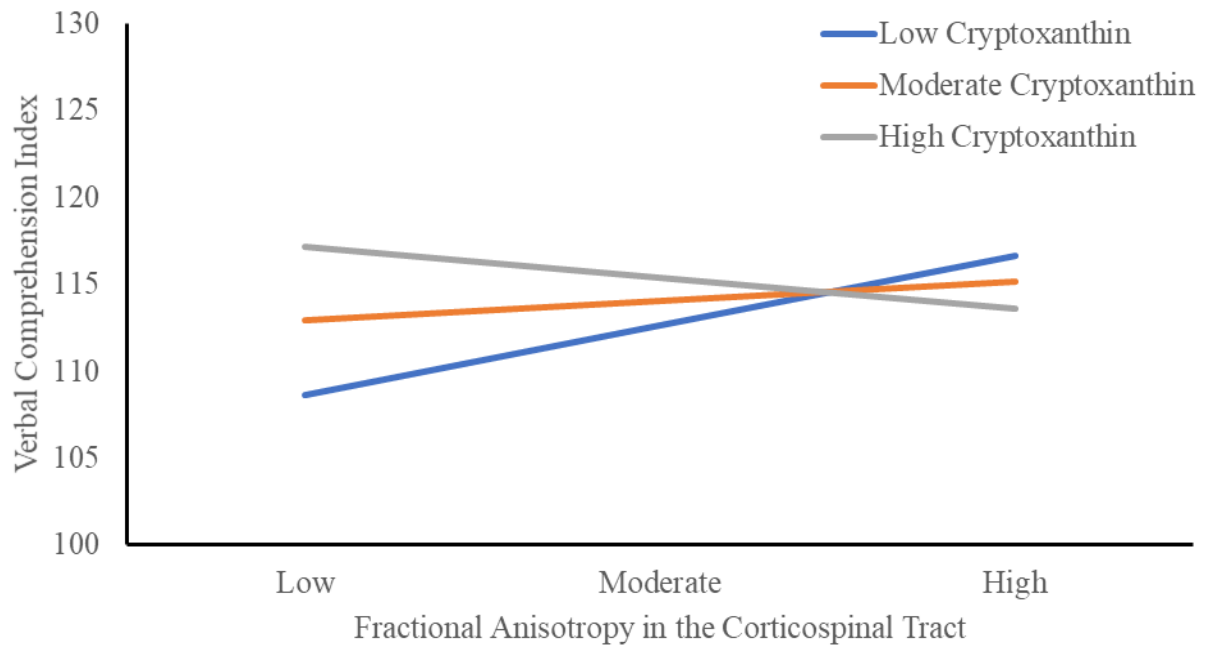


Figure 2.27 | Cryptoxanthin status conditionally moderates the relationship between fractional anisotropy in the corticospinal tract and crystallized intelligence. Low status and FA are defined as one *SD* below the mean; high status and FA are defined as one *SD* above the mean

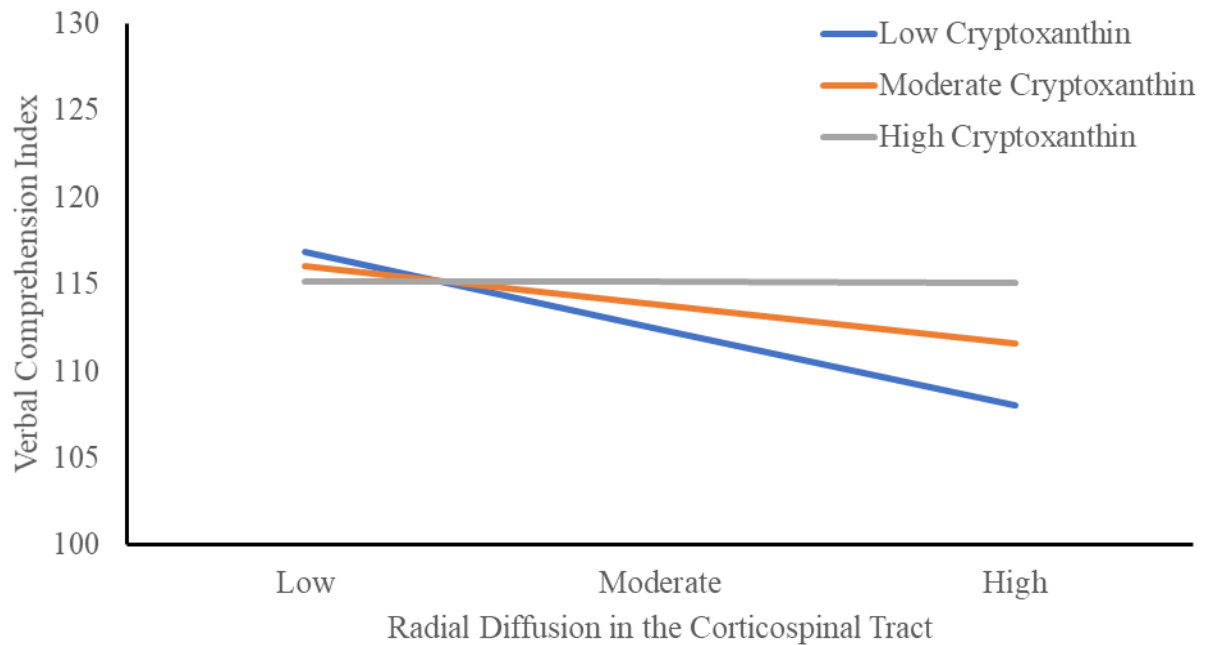


Figure 2.28 | Cryptoxanthin status conditionally moderates the relationship between RD in the corticospinal tract and crystallized intelligence. When RD is high, cryptoxanthin status significantly influences crystallized intelligence score. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean

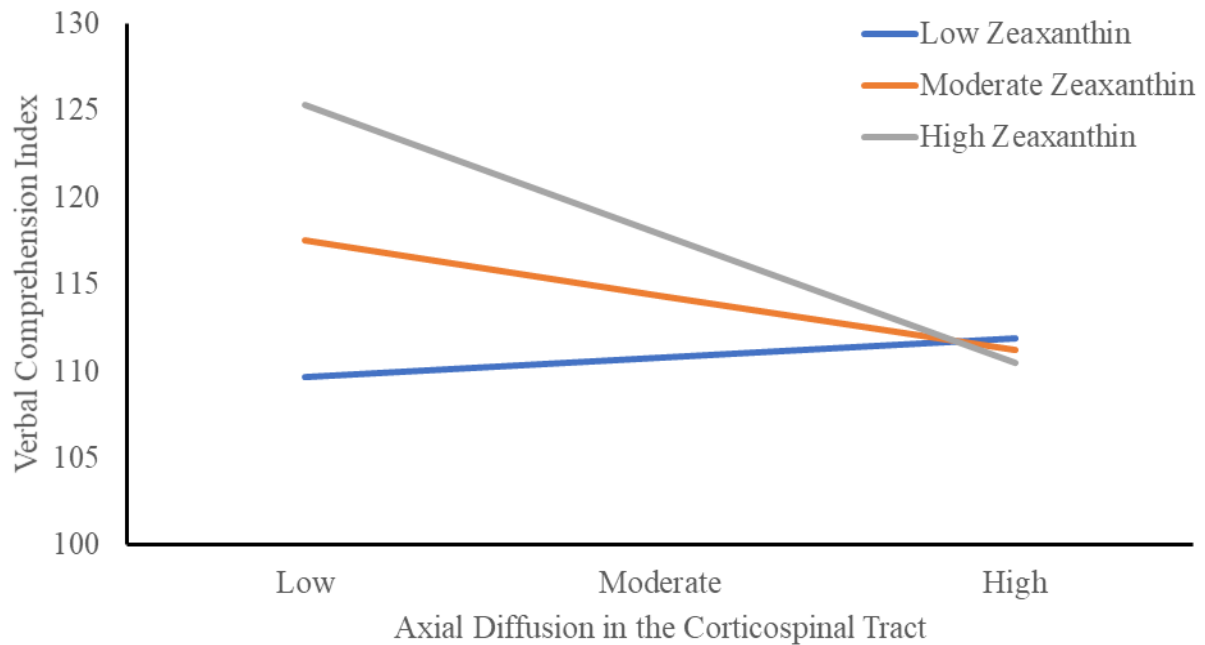


Figure 2.29 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the corticospinal tract and crystallized intelligence. When AD is moderate or high, zeaxanthin status significantly influences crystallized intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean

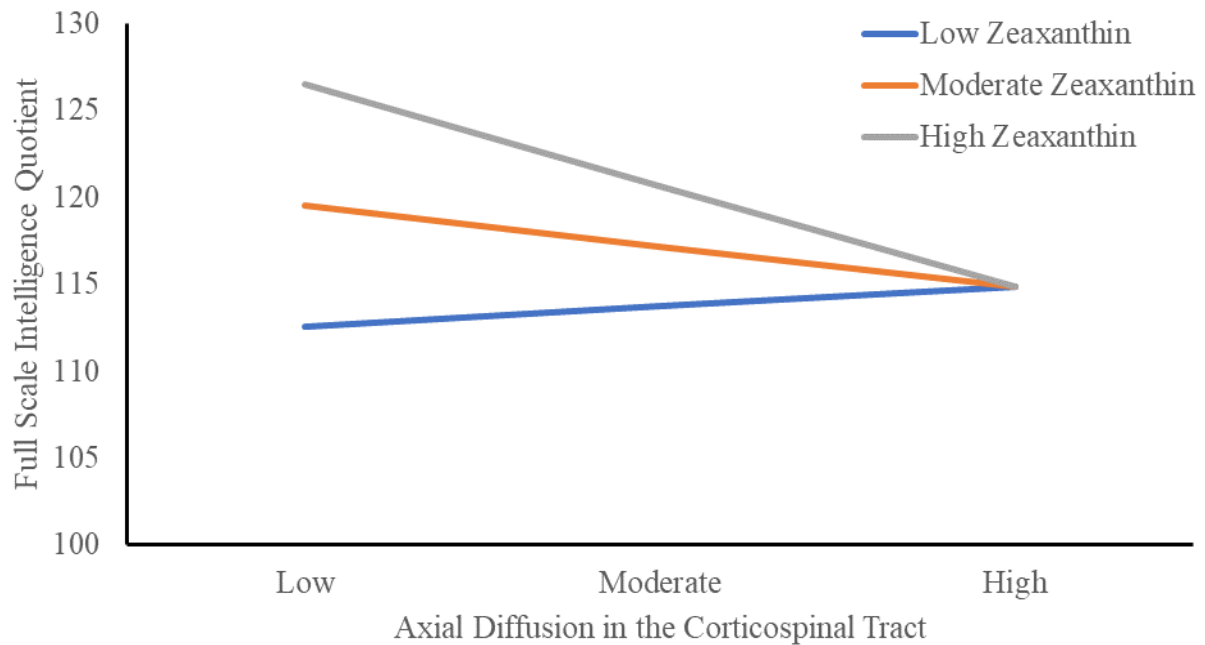


Figure 2.30 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the corticospinal tract and general intelligence. When AD is low or moderate, zeaxanthin status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

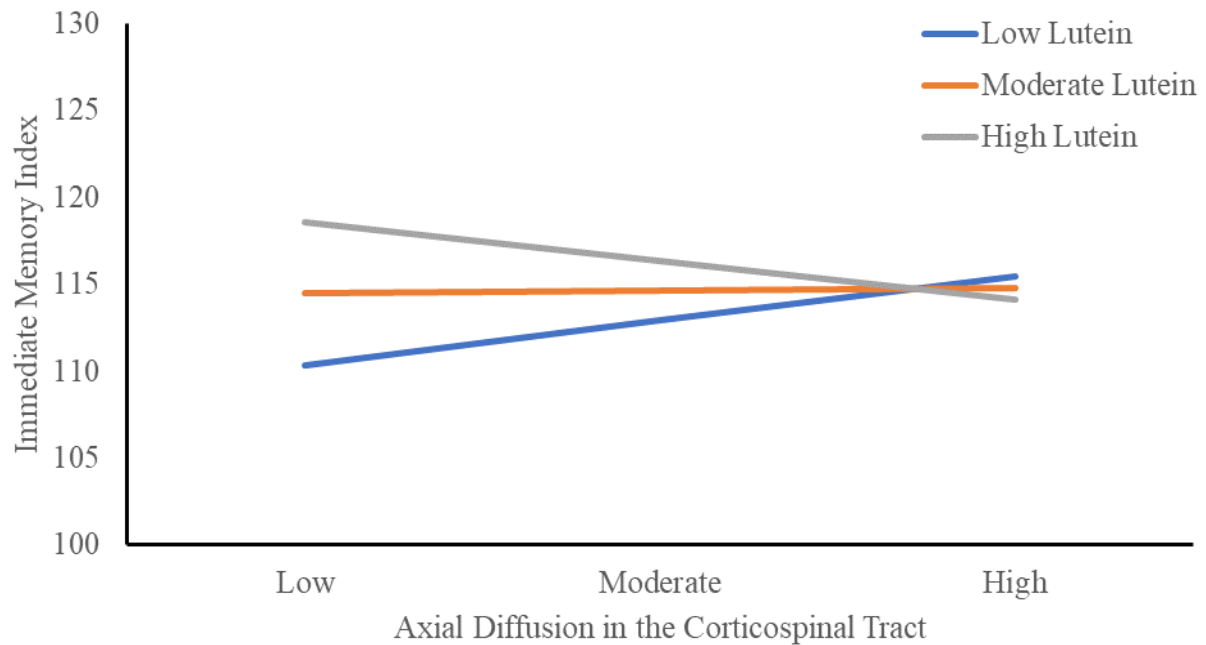


Figure 2.31 | Lutein status conditionally moderates the relationship between axial diffusion in the corticospinal tract and immediate memory. When AD is low, lutein status significantly influences immediate memory score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

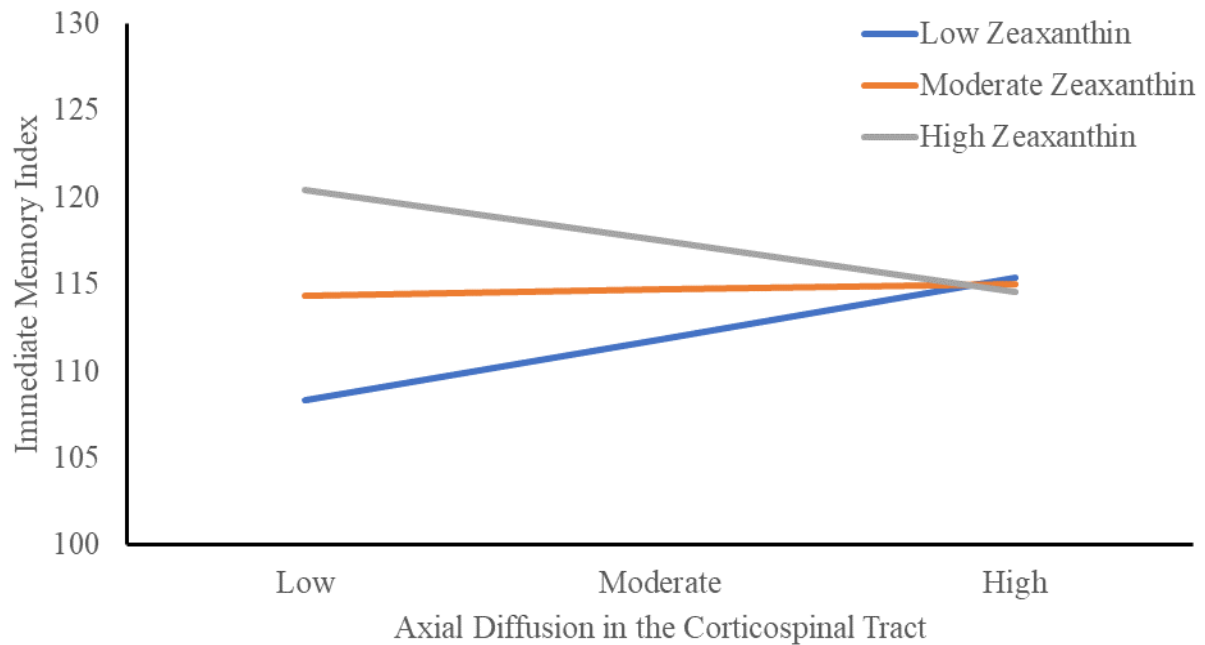


Figure 2.32 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the corticospinal tract and immediate memory. When AD is moderate or low, zeaxanthin status significantly influences immediate memory score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

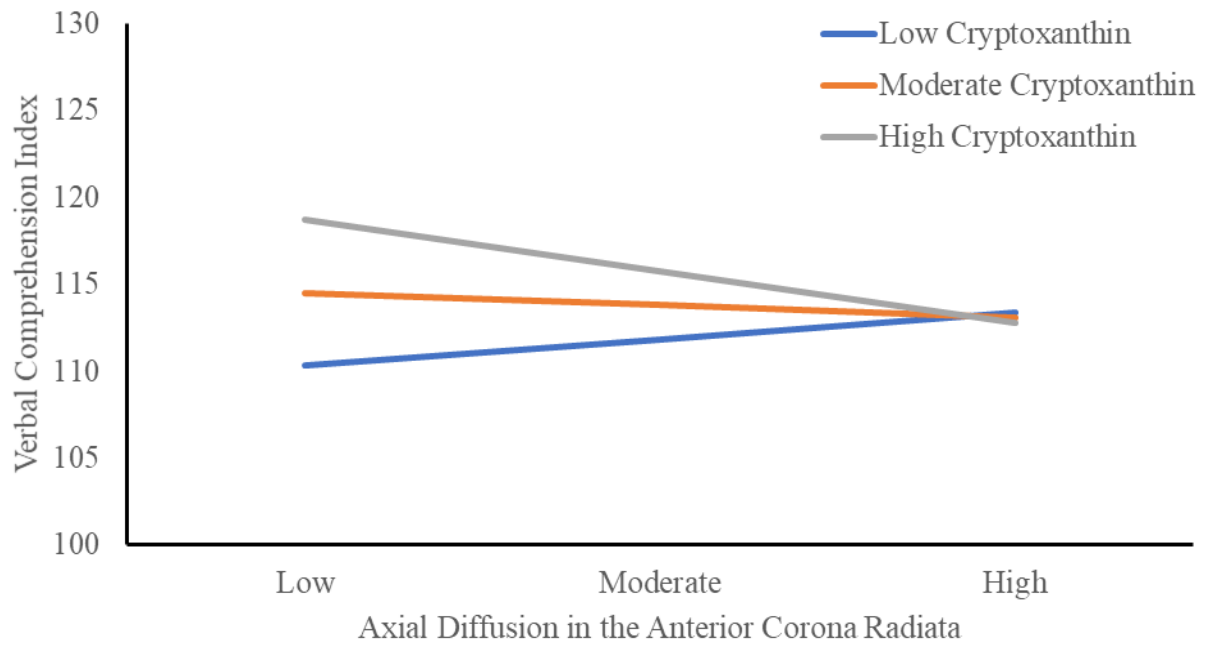


Figure 2.33 | Cryptoxanthin status conditionally moderates the relationship between axial diffusion in the anterior corona radiata and crystallized intelligence. When AD is low, cryptoxanthin status significantly influences crystallized intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

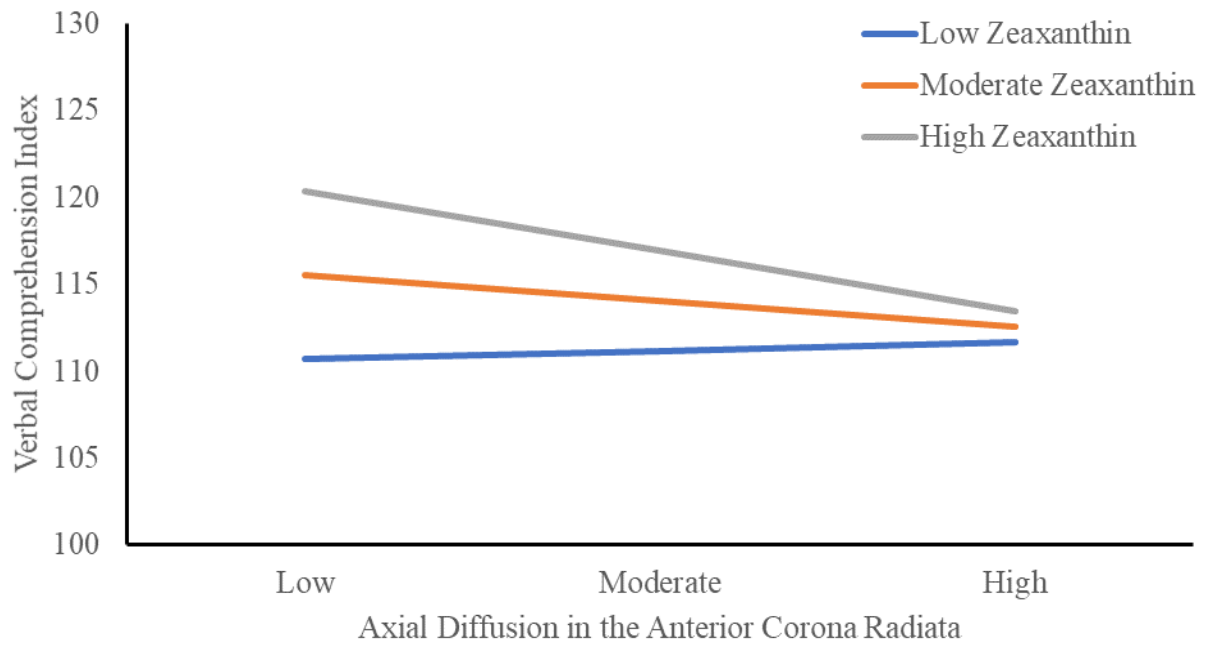


Figure 2.34 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the anterior corona radiata and crystallized intelligence. When AD is moderate or low, zeaxanthin status significantly influences crystallized intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

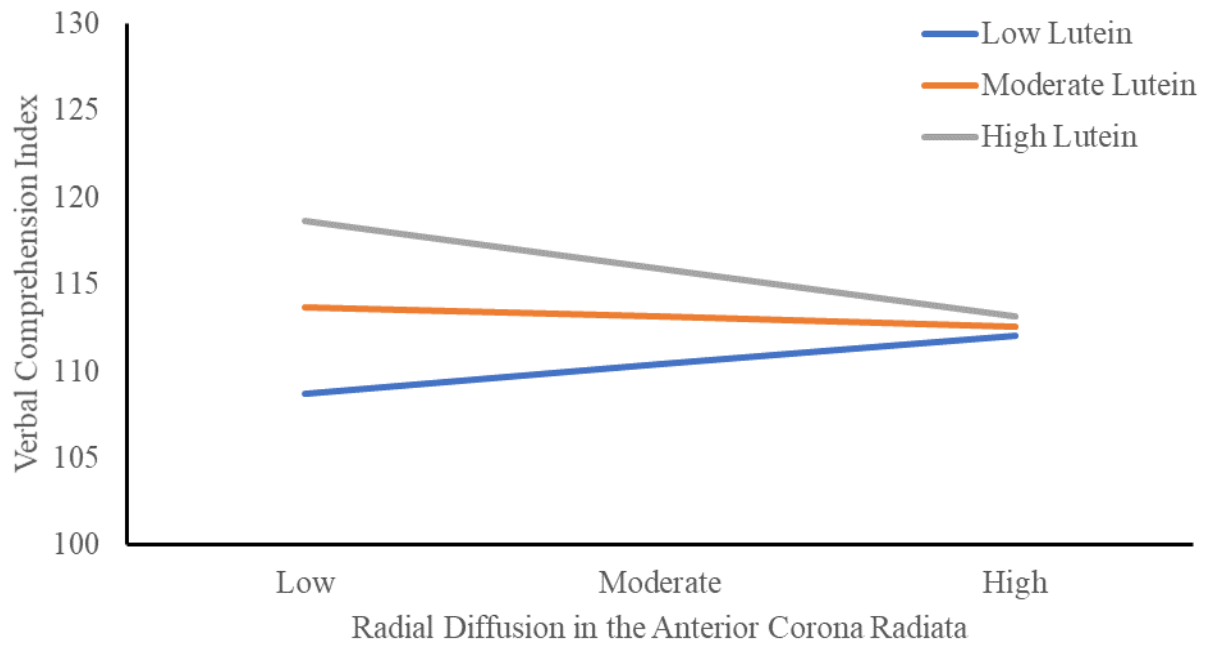


Figure 2.35 | Lutein status conditionally moderates the relationship between radial diffusion in the anterior corona radiata and crystallized intelligence. When RD is moderate or low, lutein status significantly influences crystallized intelligence score. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

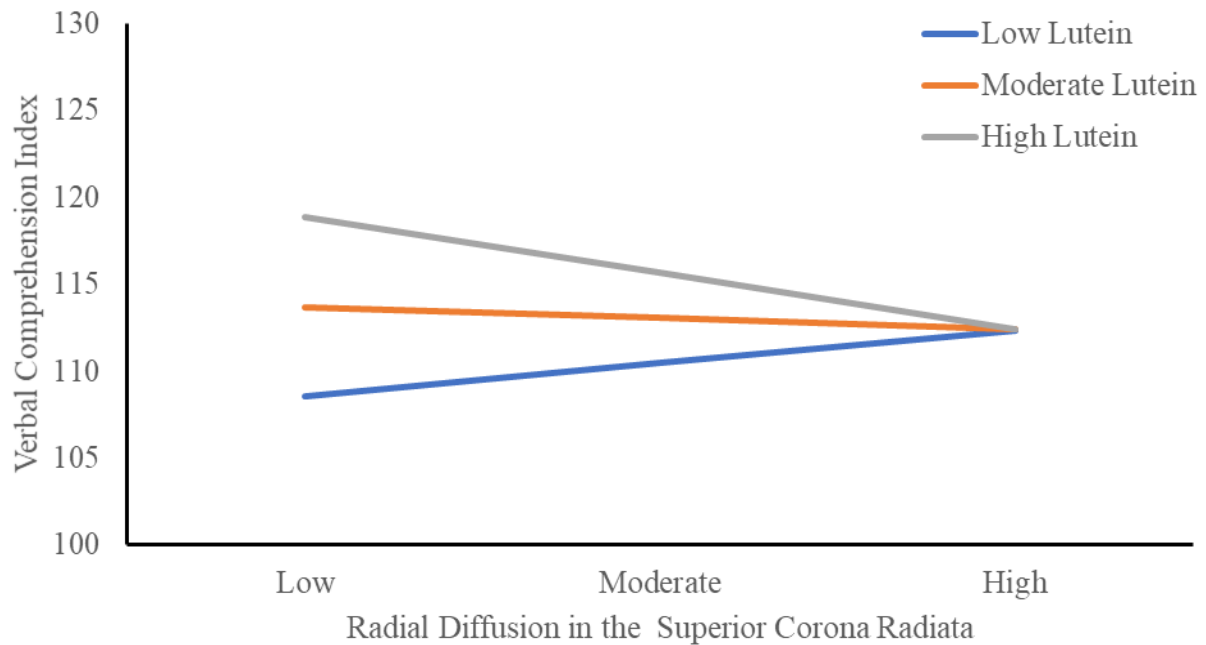


Figure 2.36 | Lutein status conditionally moderates the relationship between radial diffusion in the superior corona radiata and crystallized intelligence. When RD is moderate or low, lutein status significantly influences crystallized intelligence score. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

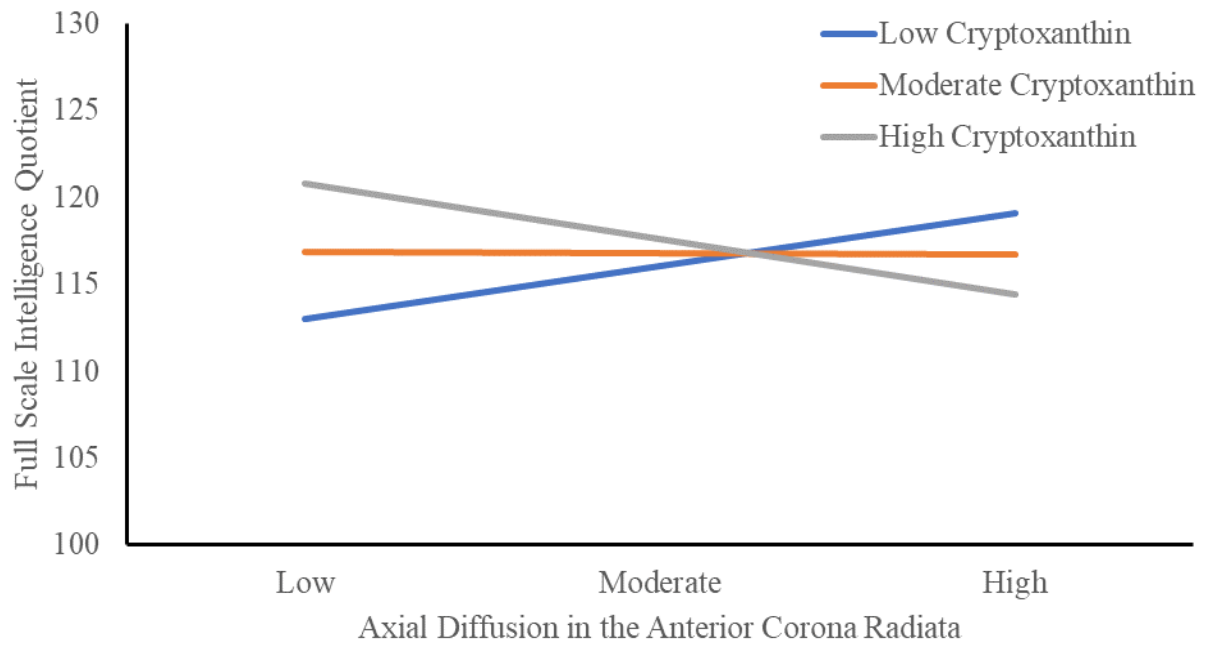


Figure 2.37 | Cryptoxanthin status conditionally moderates the relationship between axial diffusion in the anterior corona radiata and general intelligence. When AD low, cryptoxanthin status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

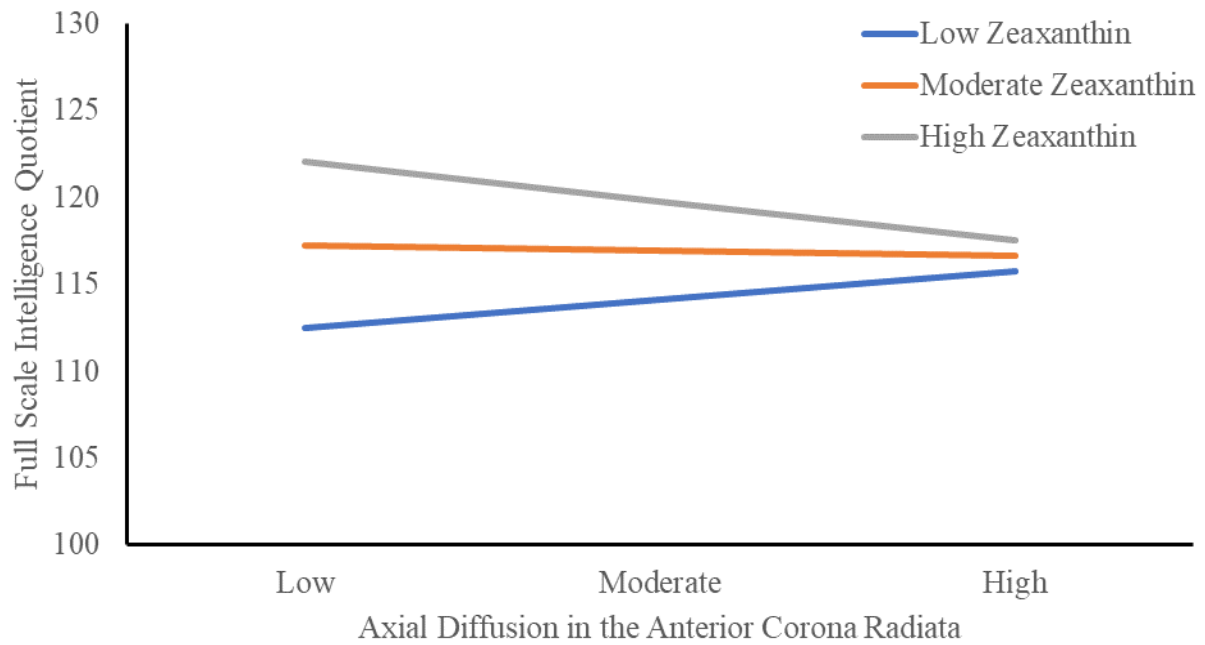


Figure 2.38 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the anterior corona radiata and general intelligence. When AD is moderate or low, zeaxanthin status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

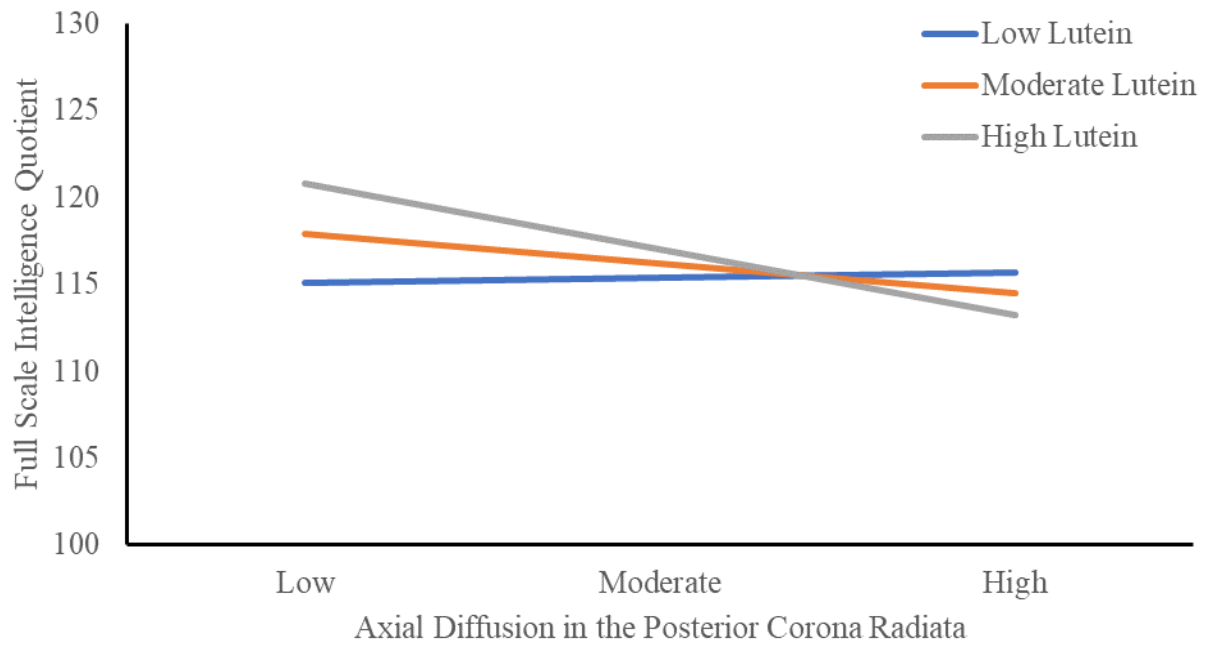


Figure 2.39 | Lutein status conditionally moderates the relationship between axial diffusion in the posterior corona radiata and general intelligence. When AD is low, lutein status significantly influences general intelligence score. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

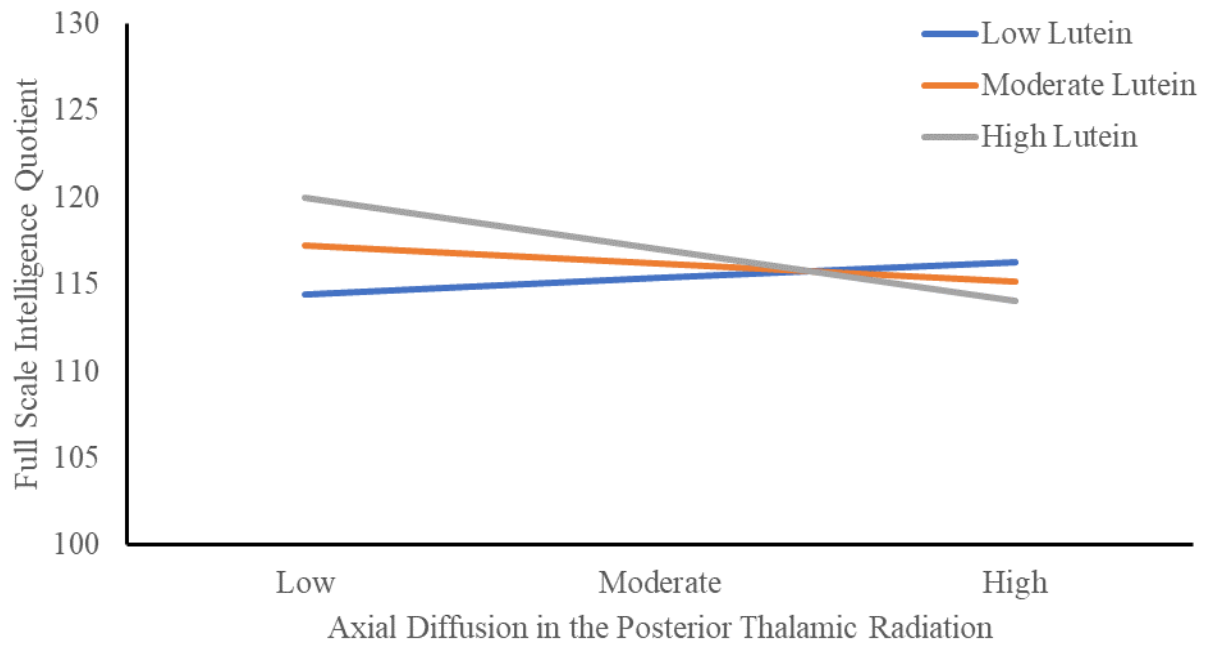


Figure 2.40 | Lutein status conditionally moderates the relationship between axial diffusion in the posterior thalamic radiation and general intelligence. When AD is low, lutein status significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

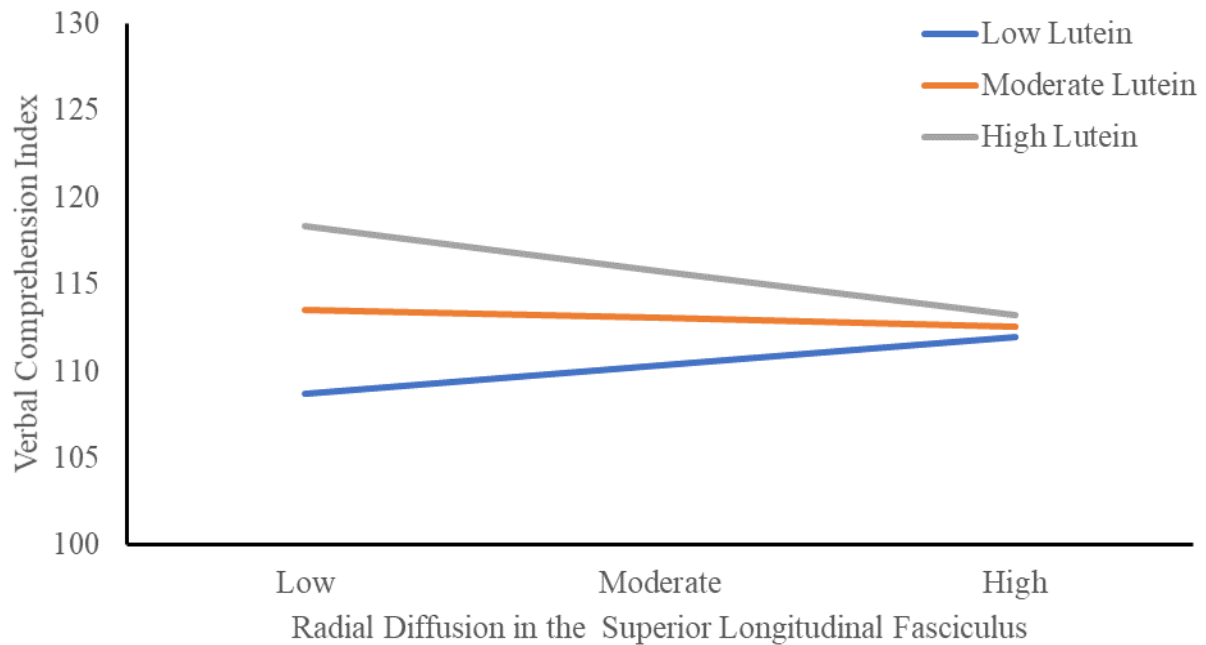


Figure 2.41 | Lutein status conditionally moderates the relationship between radial diffusion in the superior longitudinal fasciculus and crystallized intelligence. When RD is low or moderate, lutein status significantly influences crystallized intelligence. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

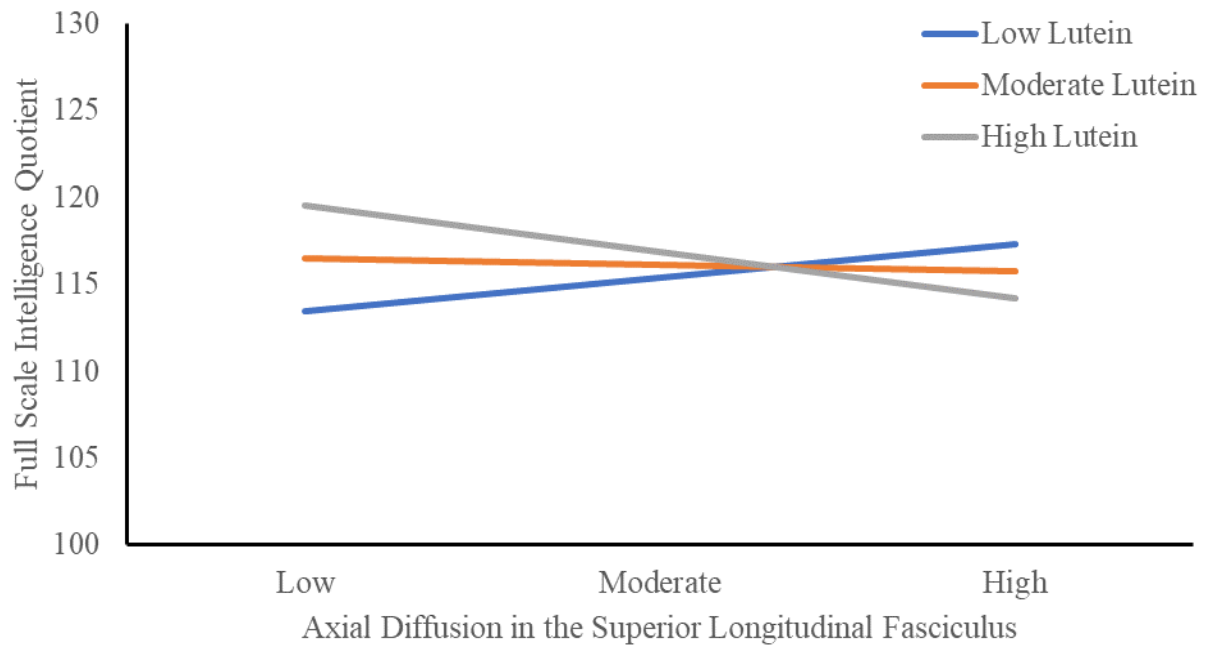


Figure 2.42 | Lutein status conditionally moderates the relationship between axial diffusion in the superior longitudinal fasciculus and general intelligence. When AD is low or moderate, lutein status significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

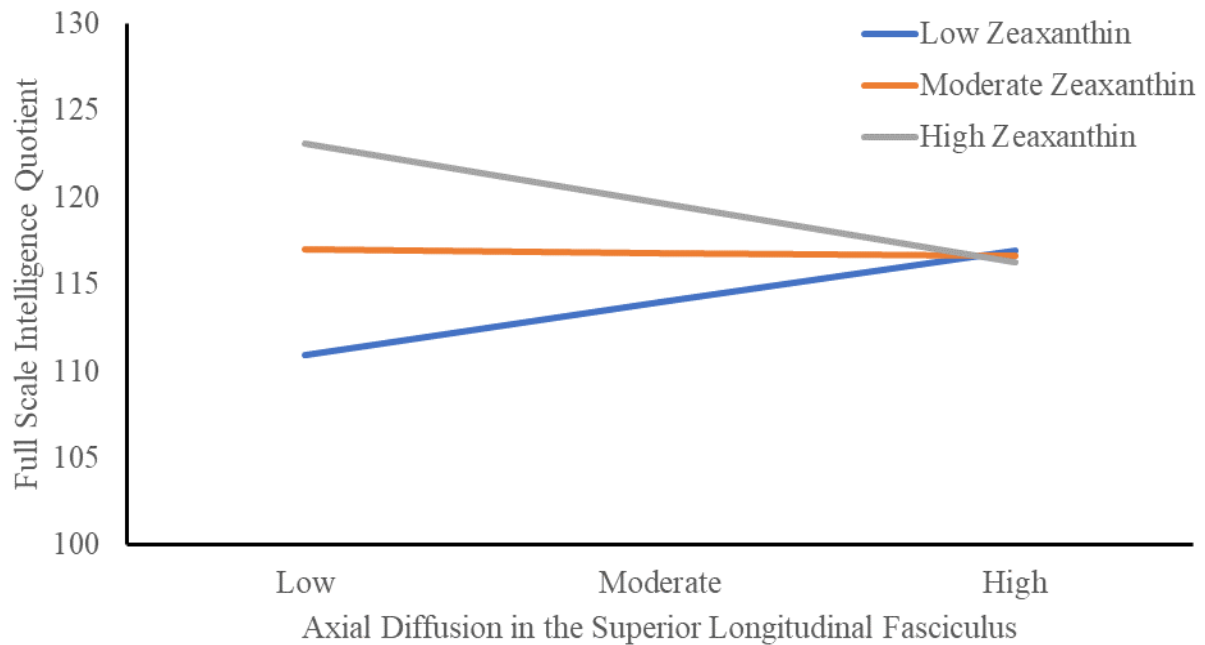


Figure 2.43 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the superior longitudinal fasciculus and general intelligence. When AD is low or moderate, zeaxanthin status significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

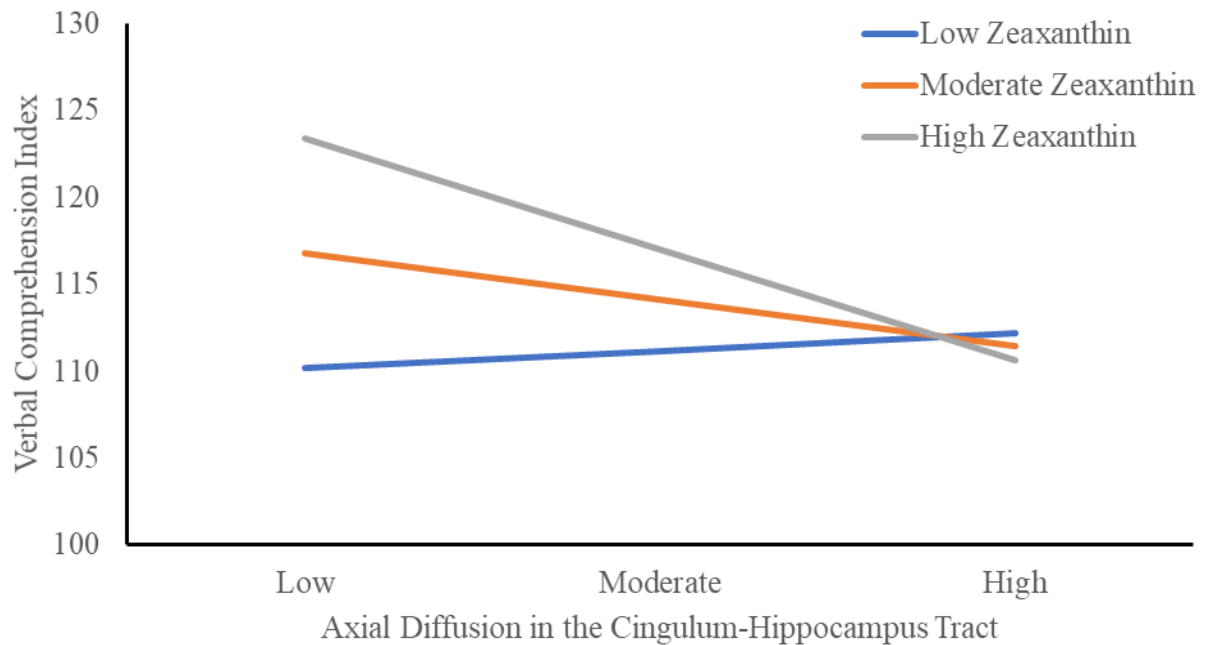


Figure 2.44 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the cingulum – hippocampus tract and crystallized intelligence. When AD is low or moderate, zeaxanthin status significantly influences crystallized intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

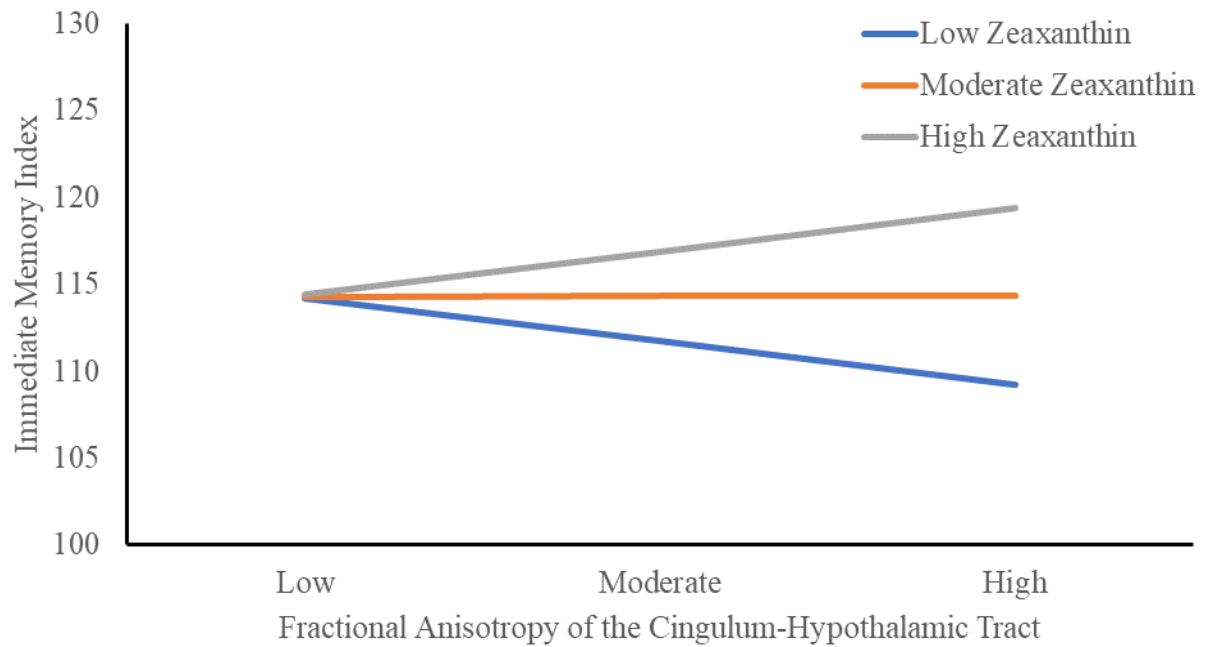


Figure 2.45 | Zeaxanthin status conditionally moderates the relationship between fractional anisotropy in the cingulum – hippocampus tract and immediate memory. When FA is moderate or high, zeaxanthin status significantly influences immediate memory. Low status and FA are defined as one *SD* below the mean; high status and FA are defined as one *SD* above the mean.

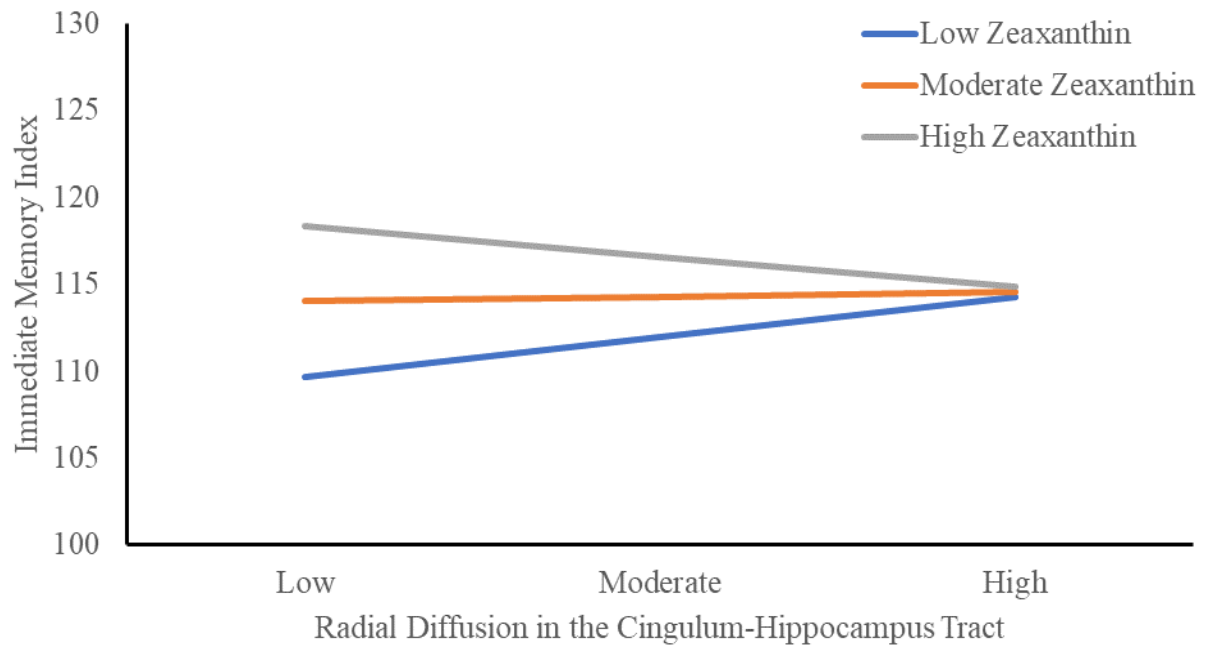


Figure 2.46 | Zeaxanthin status conditionally moderates the relationship between radial diffusion in the cingulum – hippocampus tract and immediate memory. When RD is low or moderate, zeaxanthin status significantly influences immediate memory. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

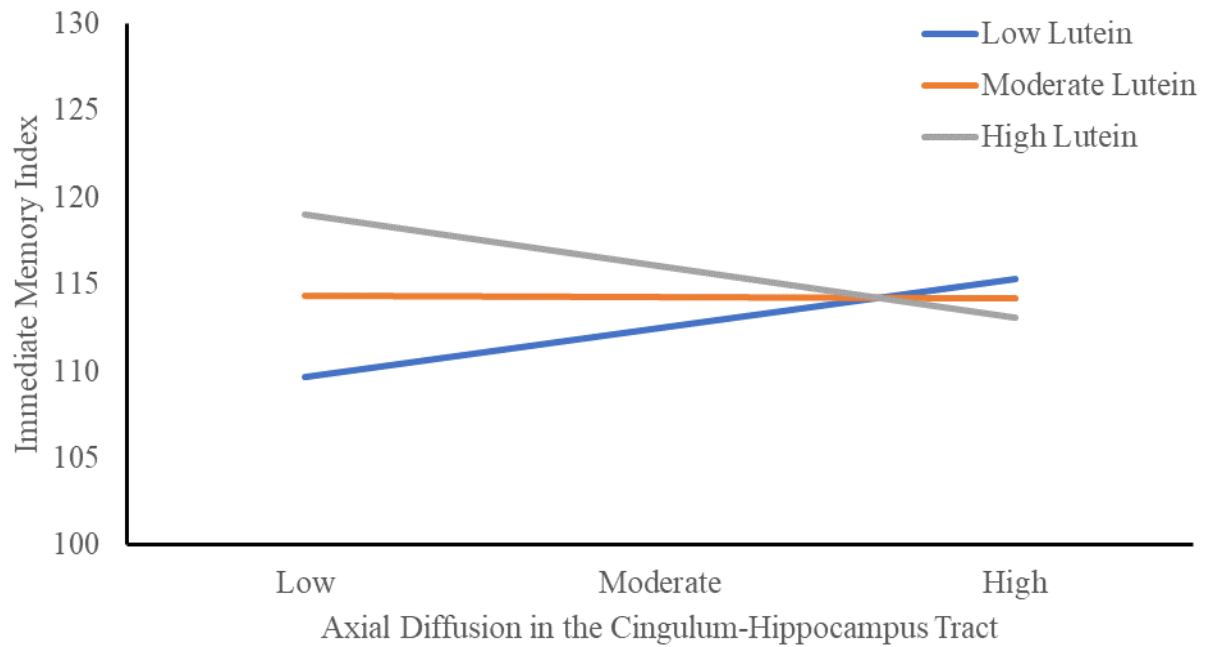


Figure 2.47 | Lutein status conditionally moderates the relationship between axial diffusion in the cingulum – hippocampus tract and immediate memory. When AD is low lutein status significantly influences immediate memory. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

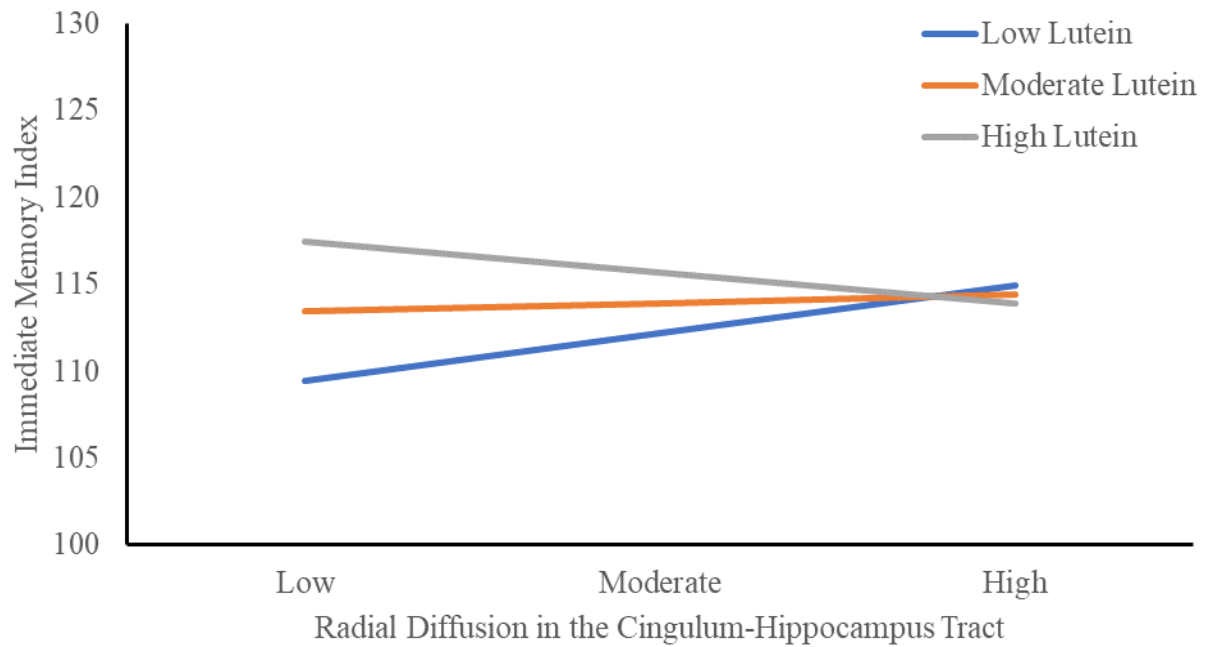


Figure 2.48 | Lutein status conditionally moderates the relationship between radial diffusion in the cingulum – hippocampus tract and immediate memory. When RD is low, lutein status significantly influences immediate memory. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

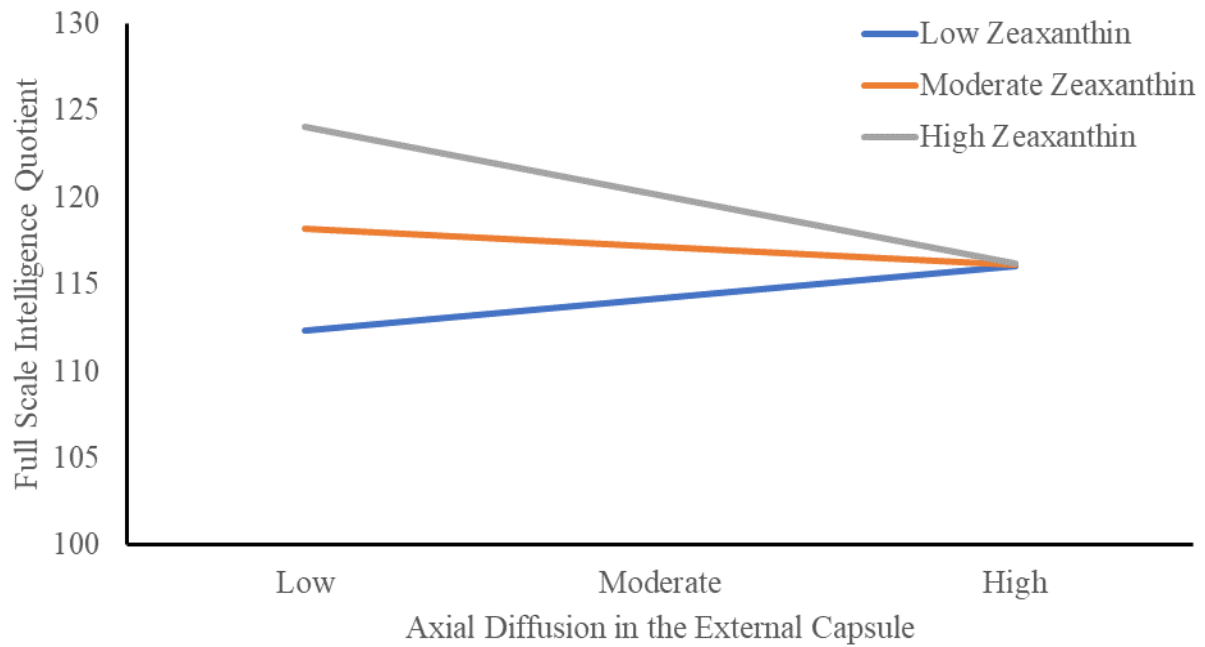


Figure 2.49 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the external capsule and general intelligence. When AD is low or moderate, zeaxanthin status significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

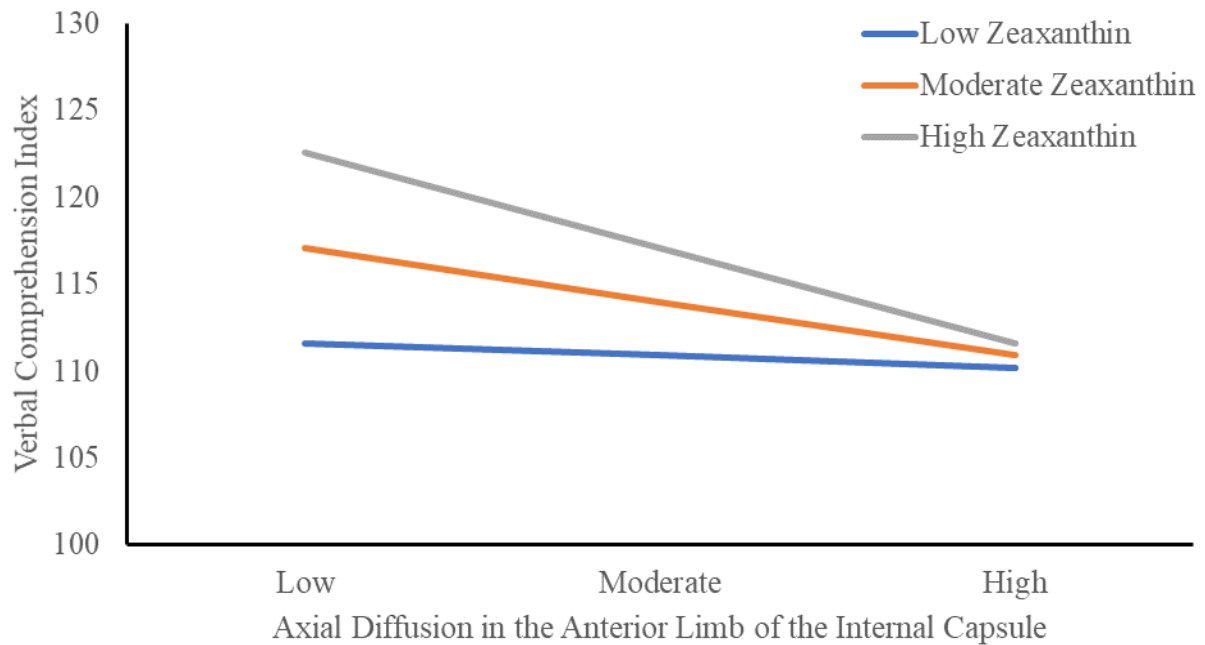


Figure 2.50 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the anterior limb of the internal capsule and crystallized intelligence. When AD is low or moderate, zeaxanthin status significantly influences crystallized intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

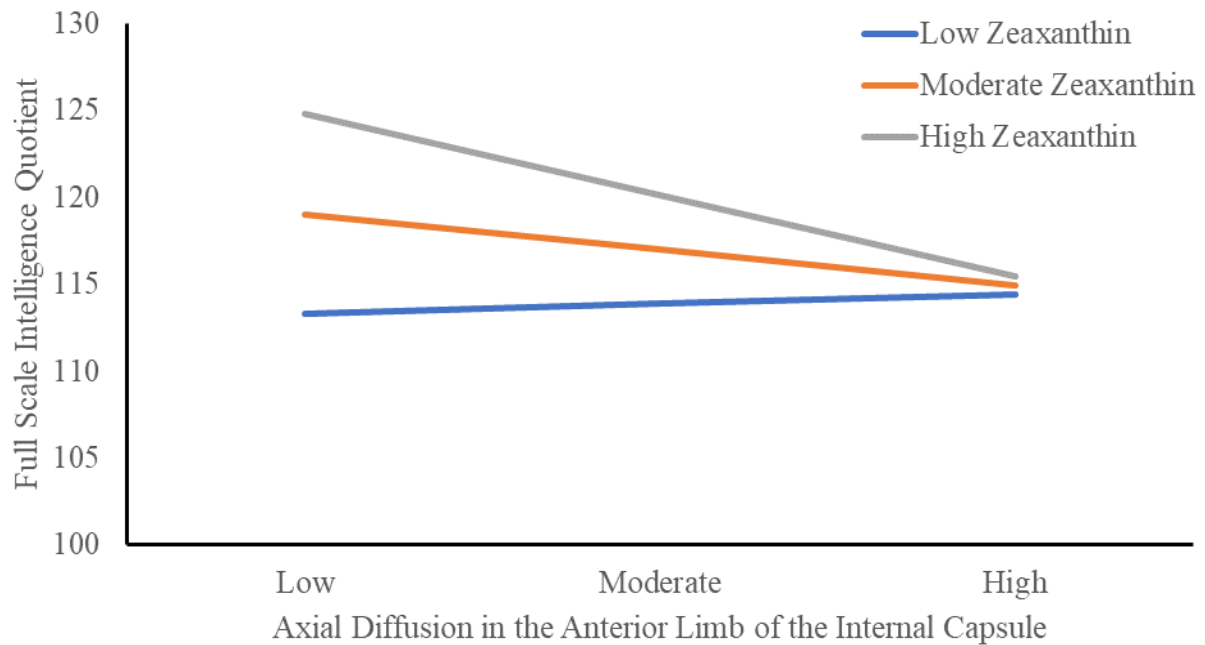


Figure 2.51 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the anterior limb of the internal capsule and general intelligence. When AD is low or moderate, zeaxanthin status significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

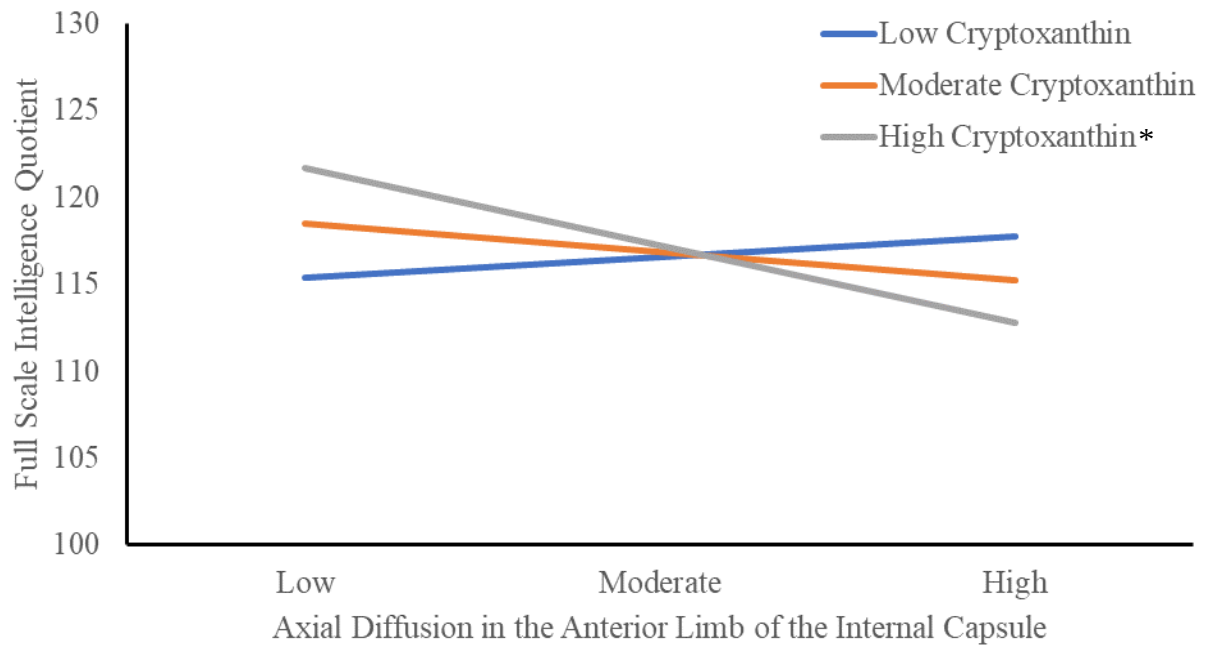


Figure 2.52 | Cryptoxanthin status conditionally moderates the relationship between axial diffusion in the anterior limb of the internal capsule and general intelligence. When cryptoxanthin status is high, it significantly moderates the relationship between AD and general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean. $*p < .05$

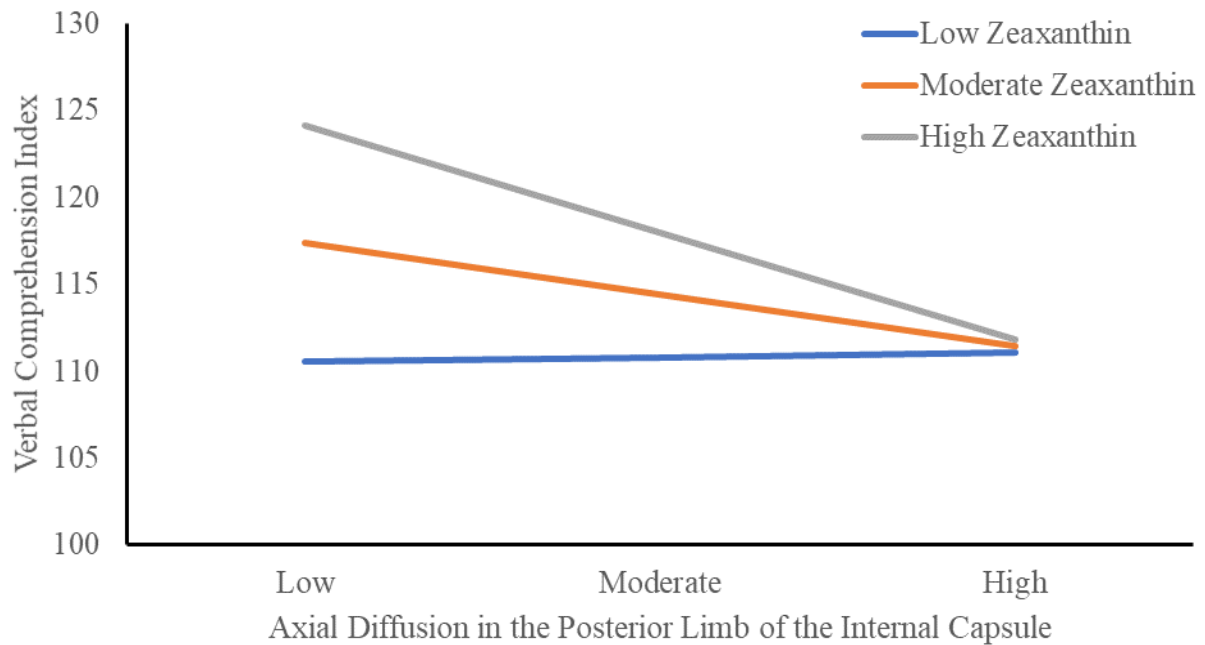


Figure 2.53 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the posterior limb of the internal capsule and crystallized intelligence. When AD is low or moderate, zeaxanthin status significantly influences crystallized intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

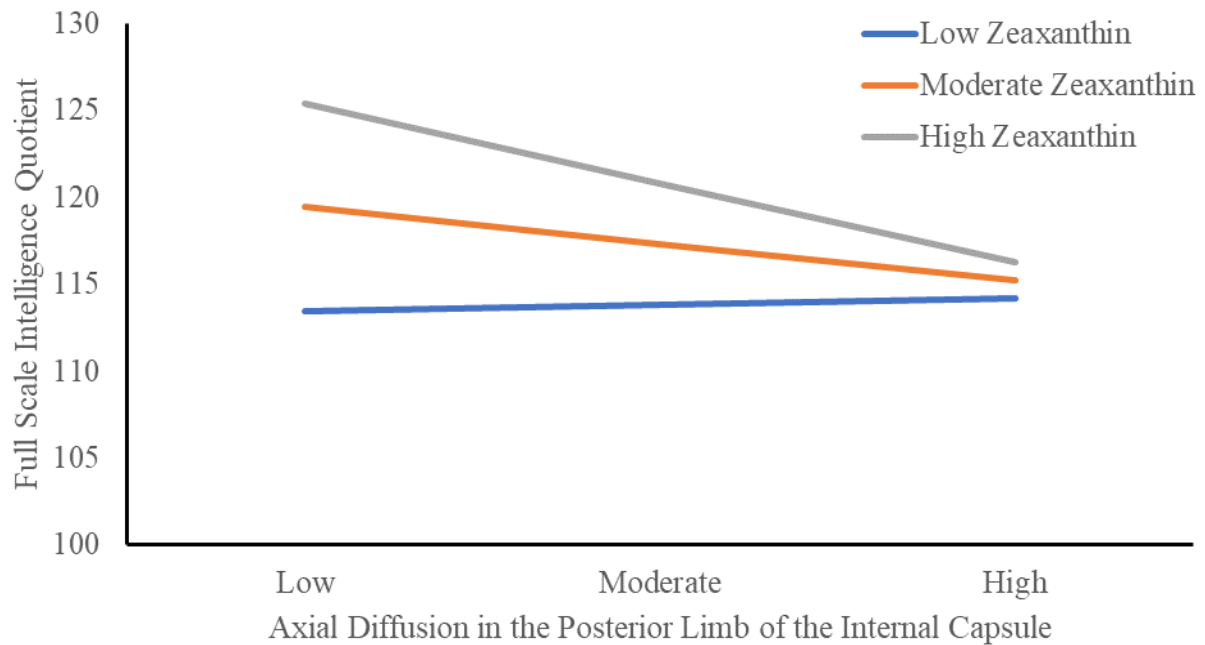


Figure 2.54 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the posterior limb of the internal capsule and general intelligence. When AD is low or moderate, zeaxanthin status significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

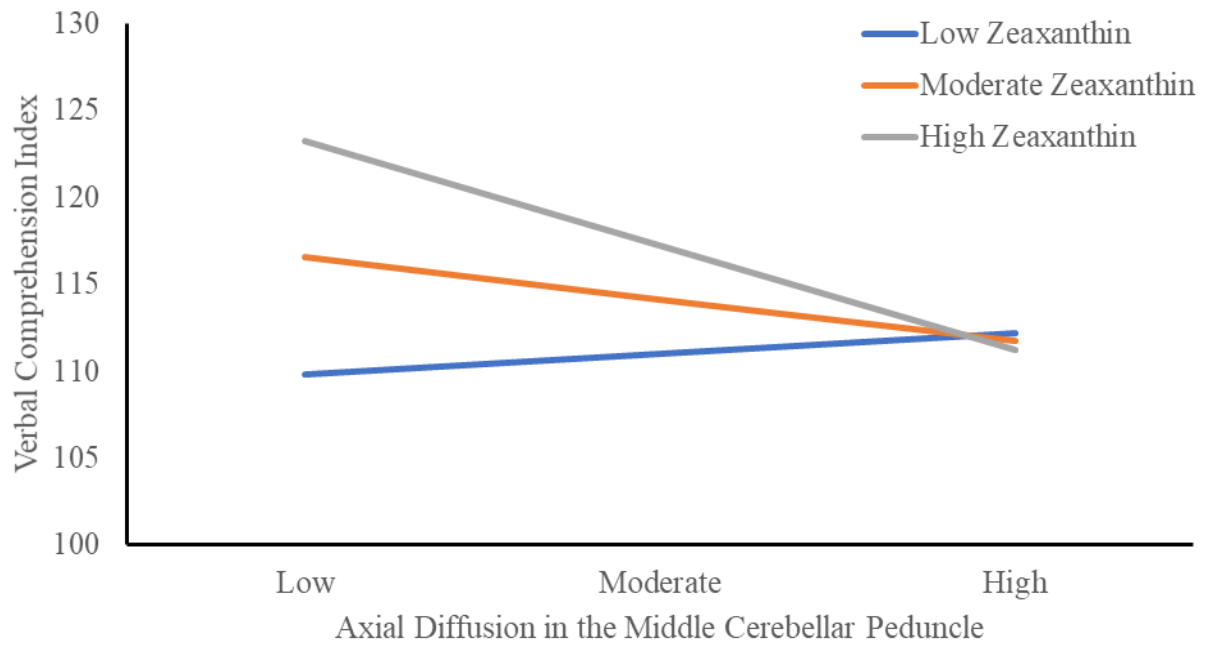


Figure 2.55 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the middle cerebellar peduncle and crystallized intelligence. When AD is low or moderate, zeaxanthin status significantly influences crystallized intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

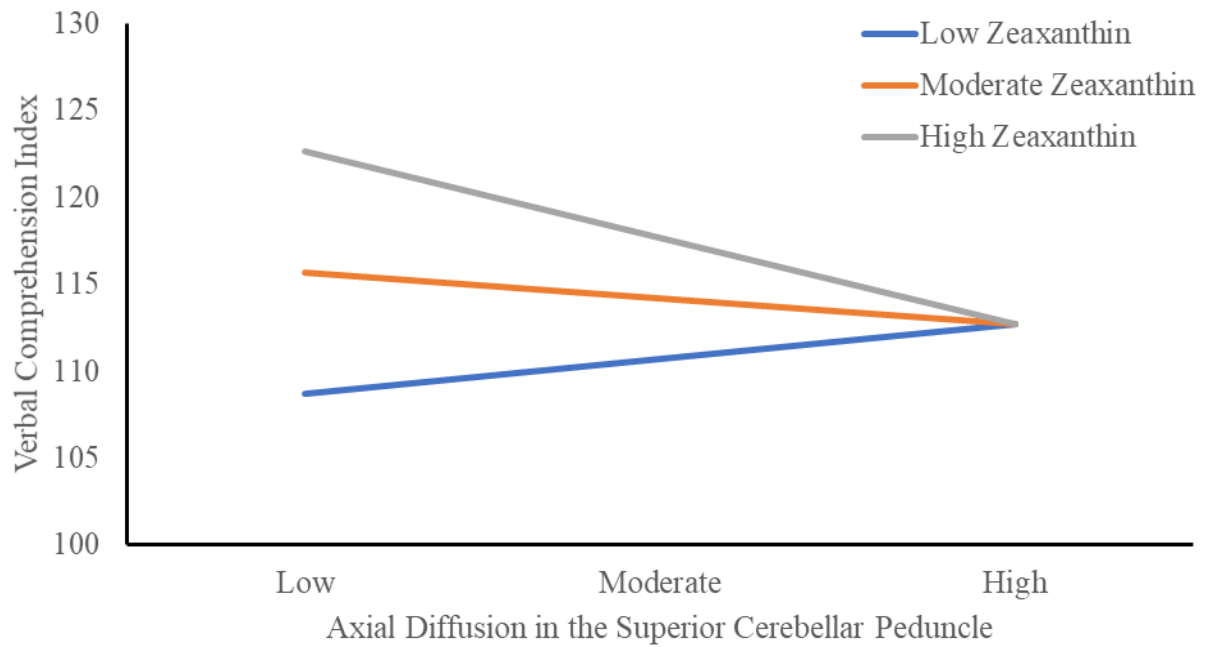


Figure 2.56 | Zeaxanthin status conditionally moderates the relationship between axial diffusion in the superior cerebellar peduncle and crystallized intelligence. When AD is low or moderate, zeaxanthin status significantly influences crystallized intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

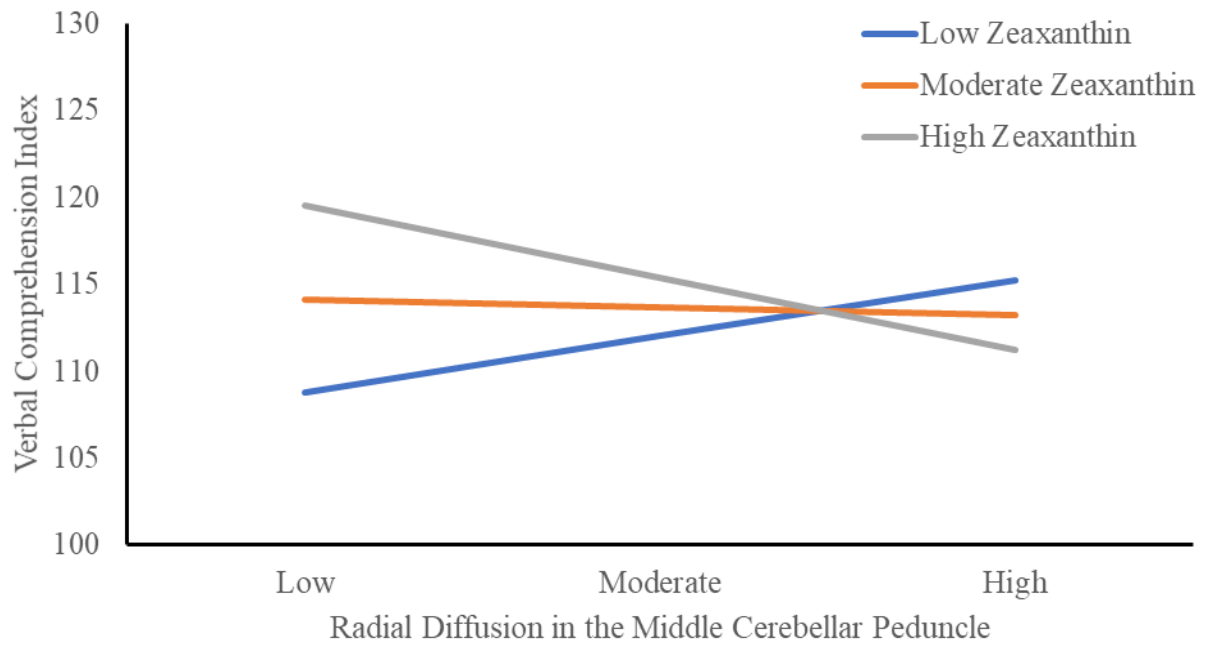


Figure 2.57 | Zeaxanthin status conditionally moderates the relationship between radial diffusion in the middle cerebellar peduncle and crystallized intelligence. When RD is low, zeaxanthin status significantly influences crystallized intelligence. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

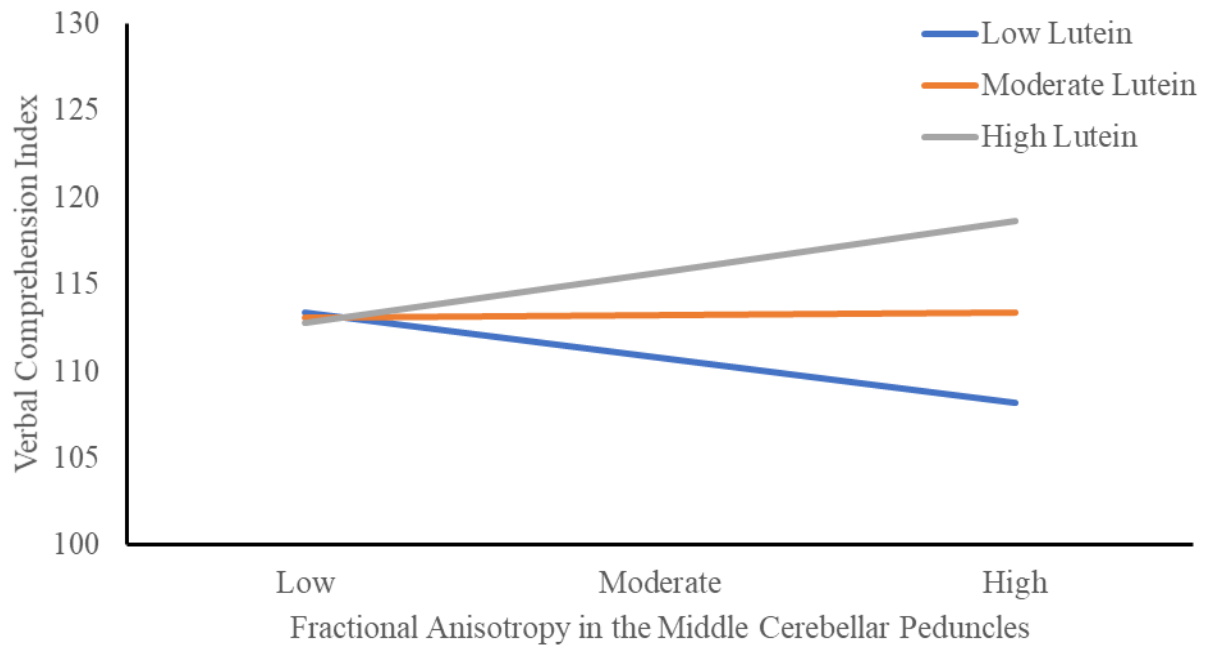


Figure 2.58 | Lutein status conditionally moderates the relationship between fractional anisotropy in the middle cerebellar peduncle and crystallized intelligence. When FA is moderate or high, lutein status significantly influences crystallized intelligence. Low status and FA are defined as one *SD* below the mean; high status and FA are defined as one *SD* above the mean.

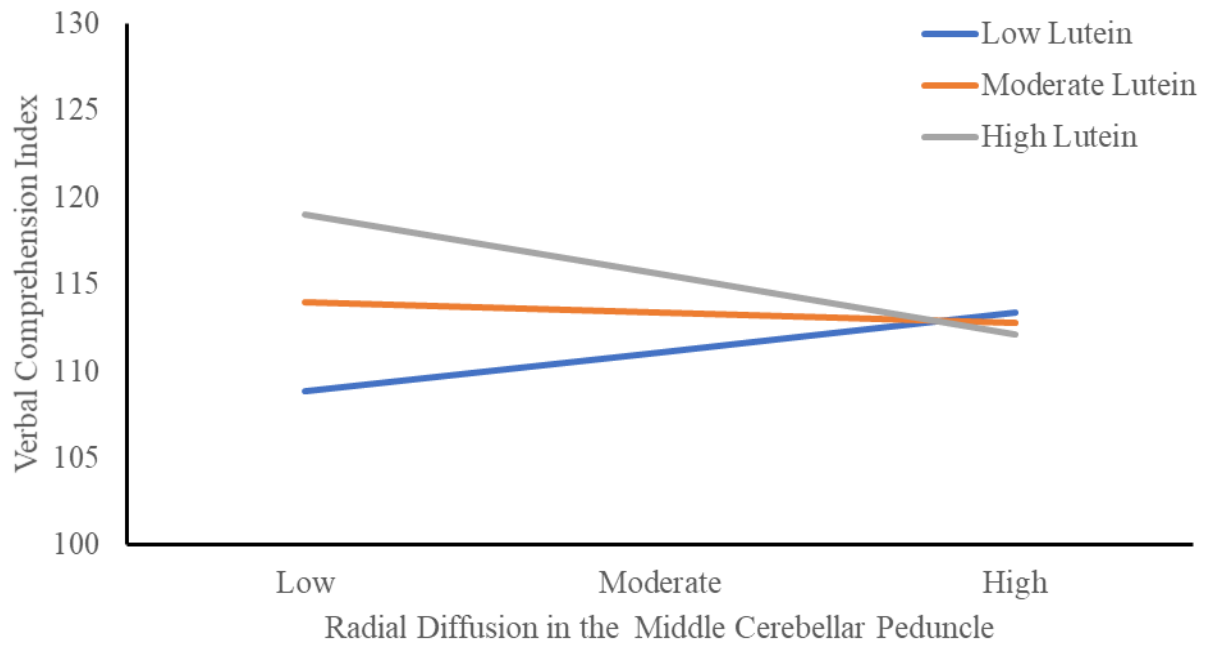


Figure 2.59 | Lutein status conditionally moderates the relationship between radial diffusion in the middle cerebellar peduncle and crystallized intelligence. When RD is low or moderate, lutein status significantly influences crystallized intelligence. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

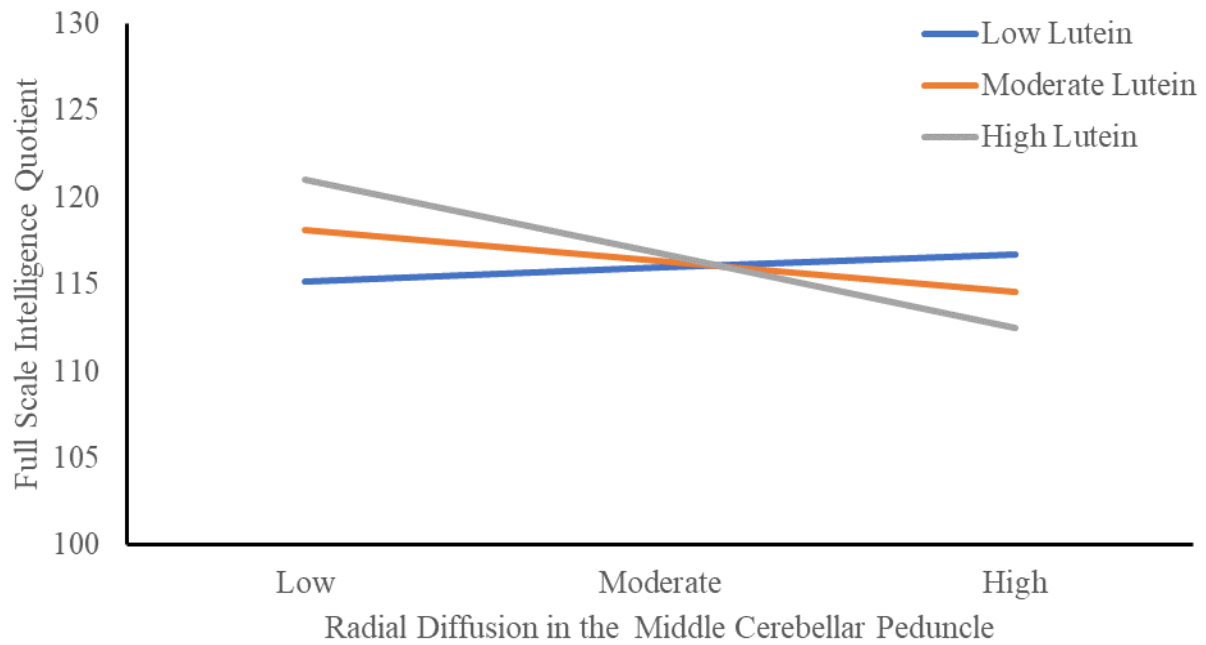


Figure 2.60 | Lutein status conditionally moderates the relationship between radial diffusion in the middle cerebellar peduncle and general intelligence. When RD is low, lutein status significantly influences general intelligence. Low status and RD are defined as one *SD* below the mean; high status and RD are defined as one *SD* above the mean.

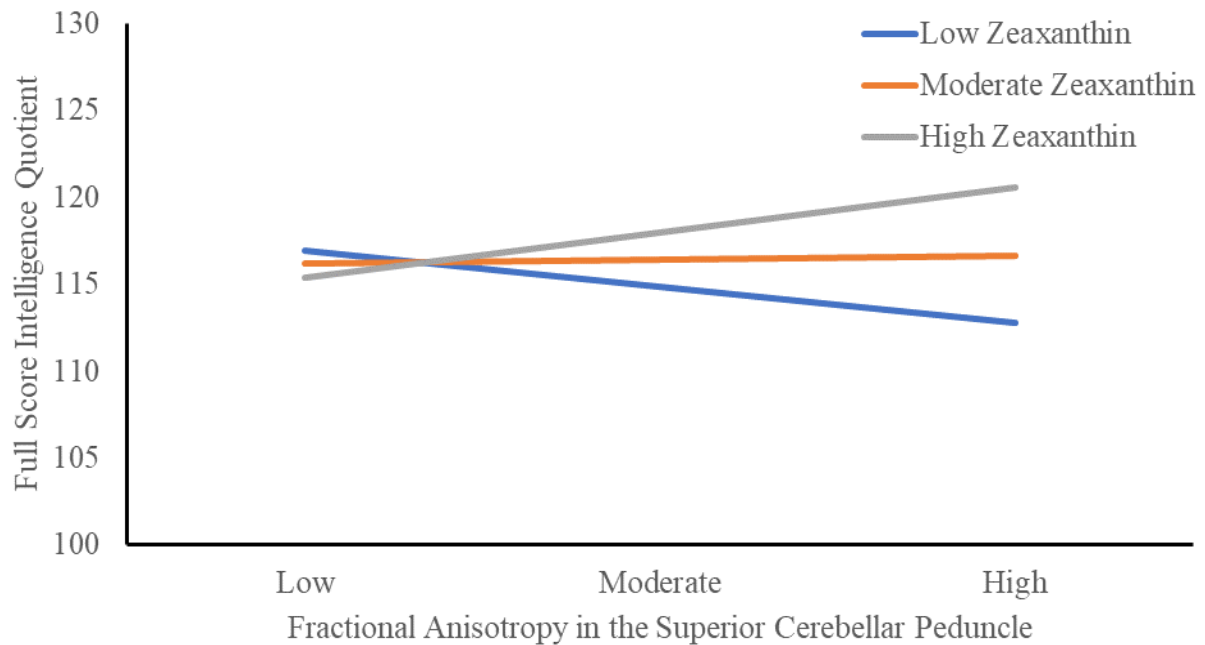


Figure 2.61 | Zeaxanthin status conditionally moderates the relationship between fractional anisotropy in the superior cerebellar peduncle and general intelligence. When FA is high, zeaxanthin status significantly influences general intelligence. Low status and FA are defined as one *SD* below the mean; high status and FA are defined as one *SD* above the mean.

Table 2.1 | DTI Regions of Interest

Global White Matter	Fornix
Corpus Callosum (genu)	Corona Radiata (anterior)
Corpus Callosum (body)	Corona Radiata (posterior)
Cingulum – Cingulate	Corona Radiata (superior)
Cingulum – Hippocampus	Internal Capsule (anterior limb)
External Capsule	Internal Capsule (posterior limb)
Cerebellar Peduncle (inferior)	Posterior Thalamic Radiation
Cerebellar Peduncle (middle)	Corticospinal Tract
Cerebellar Peduncle (superior)	Longitudinal Fasciculus (Superior)
	Uncinate Fasciculus

Table 2.2 | Neuropsychological Assessment Tasks

Assessment	Measurement	Test Composition	Test Description (Facet of Intelligence)
WMS-IV Older Adult Battery	Immediate Memory Index	Logical Memory (I)	Free recall of oral short stories (narrative memory)
		Verbal Paired Associates (I)	Associated word pairs after verbal presentation (verbal memory)
		Visual Reproduction (I)	Recreating designs from memory after viewing for 10 seconds (nonverbal visual memory)
	Delayed Memory Index	Logical Memory (II)	Free recall and detail recognition about 10 minutes after hearing short stories (long-term narrative memory)
		Verbal Paired Associates (II)	Cued recall, recognition, and free recall of associated word pairs about 10 minutes after verbal presentation (long-term verbal memory)
		Visual Reproduction (II)	Free recreation and recognition of designs about 10 minutes after viewing (long-term visual-spatial memory)
	Auditory Memory Index	Logical Memory (I & II)	See Above
		Verbal Paired Associates (I & II)	See Above
	Visual Memory Index	Visual Reproduction (I & II)	See Above
	Visual Working Memory	Symbol Span	Ordered recognition of novel, abstract visual stimuli
WASI-II	Full Scale IQ	Block Design	Match the design of a visual stimulus using colored blocks (abstract analysis of visual stimuli)
		Vocabulary	Define words presented visually and orally (crystallized intelligence; verbal concepts)
		Matrix Reasoning	Select responses from provided images to complete a matrix or series (fluid intelligence; spatial ability)
		Similarities	Describe how (2) orally presented words are similar (verbal concept formation and reasoning)
	Perceptual Reasoning Index	Block Design	See Above
		Matrix Reasoning	See Above
	Verbal Comprehension Index	Vocabulary	See Above
		Similarities	See Above
DKEFS	Trail Making Test	Task Switching	Visual scanning for alternating letters and numbers

Table 2.3 | Demographic data by moderator: xanthophylls

	Cryptoxanthin (n = 113)	Lutein (n = 112)	Zeaxanthin (n = 114)
(nmol/mL; $\bar{x} \pm SD$)	0.1598 $\pm$ 0.0906	0.3923 $\pm$ 0.1924	0.0795 $\pm$ 0.0424
Age (years; $\bar{x} \pm SD$)	68.88 $\pm$ 2.94	68.93 $\pm$ 2.95	68.96 $\pm$ 3.00
Sex (%F)	62.83	61.61	62.28
BMI ($\bar{x} \pm SD$)	25.98 $\pm$ 3.79	26.07 $\pm$ 3.75	25.99 $\pm$ 3.78
Income, n (%)			
<15k	1(0.88)	1(0.89)	1(0.88)
15-25k	5(4.42)	5(4.46)	5(4.39)
25-50k	22(19.47)	21(18.75)	22(19.30)
50-75k	23(20.35)	24(21.43)	23(20.18)
75-100k	27(23.89)	27(24.11)	28(24.56)
>100k	35(30.97)	34(30.36)	35(30.70)
Education, n (%)			
Some high school	1(0.88)	1(0.89)	1(0.88)
High school degree	11(9.73)	12(10.71)	12(10.53)
Some college	22(19.47)	22(19.64)	22(19.30)
College degree	79(69.91)	77(68.75)	79(69.30)
Facets of Intelligence, (n), $\bar{x} \pm SD$			
Immediate Memory	(110) 114.90 $\pm$ 11.19	(110) 114.05 $\pm$ 10.92	(111) 114.43 $\pm$ 11.12
Delayed Memory	(111) 112.65 $\pm$ 12.15	(111) 112.42 $\pm$ 11.90	(112) 112.88 $\pm$ 12.14
Auditory Memory	(110) 113.00 $\pm$ 11.94	(111) 112.79 $\pm$ 11.69	(111) 113.05 $\pm$ 11.85
Visual Memory	(109) 110.90 $\pm$ 10.21	(108) 110.41 $\pm$ 10.30	(110) 110.70 $\pm$ 10.34
Working Memory	(108) 13.06 $\pm$ 2.40	(107) 12.93 $\pm$ 2.33	(109) 13.04 $\pm$ 2.34
Task Switching	(109) 8.32 $\pm$ 1.95	(108) 8.23 $\pm$ 1.98	(110) 8.21 $\pm$ 1.99
Crystallized Intelligence	(108) 113.77 $\pm$ 12.11	(107) 113.27 $\pm$ 12.07	(109) 113.96 $\pm$ 12.40
Fluid Intelligence	(108) 113.91 $\pm$ 11.41	(107) 113.26 $\pm$ 11.23	(109) 113.83 $\pm$ 11.40
General Intelligence	(108) 116.88 $\pm$ 10.87	(107) 116.27 $\pm$ 10.74	(109) 116.95 $\pm$ 11.00
Volumetrics (mm³; $\bar{x} \pm SD$)			
Cuneus	5649.42 $\pm$ 811.63	5637.732 $\pm$ 793.00	5649.94 $\pm$ 801.17
Inferior Parietal	22094.82 $\pm$ 2946.31	22081.01 $\pm$ 2951.14	22097.98 $\pm$ 2933.37
Lateral Occipital	21514.01 $\pm$ 2757.92	21445.48 $\pm$ 2774.62	21524.14 $\pm$ 2744.00
Precuneus	18513.74 $\pm$ 2057.15	18538.09 $\pm$ 2026.11	18522.60 $\pm$ 2043.28
Superior Parietal	25030.45 $\pm$ 2691.73	25009.42 $\pm$ 2618.76	25010.78 $\pm$ 2625.76

Table 2.4 | Linear Regression models of ROI associated with facets of intelligence

Facet of Intelligence	<u>Cuneus</u>			<u>Inferior Parietal</u>			<u>Lateral Occipital</u>			<u>Precuneus</u>			<u>Superior Parietal</u>		
	β	β SE	R^2	β	β SE	R^2	β	β SE	R^2	β	β SE	R^2	β	β SE	R^2
Immediate Memory	.001	.001	.129 ^x	.000	.000	.137 ^x	<.001	.000	.127 ^x	.001	.001	.164*	.001	.000	.152*
Delayed Memory	<.001	.001	.103	.000	.000	.112 ^x	.000	.000	.112 ^x	.001	.001	.133 ^x	<.001	.000	.103
Auditory Memory	.000	.001	.113 ^x	.000	.000	.118 ^x	.000	.000	.118 ^x	.001	.001	.152*	.000	.000	.115 ^x
Visual Memory	.000	.001	.064	.000	.000	.065	.000	.000	.072	.001	.001	.079	.000	.000	.065
General Intelligence	-.001	.001	.228**	<-.001	.000	.225**	.000	.000	.228**	.001	.000	.244**	.001	.000	.243**
Task Switching	.000	.000	.098	<-.001	.000	.093	<-.001	.000	.098	<-.001	.000	.096	<.001	.000	.092
Crystallized Intelligence	.001	.001	.315**	.000	.000	.316**	.000	.000	.314**	<-.001	.001	.313**	.000	.000	.314**

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

Table 2.5 | F statistics from moderation analyses, FDR corrected: general intelligence (DV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Cuneus</u>						
Cryptoxanthin (<i>df</i> = 97)	3.212	0.003	0.209	0.594	0.443	0.005
Lutein (<i>df</i> = 96)	3.682	0.001	0.235	0.187	0.666	0.002
Zeaxanthin (<i>df</i> = 98)	6.146	0.000	0.334	4.262	0.042	0.029
<u>Precuneus</u>						
Cryptoxanthin (<i>df</i> = 97)	3.456	0.002	0.222	0.048	0.827	0.000
Lutein (<i>df</i> = 96)	3.992	0.000	0.250	0.409	0.524	0.003
Zeaxanthin (<i>df</i> = 98)	5.441	0.000	0.308	0.830	0.364	0.006

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.6 | F statistics from moderation analyses, FDR corrected: immediate memory (DV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Cuneus</u>						
Cryptoxanthin (<i>df</i> = 99)	3.598	0.001	0.225	2.030	0.157	0.016
Lutein (<i>df</i> = 99)	2.543	0.015	0.171	4.033	0.047	0.034
Zeaxanthin (<i>df</i> = 100)	2.863	0.007	0.186	2.267	0.135	0.018
<u>Precuneus</u>						
Cryptoxanthin (<i>df</i> = 99)	4.138	0.000	0.251	0.071	0.791	0.000
Lutein (<i>df</i> = 99)	2.985	0.005	0.194	1.876	0.174	0.015
Zeaxanthin (<i>df</i> = 100)	3.808	0.001	0.234	6.261	0.014	0.048

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.7 | Demographic data

Age, $n(\bar{x} \pm SD)$; years	99(68.8 $\pm$ 2.0)
Sex, $n(\%F)$	99(62.6)
Body Mass Index (BMI), $n(\bar{x} \pm SD)$	99(26.0 $\pm$ 3.8)
Income, n (%)	
<15k	1(1.0)
15-25k	3(3.0)
25-50k	15(15.2)
50-75k	24(24.2)
75-100k	24(24.2)
>100k	32(32.3)
Education, n (%)	
Some high school	1(1.0)
High school degree	11(11.1)
Some college	17(17.2)
College degree	70(70.7)
Xanthophyll Carotenoids, $n(\bar{x} \pm SD)$; nmol/mL	
Cryptoxanthin	94(1.557 $\times 10^{-1} \pm 0.094$)
Lutein	93(3.857 $\times 10^{-1} \pm 0.182$)
Zeaxanthin	95(7.848 $\times 10^{-2} \pm 0.043$)
Facets of Intelligence, $n(\bar{x} \pm SD)$	
Auditory Memory	94(112.7 $\pm$ 11.0)
Crystallized Intelligence	95(113.6 $\pm$ 12.7)
Delayed Memory	95(112.8 $\pm$ 11.2)
General Intelligence	93(116.4 $\pm$ 11.0)
Immediate Memory	95(114.3 $\pm$ 11.0)
Default Mode Network (DMN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(2.466 $\times 10^{-1} \pm 0.030$)
Local Efficiency	99(3.004 $\times 10^{-1} \pm 0.023$)
Small World Propensity	99(6.670 $\times 10^{-1} \pm 0.051$)
Frontoparietal Network (FPN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(2.700 $\times 10^{-1} \pm 0.046$)
Local Efficiency	99(3.295 $\times 10^{-1} \pm 0.039$)
Small World Propensity	99(6.558 $\times 10^{-1} \pm 0.077$)
Visual Network (VisN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(3.099 $\times 10^{-1} \pm 0.041$)
Local Efficiency	99(3.384 $\times 10^{-1} \pm 0.031$)
Small World Propensity	99(5.422 $\times 10^{-1} \pm 0.116$)
Dorsal Attention Network (DAN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(3.021 $\times 10^{-1} \pm 0.040$)
Local Efficiency	99(3.524 $\times 10^{-1} \pm 0.028$)
Small World Propensity	99(5.840 $\times 10^{-1} \pm 0.104$)
Ventral Attention Network (VAN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(3.328 $\times 10^{-1} \pm 0.049$)
Local Efficiency	99(3.800 $\times 10^{-1} \pm 0.041$)
Small World Propensity	99(5.179 $\times 10^{-1} \pm 0.137$)

Table 2.8 | Linear Regression models of network characteristics correlated with facets of intelligence measured by WMS – IV

	<u>Crystallized Intelligence</u>			<u>General Intelligence</u>		
	β	β SE	R^2	β	β SE	R^2
<u>Default Mode Network</u>						
Local Efficiency	-49.634	47.959	.321**	29.179	45.182	.229*
Global Efficiency	-69.755	38.955	.337**	2.181	37.225	.225*
Small World Propensity	-18.749	22.508	.318**	-51.502	20.471	.278**
<u>Frontoparietal Network</u>						
Local Efficiency	-17.157	29.070	.316**	42.801	26.949	.247**
Global Efficiency	-41.324	24.316	.335**	16.687	23.126	.229*
Small World Propensity	32.261	14.242	.351**	3.783	13.747	.225*
<u>Visual Network</u>						
Local Efficiency	-32.538	36.593	.319**	-24.058	34.405	.229*
Global Efficiency	-54.931	27.633	.343**	-29.568	26.322	.236*
Small World Propensity	17.795	9.898	.337**	5.443	9.526	.228*
<u>Dorsal Attention Network</u>						
Local Efficiency	-67.726	39.204	.336**	-79.988	36.411	.266**
Global Efficiency	-72.183	27.169	.364**	-49.129	25.971	.256**
Small World Propensity	41.165	10.024	.423**	14.812	10.146	.244**
<u>Ventral Attention Network</u>						
Local Efficiency	-77.832	26.496	.374**	-54.193	25.399	.264**
Global Efficiency	-77.399	22.529	.394**	-45.711	21.975	.262**
Small World Propensity	4.542	8.102	.315**	-0.154	7.619	.225*

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

Table 2.9 | Linear Regression models of network characteristics correlated with facets of intelligence measured by WASI – II

	<u>Auditory Memory</u>			<u>Delayed Memory</u>			<u>Immediate Memory</u>		
	β	βSE	R^2	β	βSE	R^2	β	βSE	R^2
<u>Default Mode Network</u>									
Local Efficiency	12.561	51.718	.113	18.534	52.698	.104	45.745	48.490	.136 ^x
Global Efficiency	0.984	42.522	.112	-2.304	43.343	.103	19.542	40.002	.130
Small World Propensity	-25.960	24.069	.124	-18.982	24.614	.109	-11.734	22.79	.130
<u>Frontoparietal Network</u>									
Local Efficiency	21.456	31.147	.117	12.741	31.806	.104	20.125	29.342	.132 ^x
Global Efficiency	9.987	26.475	.114	9.902	26.988	.104	12.392	24.925	.130
Small World Propensity	3.171	15.706	.113	1.139	16.013	.103	4.569	14.791	.128
<u>Visual Network</u>									
Local Efficiency	44.196	39.126	.125	11.543	40.154	.103	30.354	36.985	.134 ^x
Global Efficiency	30.617	30.109	.123	16.391	30.823	.105	18.445	28.463	.131 ^x
Small World Propensity	-0.058	10.902	.112	1.529	11.111	.103	-0.313	10.269	.127
<u>Dorsal Attention Network</u>									
Local Efficiency	30.879	42.614	.117	5.769	43.564	.103	13.170	40.239	.128
Global Efficiency	33.633	30.062	.125	18.717	30.797	.106	14.924	28.477	.130
Small World Propensity	-12.369	11.657	.123	-11.348	11.898	.112	-1.212	11.051	.127
<u>Ventral Attention Network</u>									
Local Efficiency	-22.185	29.675	.118	-53.662	29.801	.134 ^x	-40.058	27.717	.147 ^x
Global Efficiency	-7.457	25.713	.113	-26.057	26.075	.113	-11.356	24.203	.129
Small World Propensity	-0.145	8.703	.112	2.360	8.867	.103	2.029	8.195	.128

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

Table 2.10 | F statistics from moderation analyses, FDR corrected: DMN efficiency (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	5.828	.000	.365	2.268	.136	.018
Lutein (<i>df</i> = 80)	6.112	.000	.379	0.329	.568	.003
Zeaxanthin (<i>df</i> = 82)	7.503	.000	.423	3.716	.057	.026
Global Efficiency						
Cryptoxanthin (<i>df</i> = 81)	6.021	.000	.373	0.506	.479	.004
Lutein (<i>df</i> = 80)	6.614	.000	.398	0.886	.349	.007
Zeaxanthin (<i>df</i> = 82)	8.464	.000	.452	7.048	.010	.047
Small World Propensity						
Cryptoxanthin (<i>df</i> = 81)	5.568	.000	.355	0.007	.934	.000
Lutein (<i>df</i> = 80)	6.377	.000	.389	0.728	.396	.006
Zeaxanthin (<i>df</i> = 82)	7.699	.000	.429	2.002	.161	.014
<u>Immediate Memory</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	2.819	.008	.218	1.707	.195	.016
Lutein (<i>df</i> = 81)	2.092	.046	.171	4.576	.035	.047
Zeaxanthin (<i>df</i> = 82)	2.548	.016	.199	5.096	.037	.050

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.11 | F statistics from moderation analyses, FDR corrected: FPN efficiency (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	6.630	.000	.396	6.631	.012	.050
Lutein (<i>df</i> = 80)	5.786	.000	.366	0.137	.712	.001
Zeaxanthin (<i>df</i> = 82)	6.530	.000	.389	0.087	.769	.001
Global Efficiency						
Cryptoxanthin (<i>df</i> = 81)	6.096	.000	.376	2.269	.136	.018
Lutein (<i>df</i> = 80)	6.106	.000	.379	0.390	.534	.003
Zeaxanthin (<i>df</i> = 82)	7.254	.000	.414	3.516	.064	.025
Small World Propensity						
Cryptoxanthin (<i>df</i> = 81)	5.961	.000	.371	0.001	.971	.000
Lutein (<i>df</i> = 80)	6.309	.000	.387	0.187	.667	.001
Zeaxanthin (<i>df</i> = 82)	8.104	.000	.442	1.844	.178	.013
<u>Immediate Memory</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	2,973	.006	.227	2.992	.088	.029
Lutein (<i>df</i> = 81)	2.254	.032	.182	5.280	.024	.053
Zeaxanthin (<i>df</i> = 82)	2.076	.048	.168	2.338	.130	.024

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.12 | F statistics from moderation analyses, FDR corrected: DAN efficiency (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	5.911	.000	.369	1.204	.276	.009
Lutein (<i>df</i> = 80)	6.211	.000	.383	0.546	.462	.004
Zeaxanthin (<i>df</i> = 82)	7.074	.000	.408	0.442	.508	.003
Global Efficiency						
Cryptoxanthin (<i>df</i> = 81)	7.153	.000	.414	3.884	.052	.028
Lutein (<i>df</i> = 80)	7.343	.000	.423	2.813	.097	.020
Zeaxanthin (<i>df</i> = 82)	7.708	.000	.429	1.180	.281	.008
Small World Propensity						
Cryptoxanthin (<i>df</i> = 81)	9.263	.000	.478	3.936	.051	.025
Lutein (<i>df</i> = 80)	8.861	.000	.470	4.833	.031	.032
Zeaxanthin (<i>df</i> = 82)	8.968	.000	.467	0.781	.379	.005

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.13 | F statistics from moderation analyses, FDR corrected: VAN efficiency (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	7.285	.000	.418	0.136	.713	.001
Lutein (<i>df</i> = 80)	7.098	.000	.415	0.036	.850	.000
Zeaxanthin (<i>df</i> = 82)	8.266	.000	.446	1.478	.228	.010
Global Efficiency						
Cryptoxanthin (<i>df</i> = 81)	7.933	.000	.439	0.310	.580	.580
Lutein (<i>df</i> = 80)	7.714	.000	.436	1.591	.211	.011
Zeaxanthin (<i>df</i> = 82)	9.458	.000	.480	4.007	.049	.025
Small World Propensity						
Cryptoxanthin (<i>df</i> = 81)	5.449	.000	.350	0.030	.863	.000
Lutein (<i>df</i> = 80)	5.988	.000	.374	0.941	.335	.007
Zeaxanthin (<i>df</i> = 82)	6.494	.000	.388	0.124	.726	.001
<u>Delayed Memory</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 82)	1.914	.069	.157	0.001	.977	.000
Lutein (<i>df</i> = 82)	1.907	.070	.157	0.003	.958	.000
Zeaxanthin (<i>df</i> = 83)	2.258	.031	.179	1.576	.213	.016
<u>Immediate Memory</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	2.646	.012	.207	0.002	.968	0.000
Lutein (<i>df</i> = 81)	1.586	.142	.135	0.010	.919	0.000
Zeaxanthin (<i>df</i> = 82)	2.051	.050	.167	1.226	.271	0.012

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.14 | Demographic data

Age, $n(\bar{x} \pm SD)$; years	121(68.8 $\pm$ 3.0)
Sex, $n(\%F)$	121(62.0)
Body Mass Index (BMI), $n(\bar{x} \pm SD)$	121(26.0 $\pm$ 3.8)
Income, $n(\%)$	
<15k	1(0.8)
15-25k	5(4.1)
25-50k	22(18.2)
50-75k	26(21.5)
75-100k	28(23.1)
>100k	39(32.2)
Education, $n(\%)$	
Some high school	1(0.8)
High school degree	12(9.9)
Some college	22(18.2)
College degree	86(71.1)
Xanthophyll Carotenoids, $n(\bar{x} \pm SD)$; nmol/mL	
Cryptoxanthin	116(1.586 $\times 10^{-1} \pm 0.091$)
Lutein	115(3.931 $\times 10^{-1} \pm 0.190$)
Zeaxanthin	117(7.971 $\times 10^{-2} \pm 0.042$)
Facets of Intelligence, $n(\bar{x} \pm SD)$	
Crystallized Intelligence	113(114.2 $\pm$ 12.6)
General Intelligence	113(117.0 $\pm$ 11.0)
Immediate Memory	115(114.6 $\pm$ 11.2)
White Matter Integrity, $n(\bar{x} \pm SD)$	
Global White Matter AxD	115(1.266 $\times 10^{-3} \pm 4.325 \times 10^{-5}$)
Global White Matter RD	115(7.017 $\times 10^{-4} \pm 5.109 \times 10^{-5}$)
Global White Matter FA	115(6.074 $\times 10^{-1} \pm 2.451 \times 10^{-2}$)
Corpus Callosum (Genu) AxD	115(1.501 $\times 10^{-3} \pm 6.190 \times 10^{-5}$)
Corpus Callosum (Genu) RD	115(5.691 $\times 10^{-4} \pm 8.457 \times 10^{-5}$)
Corpus Callosum (Genu) FA	115(7.281 $\times 10^{-1} \pm 4.708 \times 10^{-2}$)
Corpus Callosum (Body) AxD	115(1.557 $\times 10^{-3} \pm 6.889 \times 10^{-5}$)
Corpus Callosum (Body) RD	115(6.328 $\times 10^{-4} \pm 8.040 \times 10^{-5}$)
Corpus Callosum (Body) FA	115(6.979 $\times 10^{-1} \pm 3.995 \times 10^{-2}$)
Uncinate Fasciculus AxD	115(1.162 $\times 10^{-3} \pm 7.754 \times 10^{-5}$)
Uncinate Fasciculus RD	115(7.804 $\times 10^{-4} \pm 1.371 \times 10^{-4}$)
Uncinate Fasciculus FA	115(5.394 $\times 10^{-1} \pm 5.231 \times 10^{-2}$)
Corticospinal Tract AxD	115(1.087 $\times 10^{-3} \pm 9.357 \times 10^{-5}$)
Corticospinal Tract RD	115(5.750 $\times 10^{-4} \pm 6.463 \times 10^{-5}$)
Corticospinal Tract FA	115(6.732 $\times 10^{-1} \pm 3.362 \times 10^{-2}$)
Anterior Corona Radiata AxD	115(1.154 $\times 10^{-3} \pm 4.800 \times 10^{-5}$)
Anterior Corona Radiata RD	115(8.613 $\times 10^{-4} \pm 7.420 \times 10^{-5}$)
Anterior Corona Radiata FA	115(4.700 $\times 10^{-1} \pm 3.275 \times 10^{-2}$)
Posterior Corona Radiata AxD	115(1.267 $\times 10^{-3} \pm 7.154 \times 10^{-5}$)
Posterior Corona Radiata RD	115(8.775 $\times 10^{-4} \pm 6.984 \times 10^{-5}$)
Posterior Corona Radiata FA	115(5.121 $\times 10^{-1} \pm 3.282 \times 10^{-2}$)
Superior Corona Radiata AxD	115(1.120 $\times 10^{-3} \pm 4.557 \times 10^{-5}$)
Superior Corona Radiata RD	115(7.687 $\times 10^{-4} \pm 5.936 \times 10^{-5}$)
Superior Corona Radiata FA	115(5.187 $\times 10^{-1} \pm 2.746 \times 10^{-2}$)
Posterior Thalamic Radiation AxD	115(1.409 $\times 10^{-3} \pm 7.860 \times 10^{-5}$)
Posterior Thalamic Radiation RD	115(8.048 $\times 10^{-4} \pm 1.100 \times 10^{-4}$)

Table 2.14 (cont.) | Demographic data, continued

White Matter Integrity, $n(\bar{x} \pm SD)$	
Posterior Thalamic Radiation FA	115($6.029 \times 10^{-1} \pm 4.838 \times 10^{-2}$)
Superior Longitudinal Fasciculus AxD	115($1.142 \times 10^{-3} \pm 4.072 \times 10^{-5}$)
Superior Longitudinal Fasciculus RD	115($7.976 \times 10^{-4} \pm 5.769 \times 10^{-5}$)
Superior Longitudinal Fasciculus FA	115($5.251 \times 10^{-1} \pm 2.761 \times 10^{-2}$)
Cingulum – Cingulate Gyrus AxD	115($1.214 \times 10^{-3} \pm 6.373 \times 10^{-5}$)
Cingulum – Cingulate Gyrus RD	115($6.854 \times 10^{-4} \pm 5.823 \times 10^{-5}$)
Cingulum – Cingulate Gyrus FA	115($6.131 \times 10^{-1} \pm 3.371 \times 10^{-2}$)
Cingulum – Hippocampus AxD	115($9.796 \times 10^{-4} \pm 9.747 \times 10^{-5}$)
Cingulum – Hippocampus RD	115($5.644 \times 10^{-4} \pm 7.716 \times 10^{-5}$)
Cingulum – Hippocampus FA	115($6.576 \times 10^{-1} \pm 4.414 \times 10^{-2}$)
External Capsule AxD	115($1.135 \times 10^{-3} \pm 4.970 \times 10^{-5}$)
External Capsule RD	115($8.807 \times 10^{-4} \pm 7.574 \times 10^{-5}$)
External Capsule FA	115($4.694 \times 10^{-1} \pm 2.666 \times 10^{-2}$)
Anterior Limb of the Internal Capsule AxD	115($1.191 \times 10^{-3} \pm 5.548 \times 10^{-5}$)
Anterior Limb of the Internal Capsule RD	115($6.812 \times 10^{-4} \pm 6.346 \times 10^{-5}$)
Anterior Limb of the Internal Capsule FA	115($6.091 \times 10^{-1} \pm 2.969 \times 10^{-2}$)
Posterior Limb of the Internal Capsule AxD	115($1.252 \times 10^{-3} \pm 5.883 \times 10^{-5}$)
Posterior Limb of the Internal Capsule RD	115($5.543 \times 10^{-4} \pm 6.460 \times 10^{-5}$)
Posterior Limb of the Internal Capsule FA	115($7.052 \times 10^{-1} \pm 3.659 \times 10^{-2}$)
Inferior Cerebellar Peduncle AxD	115($1.177 \times 10^{-3} \pm 5.956 \times 10^{-5}$)
Inferior Cerebellar Peduncle RD	115($7.020 \times 10^{-4} \pm 5.152 \times 10^{-5}$)
Inferior Cerebellar Peduncle FA	115($5.940 \times 10^{-1} \pm 3.472 \times 10^{-2}$)
Middle Cerebellar Peduncle AxD	115($1.142 \times 10^{-3} \pm 6.353 \times 10^{-5}$)
Middle Cerebellar Peduncle RD	115($5.650 \times 10^{-4} \pm 5.055 \times 10^{-5}$)
Middle Cerebellar Peduncle FA	115($6.808 \times 10^{-1} \pm 2.927 \times 10^{-2}$)
Superior Cerebellar Peduncle AxD	115($1.442 \times 10^{-3} \pm 9.764 \times 10^{-5}$)
Superior Cerebellar Peduncle RD	115($5.634 \times 10^{-4} \pm 5.476 \times 10^{-5}$)
Superior Cerebellar Peduncle FA	115($7.318 \times 10^{-1} \pm 2.959 \times 10^{-2}$)
Fornix AxD	115($2.181 \times 10^{-3} \pm 2.812 \times 10^{-4}$)
Fornix RD	115($1.905 \times 10^{-3} \pm 5.622 \times 10^{-4}$)
Fornix FA	115($4.370 \times 10^{-1} \pm 9.873 \times 10^{-2}$)

Table 2.15 | Linear Regression models of white matter tract characteristics associated with facets of intelligence

	<u>Immediate Memory</u>			<u>General Intelligence</u>			<u>Crystallized Intelligence</u>		
	β	β SE	R^2	β	β SE	R^2	β	β SE	R^2
<u>Global White Matter</u>									
Axial Diffusion	16976.766	25052.999	.131 ^x	-29768.74	23105.30	.237**	-50927.96	24589.35	.341**
Radial Diffusion	-14929.49	20462.207	.132 ^x	-36852.81	18677.91	.253**	-10047.98	20484.51	.315**
Fractional Anisotropy	36.142	42.328	.133 ^x	66.524	38.850	.246**	-0.098	42.464	.313**
<u>Corpus Callosum (Genu)</u>									
Axial Diffusion	3236.041	17283.629	.128 ^x	-19165.59	15923.79	.236**	-25373.72	17098.01	.328**
Radial Diffusion	-5155.087	12317.989	.129 ^x	-13862.97	11354.16	.236**	2780.386	12321.764	.313**
Fractional Anisotropy	10.396	22.113	.129 ^x	15.734	20.476	.229**	-15.595	22.076	.316**
<u>Corpus Callosum (Body)</u>									
Axial Diffusion	11088.381	15178.727	.132 ^x	-11698.80	14069.56	.230**	-20070.48	15082.92	.325**
Radial Diffusion	-2571.794	12914.353	.128 ^x	-12166.23	11922.03	.233**	-780.542	12912.898	.313**
Fractional Anisotropy	9.697	26.008	.128 ^x	18.257	24.075	.229**	-4.782	26.013	.313**
<u>Uncinate Fasciculus</u>									
Axial Diffusion	-10308.424	13531.074	.132 ^x	808.558	12587.30	.225**	3511.904	13560.45	.313**
Radial Diffusion	-6990.842	7577.493	.134 ^x	-8783.762	7004.447	.237**	926.829	7605.713	.313**
Fractional Anisotropy	7.060	20.040	.128 ^x	29.000	18.378	.243**	8.660	20.027	.314**
<u>Corticospinal Tract</u>									
Axial Diffusion	9519.857	12357.554	.132 ^x	-17046.10	11372.01	.242**	-31359.39	11993.82	.356**
Radial Diffusion	8176.747	17119.973	.129 ^x	-29688.90	15625.24	.251**	-37576.92	16724.99	.345**
Fractional Anisotropy	-5.253	32.461	.127 ^x	50.745	29.696	.246**	40.844	32.203	.324**
<u>Anterior Corona Radiata</u>									
Axial Diffusion	10349.738	22077.537	.129 ^x	-16620.03	20436.48	.230**	-33140.83	21849.51	.328**
Radial Diffusion	-15833.619	14142.837	.138 ^x	-26829.82	12928.82	.256**	-9032.61	14195.60	.316**
Fractional Anisotropy	43.866	31.844	.143 ^x	62.667	29.157	.258**	8.248	32.114	.313**
<u>Posterior Corona Radiata</u>									
Axial Diffusion	-13817.017	14919.089	.134 ^x	-24410.09	13685.38	.248**	-17155.47	14879.56	.322**
Radial Diffusion	-9695.75	14974.456	.131 ^x	-24502.83	13706.49	.248**	-15267.18	14923.96	.320**
Fractional Anisotropy	11.969	31.714	.128 ^x	40.023	29.173	.239**	31.956	31.569	.320**
<u>Superior Corona Radiata</u>									
Axial Diffusion	-27853.391	23079.916	.139 ^x	-22772.65	21442.06	.233**	-17910.21	23166.55	.317**
Radial Diffusion	-15155.261	17623.727	.133 ^x	-30252.64	16131.54	.251**	-13049.68	17633.95	.317**
Fractional Anisotropy	5.315	38.163	.127 ^x	64.986	34.817	.250**	37.542	37.974	.320**
<u>Posterior Thalamic Radiation</u>									
Axial Diffusion	2843.649	13669.472	.128 ^x	-13565.32	12612.29	.234**	-14391.70	13593.93	.320**
Radial Diffusion	-8789.800	9496.924	.134 ^x	-16483.41	8694.51	.251**	-1761.176	9531.640	.313**
Fractional Anisotropy	16.780	21.476	.132 ^x	34.413	19.689	.247**	-1.430	21.533	.313**
<u>Superior Longitudinal Fasciculus</u>									
Axial Diffusion	8015.174	26308.767	.128 ^x	-9870.85	24397.58	.226**	-35718.50	26074.23	.325**
Radial Diffusion	-26252.726	18020.244	.145 ^x	-37205.85	16480.10	.262**	-4251.16	18193.13	.313**
Fractional Anisotropy	54.703	37.477	.145 ^x	88.966	33.998	.274**	22.223	37.784	.315**

Table 2.15 (cont.) | White matter tract regression models, continued

	<u>Immediate Memory</u>			<u>General Intelligence</u>			<u>Crystallized Intelligence</u>		
	β	β SE	R^2	β	β SE	R^2	β	β SE	R^2
<u>Cingulum (Cingulate Gyrus)</u>									
Axial Diffusion	6408.55	16590.91	.128 ^x	-749.670	15402.00	.225**	-13080.92	16547.46	.317**
Radial Diffusion	-19270.51	17963.94	.137 ^x	-24510.24	16580.15	.241**	13575.18	18007.80	.317**
Fractional Anisotropy	29.738	31.196	.135 ^x	36.884	28.836	.237**	-27.498	31.204	.318**
<u>Cingulum (Hippocampus)</u>									
Axial Diffusion	6525.53	11038.20	.130 ^x	-15287.50	10144.86	.242**	-15503.65	10946.47	.326**
Radial Diffusion	-2694.76	13938.16	.128 ^x	-17450.99	12816.59	.239**	-12106.32	13885.04	.318**
Fractional Anisotropy	12.030	24.273	.129 ^x	17.435	22.478	.229**	6.687	24.285	.314**
<u>External Capsule</u>									
Axial Diffusion	-6719.71	21774.31	.129 ^x	-14758.00	20156.06	.229**	-29776.28	21680.69	.319**
Radial Diffusion	-15271.91	13731.88	.138 ^x	-12767.39	12751.88	.232**	-2177.612	13807.67	.313**
Fractional Anisotropy	27.360	38.657	.131 ^x	31.341	35.813	.231**	1.622	38.738	.313**
<u>Internal Capsule (Anterior Limb)</u>									
Axial Diffusion	3823.171	19185.32	.128 ^x	-26783.81	17602.68	.242**	-42568.70	18714.73	.346**
Radial Diffusion	-8356.081	16849.784	.129 ^x	-12050.63	15604.21	.229**	-9331.184	16839.55	.315**
Fractional Anisotropy	29.954	35.415	.133 ^x	16.843	32.925	.227**	-16.800	35.488	.315**
<u>Internal Capsule (Posterior Limb)</u>									
Axial Diffusion	6994.316	17674.130	.129 ^x	-10554.76	16375.06	.228**	-21502.92	17553.74	.323**
Radial Diffusion	20.284	16390.575	.127 ^x	319.880	15205.26	.225**	9655.122	16357.99	.315**
Fractional Anisotropy	-7.067	29.262	.128 ^x	-7.826	27.143	.225**	-26.975	29.140	.319**
<u>Inferior Cerebellar Peduncle</u>									
Axial Diffusion	63949.65	16910.86	.233**	16650.87	16650.37	.232**	-	17982.52	.317**
							133333.52		
Radial Diffusion	5931.714	20804.68	.128 ^x	-24544.48	19154.18	.237**	10629.44	20780.23	.315**
Fractional Anisotropy	26.985	30.228	.134 ^x	48.463	27.737	.247**	-20.387	30.268	.316**
<u>Middle Cerebellar Peduncle</u>									
Axial Diffusion	231.728	18584.481	.127 ^x	-14249.12	17182.74	.230**	-36017.01	18233.72	.338**
Radial Diffusion	5759.897	21039.41	.128 ^x	-30208.31	19294.52	.243**	-9728.007	21018.92	.314**
Fractional Anisotropy	-16.231	35.770	.129 ^x	42.790	32.945	.237**	-2.503	35.794	.313**
<u>Superior Cerebellar Peduncle</u>									
Axial Diffusion	7706.320	11915.539	.131 ^x	-5992.25	11060.17	.227**	-14068.12	11854.511	.322**
Radial Diffusion	-7116.577	19769.158	.128 ^x	-13304.95	18303.63	.229**	-202.696	19775.82	.313**
Fractional Anisotropy	22.328	36.251	.130 ^x	38.136	33.479	.235**	-16.244	36.271	.314**
<u>Fornix</u>									
Axial Diffusion	-	3780.656	.211**	-4256.14	3664.99	.235**	-832.101	3974.721	.313**
	12576.528								
Radial Diffusion	-6799.959	1948.451	.219**	-2594.86	1893.11	.239**	667.202	2057.738	.314**
Fractional Anisotropy	35.653	10.943	.208**	17.872	10.510	.246**	-2.711	11.482	.313**

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

Table 2.16 | F statistics from moderation analyses, FDR corrected: global white matter (IV)

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.476	.000	.353	0.171	.680	.001
Lutein (<i>df</i> = 94)	6.940	.000	.371	3.407	.068	.023
Zeaxanthin (<i>df</i> = 97)	7.060	.000	.368	0.574	.450	.004
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.488	.000	.387	1.566	.214	.010
Lutein (<i>df</i> = 94)	8.465	.000	.419	5.827	.018	.036
Zeaxanthin*	-	-	-	-	-	-
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.529	.000	.355	0.407	.525	.003
Lutein (<i>df</i> = 94)	7.133	.000	.378	4.407	.038	.029
Zeaxanthin (<i>df</i> = 97)	7.309	.000	.376	1.977	.163	.013
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.626	.001	.234	0.731	.395	.006
Lutein (<i>df</i> = 94)	4.529	.000	.278	3.438	.067	.026
Zeaxanthin (<i>df</i> = 97)	5.409	.000	.309	1.500	.224	.011
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.845	.001	.245	3.457	.066	.028
Lutein (<i>df</i> = 94)	5.179	.000	.306	7.618	.007	.056
Zeaxanthin*	-	-	-	-	-	-
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.770	.001	.241	1.039	.311	.008
Lutein (<i>df</i> = 94)	4.879	.000	.293	4.388	.039	.033
Zeaxanthin (<i>df</i> = 97)	5.769	.000	.322	2.685	.105	.019
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.800	.001	.239	0.370	.544	.003
Lutein (<i>df</i> = 97)	2.389	.022	.165	0.511	.476	.004
Zeaxanthin (<i>df</i> = 99)	2.739	.009	.181	0.032	.859	.000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.757	.001	.237	0.107	.744	.001
Lutein (<i>df</i> = 97)	2.984	.005	.198	4.220	.043	.035
Zeaxanthin*	-	-	-	-	-	-
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.750	.001	.236	0.202	.654	.002
Lutein (<i>df</i> = 97)	2.424	.020	.167	0.776	.381	.007
Zeaxanthin (<i>df</i> = 99)	2.717	.010	.180	0.016	.899	.000

All significant overall models remained significant after FDR correction; significant interactions are in bold.

*Collinearity exists with the intercept term of the moderation analysis

**Table 2.17 | F statistics from moderation analyses, FDR corrected:
genu of the corpus callosum (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.328	.002	.219	1.053	.307	.009
Lutein (<i>df</i> = 94)	4.048	.000	.256	2.590	.111	.020
Zeaxanthin (<i>df</i> = 97)	5.358	.000	.306	2.083	.152	.015
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	4.422	.000	.271	7.163	.009	.055
Lutein (<i>df</i> = 94)	4.449	.000	.275	4.018	.048	.031
Zeaxanthin (<i>df</i> = 97)	5.952	.000	.329	4.713	.032	.033
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.530	.001	.229	1.721	.193	.014
Lutein (<i>df</i> = 94)	4.198	.000	.263	3.065	.083	.024
Zeaxanthin (<i>df</i> = 97)	5.588	.000	.316	2.932	.090	.021
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.882	.000	.242	1.017	.316	.008
Lutein (<i>df</i> = 97)	2.317	.026	.160	0.081	.776	.001
Zeaxanthin (<i>df</i> = 99)	2.900	.006	.190	1.207	.274	.010
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.658	.001	.232	0.184	.669	.002
Lutein (<i>df</i> = 97)	2.510	.016	.172	1.452	.231	.012
Zeaxanthin (<i>df</i> = 99)	3.740	.001	.232	6.773	.011	.052
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.870	.000	.242	0.913	.342	.007
Lutein (<i>df</i> = 97)	2.304	.026	.160	0.041	.841	.000
Zeaxanthin (<i>df</i> = 99)	2.761	.008	.182	0.356	.552	.003

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.18 | F statistics from moderation analyses, FDR corrected:
body of the corpus callosum (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.750	.001	.236	0.105	.746	.001
Lutein (<i>df</i> = 97)	2.299	.027	.159	0.031	.861	.000
Zeaxanthin (<i>df</i> = 99)	3.120	.004	.201	2.625	.108	.021
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.926	.000	.245	0.400	.529	.003
Lutein (<i>df</i> = 97)	3.075	.004	.202	4.640	.034	.038
Zeaxanthin (<i>df</i> = 99)	4.032	.000	.246	7.511	.007	.057
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.702	.001	.234	0.149	.701	.001
Lutein (<i>df</i> = 97)	2.299	.027	.159	0.002	.966	.000
Zeaxanthin (<i>df</i> = 99)	2.887	.006	.189	1.216	.273	.010

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.19 | F statistics from moderation analyses, FDR corrected: uncinata fasciculus (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
General Intelligence						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.905	.000	.248	1.875	.174	.015
Lutein (<i>df</i> = 94)	3.926	.000	.250	0.874	.352	.007
Zeaxanthin (<i>df</i> = 97)	6.022	.000	.332	4.388	.039	.030
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.494	.001	.227	2.368	.127	.019
Lutein (<i>df</i> = 94)	3.936	.000	.251	2.074	.153	.016
Zeaxanthin (<i>df</i> = 97)	5.121	.000	.297	0.845	.360	.006
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	4.081	.000	.256	4.375	.039	.034
Lutein (<i>df</i> = 94)	3.993	.000	.254	1.535	.218	.012
Zeaxanthin (<i>df</i> = 97)	5.825	.000	.324	3.980	.049	.028

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.20 | F statistics from moderation analyses, FDR corrected: corticospinal tract (IV)

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	8.046	.000	.404	7.421	.008	.047
Lutein (<i>df</i> = 94)	6.557	.000	.358	0.353	.554	.002
Zeaxanthin (<i>df</i> = 97)	7.207	.000	.373	0.562	.455	.004
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.760	.000	.395	0.584	.447	.004
Lutein (<i>df</i> = 94)	8.181	.000	.410	1.602	.209	.010
Zeaxanthin (<i>df</i> = 97)	10.799	.000	.471	11.11	.001	.061
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	8.229	.000	.409	5.078	.026	.032
Lutein (<i>df</i> = 94)	7.361	.000	.385	0.511	.476	.003
Zeaxanthin (<i>df</i> = 97)	8.260	.000	.405	2.675	.105	.016
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.662	.001	.236	0.783	.379	.006
Lutein (<i>df</i> = 94)	4.177	.000	.262	0.003	.957	.000
Zeaxanthin (<i>df</i> = 97)	5.370	.000	.307	0.158	.692	.001
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.547	.001	.230	0.438	.510	.004
Lutein (<i>df</i> = 94)	4.506	.000	.277	2.432	.122	.019
Zeaxanthin (<i>df</i> = 97)	7.035	.000	.367	7.290	.008	.048
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.789	.001	.242	0.856	.357	.007
Lutein (<i>df</i> = 94)	4.400	.000	.272	0.138	.711	.001
Zeaxanthin (<i>df</i> = 97)	5.784	.000	.323	1.019	.315	.007
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.734	.001	.235	0.631	.429	.005
Lutein (<i>df</i> = 97)	2.385	.022	.164	0.611	.436	.005
Zeaxanthin (<i>df</i> = 99)	2.767	.008	.183	0.259	.612	.002
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.805	.001	.239	0.469	.495	.004
Lutein (<i>df</i> = 97)	3.015	.005	.199	4.806	.031	.040
Zeaxanthin (<i>df</i> = 99)	3.537	.001	.222	5.312	.023	.042
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.853	.001	.241	1.230	.270	.010
Lutein (<i>df</i> = 97)	2.315	.026	.160	0.119	.731	.001
Zeaxanthin (<i>df</i> = 99)	2.745	.009	.182	0.001	.974	.000

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.21 | F statistics from moderation analyses, FDR corrected:
anterior corona radiata (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.505	.000	.354	0.025	.876	.000
Lutein (<i>df</i> = 94)	6.684	.000	.363	2.086	.152	.014
Zeaxanthin (<i>df</i> = 97)	6.919	.000	.363	0.001	.976	.000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.372	.000	.383	4.114	.045	.027
Lutein (<i>df</i> = 94)	7.187	.000	.380	3.246	.075	.021
Zeaxanthin (<i>df</i> = 97)	8.333	.000	.407	4.295	.041	.026
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.707	.000	.361	1.136	.289	.008
Lutein (<i>df</i> = 94)	7.155	.000	.378	4.249	.042	.028
Zeaxanthin (<i>df</i> = 97)	7.263	.000	.375	1.379	.243	.009
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.978	.000	.251	0.623	.432	.005
Lutein (<i>df</i> = 94)	4.752	.000	.288	2.942	.090	.022
Zeaxanthin (<i>df</i> = 97)	5.619	.000	.317	0.826	.366	.006
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	4.402	.000	.270	7.925	.006	.061
Lutein (<i>df</i> = 94)	4.244	.000	.265	3.420	.068	.027
Zeaxanthin (<i>df</i> = 97)	5.878	.000	.326	4.579	.035	.032
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	4.149	.000	.259	2.825	.096	.022
Lutein (<i>df</i> = 94)	4.883	.000	.294	3.915	.051	.029
Zeaxanthin (<i>df</i> = 97)	5.966	.000	.330	2.594	.110	.018

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.22 | F statistics from moderation analyses, FDR corrected:
superior corona radiata (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.708	.000	.361	0.740	.392	.005
Lutein (<i>df</i> = 94)	6.792	.000	.366	2.308	.132	.016
Zeaxanthin (<i>df</i> = 97)	7.128	.000	.370	0.947	.333	.006
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.525	.000	.355	0.150	.700	.001
Lutein (<i>df</i> = 94)	6.941	.000	.371	2.047	.156	.014
Zeaxanthin (<i>df</i> = 97)	7.804	.000	.392	2.413	.124	.015
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.744	.000	.362	1.432	.234	.010
Lutein (<i>df</i> = 94)	7.237	.000	.381	4.521	.036	.030
Zeaxanthin (<i>df</i> = 97)	7.297	.000	.376	1.652	.202	.011

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.23 | F statistics from moderation analyses, FDR corrected:
posterior corona radiata (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.378	.002	.222	0.496	.483	.004
Lutein (<i>df</i> = 94)	3.925	.000	.250	1.187	.279	.010
Zeaxanthin (<i>df</i> = 97)	5.208	.000	.300	0.938	.335	.007
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.734	.001	.239	1.614	.207	.013
Lutein (<i>df</i> = 94)	5.009	.000	.299	4.683	.033	.035
Zeaxanthin (<i>df</i> = 97)	5.596	.000	.316	1.588	.211	.011
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.563	.001	.231	0.992	.322	.008
Lutein (<i>df</i> = 94)	4.391	.000	.272	2.275	.135	.018
Zeaxanthin (<i>df</i> = 97)	5.386	.000	.308	1.277	.261	.009

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.24 | F statistics from moderation analyses, FDR corrected:
posterior thalamic radiation (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.491	.001	.227	0.320	.573	.003
Lutein (<i>df</i> = 94)	3.998	.000	.254	0.665	.417	.005
Zeaxanthin (<i>df</i> = 97)	5.116	.000	.297	0.062	.804	.000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.564	.001	.231	2.236	.138	.018
Lutein (<i>df</i> = 94)	4.635	.000	.283	4.737	.032	.036
Zeaxanthin (<i>df</i> = 97)	5.450	.000	.310	1.856	.176	.013
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.592	.001	.232	0.550	.460	.004
Lutein (<i>df</i> = 94)	4.343	.000	.270	2.150	.146	.017
Zeaxanthin (<i>df</i> = 97)	5.181	.000	.299	0.015	.902	.000

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.25 | F statistics from moderation analyses, FDR corrected:
superior longitudinal fasciculus (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.493	.000	.354	0.113	.738	.001
Lutein (<i>df</i> = 94)	6.996	.000	.373	3.031	.085	.020
Zeaxanthin (<i>df</i> = 97)	7.012	.000	.366	0.228	.634	.002
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.650	.000	.359	0.001	.970	.000
Lutein (<i>df</i> = 94)	7.336	.000	.384	3.876	.052	.025
Zeaxanthin*	-	-	-	-	-	-
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.500	.000	.354	0.320	.573	.002
Lutein (<i>df</i> = 94)	7.146	.000	.378	4.249	.042	.028
Zeaxanthin (<i>df</i> = 97)	7.168	.000	.372	1.244	.267	.008
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	4.069	.000	.255	0.206	.651	.002
Lutein (<i>df</i> = 94)	5.365	.000	.314	2.972	.088	.022
Zeaxanthin (<i>df</i> = 97)	5.689	.000	.319	0.535	.466	.004
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.229	.003	.214	0.741	.392	.006
Lutein (<i>df</i> = 94)	4.527	.000	.278	5.644	.020	.043
Zeaxanthin (<i>df</i> = 97)	6.182	.000	.338	6.933	.010	.047
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.815	.001	.243	0.421	.518	.003
Lutein (<i>df</i> = 94)	5.257	.000	.309	3.873	.052	.028
Zeaxanthin (<i>df</i> = 97)	5.653	.000	.318	1.392	.241	.010

All significant overall models remained significant after FDR correction; significant interactions are in bold

*Collinearity exists with the intercept term of the moderation analysis

**Table 2.26 | F statistics from moderation analyses, FDR corrected:
cingulum – hippocampus (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.531	.000	.355	0.002	.965	.000
Lutein (<i>df</i> = 94)	6.276	.000	.348	0.028	.867	.000
Zeaxanthin (<i>df</i> = 97)	6.929	.000	.364	0.053	.819	.000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.941	.000	.369	0.293	.589	.002
Lutein (<i>df</i> = 94)	7.621	.000	.393	3.574	.062	.023
Zeaxanthin (<i>df</i> = 97)	9.632	.000	.443	9.980	.002	.057
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.707	.000	.361	0.054	.818	.000
Lutein (<i>df</i> = 94)	6.479	.000	.355	0.388	.535	.003
Zeaxanthin (<i>df</i> = 97)	7.077	.000	.368	0.033	.856	.000
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.896	.000	.243	1.294	.258	.010
Lutein (<i>df</i> = 97)	2.814	.008	.188	3.491	.065	.029
Zeaxanthin (<i>df</i> = 99)	3.843	.001	.237	7.478	.007	.058
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.872	.000	.242	0.101	.752	.001
Lutein (<i>df</i> = 97)	3.237	.003	.211	6.187	.015	.050
Zeaxanthin (<i>df</i> = 99)	2.956	.005	.193	1.256	.265	.010
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.901	.000	.243	0.703	.404	.006
Lutein (<i>df</i> = 97)	3.067	.004	.202	5.148	.026	.042
Zeaxanthin (<i>df</i> = 99)	3.446	.002	.218	4.859	.030	.038

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 2.27 | F statistics from moderation analyses, FDR corrected: external capsule (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.493	.001	.227	1.297	.258	.010
Lutein (<i>df</i> = 94)	4.191	.000	.263	3.176	.078	.025
Zeaxanthin (<i>df</i> = 97)	5.331	.000	.305	2.009	.160	.014
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.423	.002	.224	1.567	.214	.013
Lutein (<i>df</i> = 94)	4.152	.000	.261	2.514	.116	.020
Zeaxanthin (<i>df</i> = 97)	6.249	.000	.340	6.045	.016	.041
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.790	.001	.242	3.116	.081	.025
Lutein (<i>df</i> = 94)	4.207	.000	.264	2.823	.096	.022
Zeaxanthin (<i>df</i> = 97)	5.648	.000	.318	3.217	.076	.023

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.28 | F statistics from moderation analyses, FDR corrected:
anterior limb of the internal capsule (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.461	.000	.352	0.004	.952	.000
Lutein (<i>df</i> = 94)	6.450	.000	.354	0.847	.360	.006
Zeaxanthin (<i>df</i> = 97)	7.119	.000	.370	0.532	.467	.004
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.888	.000	.399	2.491	.118	.016
Lutein (<i>df</i> = 94)	8.100	.000	.408	3.141	.080	.020
Zeaxanthin (<i>df</i> = 97)	9.737	.000	.445	5.367	.023	.031
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.670	.000	.360	0.906	.344	.006
Lutein (<i>df</i> = 94)	6.902	.000	.370	2.845	.095	.019
Zeaxanthin (<i>df</i> = 97)	7.301	.000	.376	1.802	.183	.012
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.192	.003	.212	0.043	.836	.000
Lutein (<i>df</i> = 94)	3.844	.001	.246	1.072	.303	.009
Zeaxanthin (<i>df</i> = 97)	5.264	.000	.303	1.721	.193	.012
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	4.216	.000	.262	4.611	.034	.036
Lutein (<i>df</i> = 94)	4.484	.000	.276	2.527	.115	.020
Zeaxanthin (<i>df</i> = 97)	6.994	.000	.366	7.147	.009	.047
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.508	.001	.228	1.810	.182	.015
Lutein (<i>df</i> = 94)	4.233	.000	.265	3.172	.078	.025
Zeaxanthin (<i>df</i> = 97)	5.683	.000	.319	3.866	.052	.027

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.29 | F statistics from moderation analyses, FDR corrected:
posterior limb of the internal capsule (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.787	.000	.364	0.460	.499	.003
Lutein (<i>df</i> = 94)	6.638	.000	.361	0.252	.617	.002
Zeaxanthin (<i>df</i> = 97)	7.444	.000	.380	0.240	.625	.002
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.192	.000	.377	1.066	.304	.007
Lutein (<i>df</i> = 94)	7.110	.000	.377	2.154	.146	.014
Zeaxanthin (<i>df</i> = 97)	9.989	.000	.452	10.72	.002	.061
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.745	.000	.362	1.062	.305	.007
Lutein (<i>df</i> = 94)	6.598	.000	.360	0.904	.344	.006
Zeaxanthin (<i>df</i> = 97)	7.312	.000	.376	1.056	.307	.007
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.143	.003	.209	0.127	.723	.001
Lutein (<i>df</i> = 94)	3.633	.001	.236	0.141	.708	.001
Zeaxanthin (<i>df</i> = 97)	5.160	.000	.298	0.475	.492	.003
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.316	.002	.218	0.413	.522	.003
Lutein (<i>df</i> = 94)	4.085	.000	.258	2.398	.125	.019
Zeaxanthin (<i>df</i> = 97)	6.594	.000	.352	6.925	.010	.046
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.173	.003	.211	0.385	.536	.003
Lutein (<i>df</i> = 94)	3.720	.001	.240	0.787	.377	.006
Zeaxanthin (<i>df</i> = 97)	5.264	.000	.303	1.637	.204	.012

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 2.30 | F statistics from moderation analyses, FDR corrected:
middle cerebellar peduncle (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.477	.000	.353	0.036	.849	.000
Lutein (<i>df</i> = 94)	7.107	.000	.377	4.321	.040	.029
Zeaxanthin (<i>df</i> = 97)	7.152	.000	.371	1.111	.294	.007
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.245	.000	.379	1.153	.286	.008
Lutein (<i>df</i> = 94)	7.441	.000	.388	1.932	.168	.013
Zeaxanthin (<i>df</i> = 97)	9.605	.000	.442	9.336	.003	.054
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.552	.000	.356	0.589	.445	.004
Lutein (<i>df</i> = 94)	7.355	.000	.385	5.608	.020	.037
Zeaxanthin (<i>df</i> = 97)	8.022	.000	.398	5.626	.020	.035
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.279	.002	.216	0.000	.997	.000
Lutein (<i>df</i> = 94)	4.338	.000	.270	3.192	.077	.025
Zeaxanthin (<i>df</i> = 97)	5.454	.000	.310	1.866	.175	.013
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.354	.002	.220	0.917	.341	.008
Lutein (<i>df</i> = 94)	3.875	.001	.248	0.910	.343	.007
Zeaxanthin (<i>df</i> = 97)	5.470	.000	.311	2.029	.158	.014
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.424	.002	.224	0.424	.516	.004
Lutein (<i>df</i> = 94)	4.692	.000	.285	4.595	.035	.035
Zeaxanthin*	-	-	-	-	-	-

All significant overall models remained significant after FDR correction; significant interactions are in bold

*Collinearity exists with the intercept term of the moderation analysis

**Table 2.31 | F statistics from moderation analyses, FDR corrected:
superior cerebellar peduncle (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.629	.000	.358	0.430	.514	.003
Lutein (<i>df</i> = 94)	7.102	.000	.377	3.659	.059	.024
Zeaxanthin (<i>df</i> = 97)	7.468	.000	.381	1.897	.172	.012
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.716	.000	.361	0.023	.879	.000
Lutein (<i>df</i> = 94)	6.741	.000	.365	0.638	.426	.004
Zeaxanthin (<i>df</i> = 97)	8.220	.000	.404	5.008	.028	.037
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.821	.000	.365	1.876	.174	.012
Lutein (<i>df</i> = 94)	6.716	.000	.364	2.283	.134	.016
Zeaxanthin (<i>df</i> = 97)	7.520	.000	.383	2.809	.097	.018
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.244	.003	.215	0.182	.670	.002
Lutein (<i>df</i> = 94)	4.311	.000	.268	3.696	.058	.029
Zeaxanthin (<i>df</i> = 97)	5.736	.000	.321	4.360	.039	.030
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.178	.003	.211	0.254	.616	.002
Lutein (<i>df</i> = 94)	3.703	.001	.240	0.288	.593	.002
Zeaxanthin (<i>df</i> = 97)	5.022	.000	.293	0.000	.995	.000
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.142	.003	.209	0.033	.855	.000
Lutein (<i>df</i> = 94)	4.141	.000	.261	3.048	.084	.024
Zeaxanthin (<i>df</i> = 97)	5.447	.000	.310	2.746	.101	.020

All significant overall models remained significant after FDR correction; significant interactions are in bold

CHAPTER 3: INFLAMMATION BIOMARKERS AND BRAIN BEHAVIOR, STRUCTURE, AND FUNCTION IN HEALTHY, AGING ADULTS

3.1 *Chapter Overview*

The fundamental question of this chapter asks whether peripheral inflammation biomarkers influence relationships between neurological markers of brain health and measures of memory and intelligence. I will address this fundamental question systematically using the following series of constituent hypotheses:

- 1. Do inflammation biomarkers influence relationships between grey matter volume and facets of intelligence?*
- 2. Do inflammation biomarkers influence relationships between efficiency of intrinsic connectivity networks and facets of intelligence?*
- 3. Do inflammation biomarkers influence relationships between white matter microstructure and facets of intelligence?*

This program of questions advances the understanding of healthy brain aging through the lens of psychoneuroimmunology by elucidating the nature of influence between inflammation biomarkers and markers of brain health using an exploratory system of analyses in an observational, cross-sectional study of healthy elders.

3.2 ***Introduction***

Psychoneuroimmunology integrates psychology, neuroscience, and immunology to understand how the three factors interact. Most notably, research in this field investigates sickness behavior to understand how peripheral invaders affect neurobiological systems to yield psychological effects in the form of cognitive impairment, otherwise known as the “brain fog” experienced during acute sickness. Within psychoneuroimmunology exists a subfield focused on the low-level, systemic inflammation believed to contribute to age-related cognitive decline termed “inflamm-aging,” (Franceschi et. al., 2000). This systemic inflammation is thought to exert influence on cognitive function by contributing to oxidative stress within the CNS and blood brain barrier (BBB) disruption (Montagne et. al., 2015; Salminen et. al., 2008).

To study inflamm-aging *in vivo*, markers of peripheral inflammation and oxidative stress are often evaluated in relation to cognitive decline, however the results are inconsistent when studying non-demented older adults (Berr et.a al., 2000; Hajjar et. al., 2018; Walker et. al, 2019). Additionally, the number of studies incorporating cognitive neuroscience methods to understand inflamm-aging in non-demented adults is small. One study found that some inflammation biomarkers are associated with smaller whole-brain grey matter volumes (Gu et. al., 2017), which suggests a possible connection to lower cognitive performance (Aljondi et. al., 2019; Rusinek et. al., 2003). Another study found that in non-demented adults DMN connectivity associated with systemic inflammation, but it is unclear how inflammation relates to other ICNs (Marsland et. al., 2017; Schrepf et. al., 2018). Interestingly, white matter integrity has been studied in relation to inflammation in chronic disease, but not much is known about this relationship in normal aging. Peripheral inflammation biomarkers have been linked to decreased

white matter integrity in those with AD (Swardfager et. al., 2017) and schizophrenia (Fu et. al., 2019); Prasad et. al., 2015) among others. Systemic inflammation in middle-aged adults has been related to decreased global white matter integrity later in life (Walker et. al., 2017), but it remains unclear how regional white matter integrity relates to inflammation or how these relationships influence cognitive function.

Though limited, evidence in this field suggests that peripheral inflammation biomarkers are a potential target for attenuating cognitive changes that occur during aging. Characterizing relationships between inflammation biomarkers, brain structure and connectivity, and cognitive performance will inform strategies to promote overall healthy brain aging in a non-invasive and relatively inexpensive manner. Here, a multi-modal cognitive neuroscience approach is applied to this field of research to understand how inflammation biomarkers in the periphery relate to brain health and cognitive function during aging and to expand on the existing literature using cognitive neuroscience methods within the field of inflamm-aging.

3.3 *Methodology*

3.3.1 *Overall Design*

Data was collected from 128 consenting individuals between the ages of 65-75 years old over four sessions. All participants were void of cognitive impairment as measured by the Mini Mental State Examination (Folstein, Folstein, & McHugh, 1975), were neurologically healthy, deemed non-depressed by a subjective questionnaire, had normal or corrected-to-normal vision, and exhibited right handedness. Exclusion criteria were: cancer within the three years prior to enrollment, contraindications for MRI, dementia, inability to complete data collection activities, mild cognitive impairment diagnosis, ongoing chemotherapy or radiation therapy, prior

participation in cognitive training or dietary intervention studies, psychiatric illness within the three years prior to enrollment, and stroke within the 12 months prior to enrollment.

Participants underwent two magnetic resonance imaging (MRI) sessions, one neuropsychological assessment, and one fasting blood draw for which they were compensated monetarily by the hour. Following Institutional Review Board protocol for both the University of Illinois at Urbana-Champaign and Carle Foundation Hospital, informed consent was obtained from all participants to begin the first data collection session.

3.3.2 *Imaging*

Imaging was performed on a Siemens Magnetom 3T Trio (Erlangen, Germany) with a 12- channel head coil.

3.3.2.1 *Volumetric Magnetic Resonance Imaging (MRI)*

Structural MRI data were obtained with 3D high-resolution (0.9mm isotropic) T1-weighted scans with magnetization-prepared 180 degrees radio-frequency pulses and rapid gradient-echo acquisition (MPRAGE; Brant-Zawadzki, Gillan, & Nitz, 1992). Images were acquired with the following parameters: repetition time (TR) = 1900 ms, echo time (TE) = 2.32 ms, inversion time (TI) = 900 ms, acceleration factor of 2 with GRAPPA. Regions of interest are listed in Table 3.1.

3.3.2.2 *Resting State Functional MRI*

Resting state fMRI data were obtained during using a blood-oxygen level-dependent (BOLD) accelerated gradient echoplanar imaging (EPI) sequence. Two, 7- minute EPI sequences

were acquired with the following parameters: 2.5 x 2.5 x 3.0 mm voxel size, 2.5mm in-plane resolution, 3mm slice thickness, 38 slices with 10% gap, FOV = 230 mm, 90-degree flip angle, TE = 25 ms, and TR = 2000 ms were acquired. MRI data were processed using Freesurfer software (fmRIB Software Library, FSL: Oxford, UK).

Intrinsic connectivity networks (ICNs) were obtained using post-processing methods outlined in Yeo et. al. (2011) and Muldoon, Bridgeford, & Bassett (2016). Figure 2.1 depicts the seven ICNs for which graph theory metrics were computed and has been repeated below for convenience. Graph theory metrics for each network include global efficiency (average pathlength), local efficiency (local node clustering), and small world propensity (optimal balance of local and global efficiency).

3.3.2.3 *Diffusion Tensor Imaging (DTI)*

Whole-brain DTI data was collected (FOV=240x240mm, 72 slices at 2mm, TE=98 ms, TR=10,000 ms, in-plane resolution = 1.875x1.875 mm, diffusion encoding direction $s = 30$, $b = 0$ s/mm² and 1000 s/mm²). Data were processed using the University of Oxford's Center for Functional Magnetic Resonance Imaging of the Brain (FMRIB) Software Library (FSL) diffusion toolbox (FDT). The eddy_correct tool was used for eddy current correction and the DTIFIT tool was used to generate fractional anisotropy (FA), radial diffusivity (RD), and axial diffusivity (AD) values and create a diffusion tensor model for each voxel. The FSL tract-based statistics toolbox (TBSS) was used to further process the DTI images to represent the white-matter tracts common to all participants. Finally, mean values were calculated using the JHU ICBM DTI-81 atlas. For this chapter, only FA, AD, and RD values for global white matter and the genu of the corpus callosum were used.

3.3.3 *Assessing Facets of Intelligence*

Participants attended two neuropsychological assessment sessions to complete several cognitive batteries used to measure facets of intelligence including task switching (Delis-Kaplan Executive Function System; DKEFS), general, fluid, and crystallized intelligence (Wechsler Abbreviated Scale of Intelligence – II; WASI), and immediate, delayed, auditory, visual, and visual working memory (Wechsler Memory Scale – IV: Older Adult Battery; WMS). Neuropsychological assessments are summarized in Table 2.2 of the previous chapter.

3.3.4 *Measuring Peripheral Biomarkers*

To measure inflammatory biomarker levels, 45mL of antecubital venous blood was drawn after a 10h fast. Blood was separated between EDTA-anticoagulated and Heparin tubes, treated according to the manufacturer's instructions, aliquoted into 1mL cryotubes, and stored at -80C. Heparin samples were analyzed by Myriad RBM via Human InflammationMAP v1.0, a Multi-Analyte Profile (MAP: Austin, TX) of 45 inflammatory biomarkers indicated in Table 3.2.

3.3.5 *Statistical Analysis*

To capture interactive effects of inflammation biomarkers, inflammation biomarker patterns (IBPs) were identified by applying a principle components analysis (PCA) to cluster 39 inflammation biomarkers (Table 3.2) into unbiased variance-sharing groups. Using R (version 3.4.4; RStudio Inc.: Boston, MA), variables were scaled and Varimax rotation was applied to elucidate components and components accounting for 5% variance or greater were retained and reconfigured (Figure 3.1). Biomarkers with absolute loading values of .25 or greater on the IBP

were considered dominant contributors to that particular pattern (Bowman et. al., 2012).

Inflammation biomarker pattern composition and explained variance are listed in Table 3.3.

3.3.5.1 *Inflammation Biomarkers and Grey Matter Volume*

First, a correlation matrix conducted in R identified significant Pearson correlations between total grey matter volume of ROIs listed in Table 3.1 and each facet of intelligence (Table 2.2). Significant correlations were followed by linear regression models performed in SPSS 26 (IBM Corp.: Armonk, NY) to determine relationships between ROI volume and facets of intelligence while accounting for covariates. All regression models used sex (F/M), education level (4 levels: some high school, high school degree, some college, college degree), income level (5 levels: >100,000, 75,000- 100,000, 50,000-75,000, 25,000-50,000, and 15,000-25,000 USD annually), body mass index (BMI, continuous), and age (continuous) as covariates. A second correlation matrix conducted in R identified significant Pearson correlations between facets of intelligence significant in linear regression models and inflammation biomarkers to select possible moderators for individual facets of intelligence. Additionally, inflammation biomarkers were chosen arbitrarily based on involvement in NF- κ B signaling and analyzed as moderators for all facets of intelligence along with all IBPs elucidated from the PCA. This list of biomarkers included: CRP, IL-8, IL-18, MCP-1, RANTES, ICAM-1, VCAM-1, MMP-3, and MMP-9.

Significant linear models ($p < .05$) were followed by moderation analyses conducted with the PROCESS macro v3.4 application in SPSS to evaluate the relationships between brain structure (independent variable, IV), serum inflammation biomarker levels (moderator, M), and facets of intelligence derived from regression models (dependent variable, DV). Significant

moderations were followed up with a Johnson-Neyman analysis (Johnson & Fay, 1950) at ± 1 standard deviation from the mean (*SD*). False discovery rate (FDR; Benjamini & Hochberg, 1995) was conducted to correct for multiple comparisons in all significant overall models. All moderation analyses used the same covariates as the regression models.

3.3.5.2 *Inflammation Biomarkers and Functional Connectivity*

Linear regression analyses were performed in SPSS 26 to determine relationships between network characteristics (local efficiency, global efficiency, and small world propensity) and the facets of intelligence used in significant volumetric analyses (auditory memory, fluid intelligence, general intelligence, immediate memory, and task switching). Functional networks were chosen based on significant ROI in volumetric moderation analyses. This included the default mode (DMN), frontoparietal (FPN), limbic (LN), somatomotor (SMN), dorsal attention (DAN), and ventral attention networks (VAN; reference Figure 2.1). All models included the five covariates used in volumetric models. Significant linear models ($p < .05$) were explored with moderation analyses using the same covariates and protocol as for the volumetric moderation analyses, substituting individual network characteristics as the IV. Significant overall models were corrected for multiple comparisons using FDR.

3.3.5.3 *Inflammation Biomarkers and White Matter Structure*

Linear regression analyses were performed in SPSS 26 to determine relationships between axial diffusivity (AxD), radial diffusivity (RD), and fractional anisotropy (FA) of global white matter and the genu of the corpus callosum, and fluid intelligence and general intelligence. All models included the five covariates used in previous models. Significant linear models ($p <$

.05) were followed up with moderation analyses using the same covariates and protocol as previous analyses, substituting individual diffusion characteristics as the IV. Significant overall models were corrected for with multiple comparisons using FDR.

3.4 Results

3.4.1 Inflammation Biomarkers and Grey Matter Volume

A correlation matrix was produced in to divulge possible relationships between regional grey matter volume of the ROIs listed in Table 3.1 and various facets of intelligence. Of the facets of intelligence listed in Table 2.1 from the previous chapter, various ROIs correlated with auditory memory, delayed memory, fluid intelligence, general intelligence, immediate intelligence, task switching, and visual working memory. Demographic, neuropsychological assessment, and volumetric MRI data are presented for inflammation biomarkers and IBPs in Table 3.4.

Linear regression models were conducted to reveal relationships between regional grey matter volume in ROIs (IV) and the facets of intelligence (DV) identified in the correlation matrix while accounting for five covariates (age, BMI, education, income, sex). At least one ROI significantly predicted ($p < .05$) each facet of intelligence except visual working memory (Table 3.5).

A series of moderation analyses were conducted between ROI cortical volumes (IV), facets of intelligence (DV) from significant regression models, and inflammation biomarkers and IBPs (M) as conceptualized in Figure 2.1 from the previous chapter. Despite some significant overall models, moderations with delayed memory as an outcome all had non-significant interaction terms (see Appendix B, Table B.1a). Additionally, despite having some significant

overall models, moderation analyses with fusiform gyrus (see Appendix B, Table B.1b), inferior temporal (see Appendix B, Table B.1c), insula (see Appendix B, Table B.1d), lateral occipital (see Appendix B, Table B.1e), lateral orbitofrontal (see Appendix B, Table B.1f), medial orbitofrontal (see Appendix B, Table B.1g), paracentral gyrus (see Appendix B, Table B.1h), pars opercularis (see Appendix B, Table B.1i), pars orbitalis (see Appendix B, Table B.1j), rostral anterior cingulate (see Appendix B, Table B.1k), superior frontal (see Appendix B, Table B.1m), or temporal pole (see Appendix B, Table B.1n) volume as focal predictors all had non-significant interaction terms.

3.4.1.1 Caudal Anterior Cingulate Volume

Many overall models including caudal anterior cingulate cortex volume (IV) and both fluid intelligence and general intelligence (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.6). When fluid intelligence was the outcome, both VCAM-1 ($F(1, 102) = 5.403, p = 0.002, \Delta R^2 = 0.040$; Figure 3.2) and IBP 2 ($F(1, 97) = 4.411, p = 0.038, \Delta R^2 = 0.035$; Figure 3.3) were significant moderators. Simple slopes analyses indicated that both moderations were conditional. When volume was small ($-1 SD; b = -0.139, t(102) = -2.004, p = 0.048; 95\% CI = [-0.277 - -0.002]$), VCAM-1 significantly moderated the relationship with fluid intelligence but not when volume was moderate ($b = -0.010, t(102) = -0.196, p = 0.845; 95\% CI = [-0.110 - 0.090]$) or large ($+1 SD; b = 0.119, t(102) = 1.487, p = 0.140; 95\% CI = [-0.040 - 0.278]$). Conversely, when volume was large ($+1 SD; b = 4.590, t(97) = 2.330, p = 0.022; 95\% CI = [0.680 - 8.501]$) or moderate ($b = 2.258, t(97) = 2.060, p = 0.042; 95\% CI = [0.094 - 5.062]$), IBP 2 moderated the relationship with fluid intelligence. IBP was not a moderator when volume was small ($-1 SD; b = 0.566, t(97)$

= 0.543, $p = 0.588$; 95% CI = [-1.503 – 2.636]). Johnson-Neyman analyses indicated 14.4% and 51.9% of the population in this dataset fell within the significance regions, respectively.

When general intelligence was the outcome, both VCAM-1 ($F(1, 102) = 5.337$, $p = 0.023$, $\Delta R^2 = 0.037$; Figure 3.4) and IBP 1 ($F(1, 97) = 4.542$, $p = 0.036$, $\Delta R^2 = 0.034$; Figure 3.5) were significant moderators. When volume was large (+1 SD ; $b = 0.172$, $t(102) = 2.665$, $p = 0.009$; 95% CI = [0.438 – 0.299]) but not moderate ($b = 0.063$, $t(102) = 1.434$, $p = 0.154$; 95% CI = [-0.024 – 0.151]) or small (-1 SD ; $b = -0.045$, $t(102) = -0.699$, $p = 0.486$; 95% CI = [-0.173 – 0.083]), VCAM-1 moderated the relationship with general intelligence. IBP 1 was a moderator when its levels were above the group average (+1 SD ; $b = 0.006$, $t(97) = 2.738$, $p = 0.007$; 95% CI = [0.002 – 0.010]). In this population, 58.6% and 36.8% of the subjects fell within the significance regions, respectively.

3.4.1.2 Entorhinal Cortex Volume

Many overall models including entorhinal cortex volume (IV) and fluid intelligence (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.7). Only complement C3 ($F(1, 102) = 5.082$, $p = 0.026$, $\Delta R^2 = 0.037$; Figure 3.6) was a significant moderator. A simple slopes analysis revealed that this moderation was significant when complement C3 was moderate ($b = 12.153$, $t(102) = 2.889$, $p = 0.005$; 95% CI = [3.808 – 20.497]) and high (+1 SD ; $b = 22.652$, $t(102) = 3.322$, $p = 0.001$; 95% CI = [9.128 – 36.175]), but not low (-1 SD ; $b = 1.654$, $t(102) = 0.291$, $p = 0.772$; 95% CI = [-9.617 – 12.925]). A Johnson-Neyman analysis indicated that 62.2% of this population fell within the significance region.

3.4.1.3 Frontal Pole Volume

Many overall models including frontal pole volume (IV) and auditory memory, delayed memory, or immediate memory (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.8). Neither delayed memory (see Appendix B, Table B.1a) nor immediate memory (see Appendix B, Table B.1p) were significantly predicted by an interaction between frontal pole volume and inflammation biomarkers or IBPs. Of the significant overall models predicting auditory memory, only IBP 6 ($F(1, 98) = 5.881, p = 0.017, \Delta R^2 = 0.046$; Figure 3.7) was a significant moderator. A simple slopes analysis indicated that IBP 6 was a moderator when frontal pole volume was large (+1 SD ; $b = 3.699, t(98) = 2.013, p = 0.047$; 95% CI = [0.526 – 7.346]) but not moderate ($b = 0.780, t(98) = 0.661, p = 0.510$; 95% CI = [-1.561 – 3.120]) or small (-1 SD ; $b = -2.140, t(98) = -1.410, p = 0.162$; 95% CI = [-5.153 – 0.873]). A Johnson-Neyman analysis revealed that 16.9% of the population fell within the significance region.

3.4.1.4 Lingual Gyrus Volume

Many overall models including lingual gyrus volume (IV) and task switching (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.9). Only CRP ($F(1, 102) = 4.382, p = 0.039, \Delta R^2 = 0.036$; Figure 3.8), VCAM-1 ($F(1, 103) = 4.958, p = 0.028, \Delta R^2 = 0.040$; Figure 3.9), and IBP 1 ($F(1, 99) = 7.392, p = 0.008, \Delta R^2 = 0.060$; Figure 3.10) significantly interacted with lingual gyrus volume.

CRP was a moderator when its levels were at ($b = -0.000, t(102) = -2.350, p = 0.021$; 95% CI = [-0.000 – -0.000]) or above the group average (+1 SD ; $b = -0.000, t(102) = -3.090, p = 0.003$; 95% CI = [-0.001 – -0.000]). In this population, 33.3% of the subjects fell within the

significance region. VCAM-1 was a moderator when volume was large (+1 *SD*; $b = -0.021$, $t(103) = -2.136$, $p = 0.035$; 95% CI = [-0.409 – -0.002]) but not moderate ($b = -0.004$, $t(103) = -0.468$, $p = 0.641$; 95% CI = [-0.021 – 0.013]) or small (-1 *SD*; $b = 0.013$, $t(103) = 1.047$, $p = 0.298$; 95% CI = [-0.012 – 0.039]) and 18.8% of this population fell within the significance region. Similarly, IBP 1 was a moderator when volume was large (+1 *SD*; $b = -0.567$, $t(99) = -2.021$, $p = 0.046$; 95% CI = [-1.124 – -0.010]) but not moderate ($b = -0.091$, $t(99) = -0.444$, $p = 0.658$; 95% CI = [-0.500 – 0.318]) or small (-1 *SD*; $b = 0.384$, $t(99) = 1.479$, $p = 0.142$; 95% CI = [-0.131 – 0.899]) and 17.6% of this population fell within the significance region.

3.4.1.5 *Posterior Cingulate Volume*

Many overall models including posterior cingulate volume (IV) and both auditory and immediate memory (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.10). Auditory memory (see Appendix B, Table B.1q) was not significantly predicted by an interaction between posterior cingulate volume and inflammation biomarkers or IBPs. Immediate memory was significantly predicted by an interaction between IL-18 and posterior cingulate volume ($F(1, 104) = 4.443$, $p = 0.037$, $\Delta R^2 = 0.034$; Figure 3.11). A simple slopes analysis indicated that this interaction was conditionally significant when IL-18 levels were at ($b = 0.003$, $t(104) = 2.388$, $p = 0.019$; 95% CI = [0.000 – 0.006]) or above the group average (+1 *SD*; $b = 0.006$, $t(104) = 3.250$, $p = 0.002$; 95% CI = [0.002 – 0.010]). A Johnson-Neyman analysis revealed that 47.8% of this population fell within the significance region.

3.4.1.6 *Precuneus Volume*

Many overall models including precuneus volume (IV) and fluid intelligence, general intelligence, or immediate memory (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.11). Neither general intelligence nor immediate memory (see Appendix B, Table B.1r) were significantly predicted by an interaction between precuneus volume and inflammation biomarkers or IBPs. At very high levels, IL-8 moderated the relationship between precuneus volume and fluid intelligence ($F(1, 75) = 4.078, p = 0.047, \Delta R^2 = 0.043$; Figure 3.12). A Johnson-Neyman analysis indicated that 8.3% of this population fell within the significance region ($> +1 SD; b = 0.002, t(75) = 1.992, p = 0.050; 95\% CI = [0.00 - 0.004]$).

3.4.1.7 *Superior Temporal Volume*

Many overall models including superior temporal volume (IV) and fluid intelligence (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.12). IBP 2 moderated the relationship between fluid intelligence and superior temporal volume ($F(1, 97) = 8.172, p = 0.005, \Delta R^2 = 0.063$; Figure 3.13). A simple slopes analysis indicated that this was a conditional moderation, most significant when IBP 2 was moderate ($b = 2.964, t(97) = 2.450, p = 0.016; 95\% CI = [0.563 - 5.299364]$ or high ($+1 SD; b = 6.040, t(97) = 2.984, p = 0.004; 95\% CI = [2.022 - 10.058]$), but not when it was low ($-1 SD; b = -0.113, t(97) = -0.105, p = 0.916; 95\% CI = [-2.235 - 2.010]$). A Johnson-Neyman analysis revealed that 60.4% of this population fell within the significance region.

3.4.1.8 Supramarginal Gyrus Volume

Many overall models including supramarginal gyrus volume (IV) and fluid intelligence (DV) were significant when inflammation biomarkers or IBPs were included as the moderator, even after FDR correction (Table 3.13). Multiple biomarkers moderated this relationship: IL-8 ($F(1, 75) = 6.129, p = 0.016, \Delta R^2 = 0.062$; Figure 3.14), ICAM-1 ($F(1, 102) = 5.740, p = 0.018, \Delta R^2 = 0.043$; Figure 3.15), complement C3 ($F(1, 102) = 4.411, p = 0.038, \Delta R^2 = 0.035$; Figure 3.16), and IBP 2 ($F(1, 97) = 4.241, p = 0.042, \Delta R^2 = 0.035$; Figure 3.17).

Simple slopes analyses indicated that IL-8 was a moderator when volume was large (+1 *SD*; $b = 1.490, t(75) = 2.333, p = 0.022$; 95% CI = [0.218 – 2.763]), but not when volume was moderate ($b = 0.641, t(97) = 1.750, p = 0.084$; 95% CI = [-0.089 – 1.371]) or small (-1 *SD*; $b = -0.208, t(97) = -0.674, p = 0.502$; 95% CI = [-0.824 – 0.407]).

ICAM-1 was a moderator when volume was large (+1 *SD*; $b = 0.921, t(102) = 2.677, p = 0.009$; 95% CI = [0.239 – 1.604]) but not moderate ($b = 0.302, t(102) = 1.111, p = 0.269$; 95% CI = [-0.237 – 0.841]) or small (-1 *SD*; $b = -0.317, t(102) = -0.785, p = 0.434$; 95% CI = [-1.118 – 0.484]).

Complement C3 was a moderator when volume was moderate ($b = 12.095, t(102) = 2.882, p = 0.005$; 95% CI = [3.770 – 20.420]) or large (+1 *SD*; $b = 22.824, t(102) = 3.546, p = 0.001$; 95% CI = [10.059 – 35.590]), but not small (-1 *SD*; $b = 1.366, t(102) = 0.246, p = 0.806$; 95% CI = [-9.651 – 12.382]).

IBP 2 was a moderator when volume was moderate ($b = 2.655, t(97) = 2.100, p = 0.038$; 95% CI = [0.146 – 5.164]) or large (+1 *SD*; $b = 4.661, t(97) = 2.349, p = 0.021$; 95% CI = [0.723 – 8.599]), but not small (-1 *SD*; $b = 0.649, t(97) = 0.603, p = 0.548$; 95% CI = [-1.486 – 2.784]).

Johnson-Neyman analyses revealed that when IL-8, ICAM-1, complement C3, and IBP 2 were moderators 32.1%, 30.6%, 59.4%, and 52.8% of subjects fell within the significance regions, respectively. *

3.4.2 *Inflammation Biomarkers and Functional Connectivity*

Linear regression models were conducted to reveal relationships between efficiency in ICNs (IV) and the facets of intelligence (DV) identified in the grey matter volume linear regressions (see section 3.4.2) while accounting for covariates. Relevant demographic, neuropsychological assessment, and ICN efficiency data are presented for inflammation biomarkers and IBPs in Table 3.14. Efficiency in at least one ICN (DMN, FPN, LN, SMN, DAN, VAN) significantly predicted ($p < .05$) each facet of intelligence (Table 3.15 and Table 3.16).

A series of moderation analyses were then conducted between efficiency in ICNs and facets of intelligence from significant regression models, and inflammation biomarkers and IBPs (M) as conceptualized in Figure 2.2. Despite some significant overall models, moderations with efficiency in the DMN as focal predictors all had non-significant interaction terms (see Appendix B, Table B.1a).

3.4.2.1 *Frontoparietal Network*

A series of moderation analyses between efficiency in the FPN and individual inflammation biomarkers and IBPs revealed many significant overall models after FDR correction when fluid intelligence, general intelligence, or immediate memory was the outcome.

Models with immediate memory as the outcome did not have significant interaction terms with individual inflammation biomarkers or IBPs (see Appendix B, Table B.2d).

When fluid intelligence was the outcome (Table 3.17), local and global efficiency did not interact with any moderators significantly (see Appendix B, Table B.2e). Both $\alpha 2$ -macroglobulin ($F(1, 83) = 4.043, p = .048, \Delta R^2 = 0.038$; Figure 3.18) and IBP 5 ($F(1, 79) = 5.368, p = .023, \Delta R^2 = 0.051$; Figure 3.19) significantly moderated the relationship between small world propensity in the FPN and fluid intelligence. Simple slopes analyses indicated that both interactions were conditional. When small world propensity is very high ($> +1 SD$; $b = 6.184, t(83) = 1.989, p = 0.000$; 95% CI = [0.000 – 12.368]) $\alpha 2$ -macroglobulin moderated the relationship between small world propensity in the FPN and fluid intelligence, and 7.6% of this population fell within the significance region. When small world propensity was high ($+1 SD$; $b = 5.051, t(79) = 3.075, p = 0.003$; 95% CI = [1.782 – 8.321]) but not moderate ($b = 1.665, t(79) = 1.425, p = 0.158$; 95% CI = [-0.660 – 3.990]) or small ($-1 SD$; $b = -1.721, t(79) = -0.830, p = 0.409$; 95% CI = [-5.850 – 2.408]), IBP 5 moderated the relationship between small world propensity in the FPN and fluid intelligence. Johnson-Neyman analysis indicated 43.2% of the population in this dataset falls within the significance region.

When general intelligence was the outcome (Table 3.18), local efficiency ($F(1, 84) = 2.944, p = .029, \Delta R^2 = 0.042$; Figure 3.20), global efficiency ($F(1, 84) = 4.980, p = .028, \Delta R^2 = 0.043$; Figure 3.21), and small world propensity ($F(1, 84) = 4.710, p = .033, \Delta R^2 = 0.041$; Figure 3.22) interacted significantly with $\alpha 2$ -macroglobulin. The interaction with local efficiency was significant when local efficiency was low ($-1 SD$; $b = 8.732, t(84) = 2.876, p = 0.005$; 95% CI = [2.695 – 14.770]) but not moderate ($b = 3.231, t(84) = 1.552, p = 0.124$; 95% CI = [-0.910 –

7.371]) or high (+1 *SD*; $b = -2.271$, $t(84) = -0.664$, $p = 0.508$; 95% CI = [-9.073 – 4.531]), and 44.1% of this population fell within the significance region.

The interaction with global efficiency was significant when global efficiency was low (-1 *SD*; $b = 7.298$, $t(84) = 2.780$, $p = 0.007$; 95% CI = [2.077 – 12.519]) but not moderate ($b = 2.524$, $t(84) = 1.162$, $p = 0.248$; 95% CI = [-1.795 – 6.842]) or high (+1 *SD*; $b = -2.251$, $t(84) = -0.658$, $p = 0.512$; 95% CI = [-9.052 – 4.549]), and 39.8% of this population fell within the significance region.

The interaction with small world propensity was significant when small world propensity was high (+1 *SD*; $b = 7.623$, $t(84) = 2.687$, $p = 0.009$; 95% CI = [1.980 – 13.266]) but not moderate ($b = 2.531$, $t(84) = 1.163$, $p = 0.248$; 95% CI = [-1.796 – 6.858]) or low (-1 *SD*; $b = -2.562$, $t(84) = -0.727$, $p = 0.470$; 95% CI = [-9.573 – 4.449]), and 37.6% of this population fell within the significance region.

The relationship between small world propensity in the FPN and general intelligence was also moderated by IBP 5 F STATISTIC (Figure 3.23). This interaction was significant when small world propensity was moderate ($b = 2.425$, $t(80) = 2.220$, $p = 0.029$; 95% CI = [0.251 – 4.598]) or high (+1 *SD*; $b = 5.858$, $t(80) = 3.810$, $p = 0.000$; 95% CI = [2.798 – 8.917]), but not low (-1 *SD*; $b = -1.008$, $t(80) = -0.524$, $p = 0.602$; 95% CI = [-4.837 – 2.821]). In this population, 60.7% of subjects fell within the significance region.

3.4.2.2 *Limbic Network*

A series of moderation analyses between efficiency in the LN and individual inflammation biomarkers and IBPs revealed many significant overall models after FDR correction when fluid intelligence, general intelligence, or immediate memory was the outcome

(Table 3.19). Models with general intelligence (see Appendix B, Table B.2f) or immediate memory (see Appendix B, Table B.2g) as the outcome did not have significant interaction terms with individual inflammation biomarkers or IBPs

When fluid intelligence was the outcome, local efficiency ($F(1, 79) = 5.686, p = .020, \Delta R^2 = 0.056$; Figure 3.24) and global efficiency ($F(1, 79) = 5.561, p = .021, \Delta R^2 = 0.055$; Figure 3.25) significantly interacted with IBP 3. Simple slopes analyses indicated that both interactions were conditional. When local efficiency was high (+1 *SD*; $b = 5.332, t(79) = 2.429, p = 0.017$; 95% CI = [0.963 – 9.702]) but not moderate ($b = 1.994, t(79) = 1.280, p = 0.204$; 95% CI = [-1.107 – 5.096]) or low (-1 *SD*; $b = -1.344, t(79) = -0.676, p = 0.501$; 95% CI = [-5.303 – 2.615]). When global efficiency was high (+1 *SD*; $b = 5.533, t(79) = 2.478, p = 0.015$; 95% CI = [1.089 – 9.976]) but not moderate ($b = 1.981, t(79) = 1.273, p = 0.207$; 95% CI = [-1.117 – 5.080]) or low (-1 *SD*; $b = -1.570, t(79) = -0.749, p = 0.456$; 95% CI = [-5.745 – 2.604]). Johnson-Neyman analyses indicated that 35.2% and 38.6% of the population fell within the significance regions, respectively.

Global efficiency also interacted with ICAM-1 ($F(1, 83) = 6.452, p = .013, \Delta R^2 = 0.059$; Figure 3.26). This interaction was significant when global efficiency was high (+1 *SD*; $b = 1.086, t(83) = 2.127, p = 0.036$; 95% CI = [0.070 – 2.101]) but not moderate ($b = 0.138, t(83) = 0.403, p = 0.688$; 95% CI = [-0.543 – 0.819]) or low, (-1 *SD*; $b = -0.810, t(83) = -1.612, p = 0.111$; 95% CI = [-1.809 – 0.189]) and 78.3% of subjects in this population fell within the significance region.

Small world propensity interacted with RANTES ($F(1, 83) = 4.964, p = .029, \Delta R^2 = 0.045$; Figure 3.27). This interaction was significant when small world propensity was high (+1 *SD*; $b = 0.212, t(83) = 2.294, p = 0.024$; 95% CI = [0.028 – 0.396]) but not moderate ($b = 0.042,$

$t(83) = 0.470, p = 0.640$; 95% CI = [-0.138 – 0.223]) or low (-1 *SD*; $b = -0.127, t(83) = -0.912, p = 0.364$; 95% CI = [-0.404 – 0.150]), and 22.8% of this population fell within the significance region.

3.4.2.3 *Somatomotor Network*

A series of moderation analyses between efficiency in the SMN and individual inflammation biomarkers and IBPs revealed many significant overall models after FDR correction when auditory memory (see Appendix B, Table B.2h), fluid intelligence (see Appendix B, Table B.2i), general intelligence (see Appendix B, Table B.2j), or immediate memory (see Appendix B, Table B.2k) was the outcome. However, moderators were only significant when fluid intelligence was the outcome (Table 3.20).

Both IL-18 ($F(1, 83) = 4.923, p = .029, \Delta R^2 = 0.046$; Figure 3.28) and IBP 3 ($F(1, 79) = 4.725, p = .033, \Delta R^2 = 0.046$; Figure 3.29) significantly interacted with global efficiency to predict fluid intelligence. When IL-18 was low (-1 *SD*; $b = 93.889, t(83) = 2.390, p = 0.019$; 95% CI = [15.756 – 172.020]) this interaction was most significant, and 33.7% of this population fell within the significance region.

When global efficiency was low (-1 *SD*; $b = 4.465, t(83) = 2.236, p = 0.028$; 95% CI = [0.490 – 8.440]) but not moderate ($b = 1.892, t(83) = 1.233, p = 0.221$; 95% CI = [-1.162 – 4.947]) or high (+1 *SD*; $b = -0.680, t(83) = -0.362, p = 0.718$; 95% CI = [-4.417 – 3.056]), IBP 3 was a significant moderator. In this population, 36.4% of subjects fell within the significance region.

3.4.2.4 Dorsal Attention Network

A series of moderation analyses between efficiency in the DAN and individual inflammation biomarkers and IBPs revealed many significant overall models after FDR correction when fluid intelligence, general intelligence, or task switching was the outcome.

Local efficiency did not interact with any of the moderators significantly when fluid intelligence (see Appendix B, Table B.2m) or general intelligence (see Appendix B, Table B.2n) was the outcome. Models with task switching as the outcome did not have significant interaction terms with individual inflammation biomarkers or IBPs (see Appendix B, Table B.1p).

For both fluid (Table 3.21) and general (Table 3.22) intelligence, IL-18 interacted with global efficiency and small world propensity. IL-18 moderated the relationship between global efficiency and fluid intelligence ($F(1, 83) = 4.219, p = 0.043, \Delta R^2 = 0.040$; Figure 3.30) when global efficiency was very high ($> +1 SD; b = 0.043, t(83) = 1.989, p = 0.050$; 95% CI = [0.000 – 0.086]). In this population, 9.8% of subjects fell within the significance region. IL-18 moderated the relationship between global efficiency and general intelligence ($F(1, 84) = 5.412, p = 0.022, \Delta R^2 = 0.046$; Figure 3.31) when global efficiency was low ($-1 SD; b = -0.028, t(84) = -2.500, p = 0.014$; 95% CI = [-0.050 – -0.006]) but not moderate ($b = -0.001, t(84) = -0.114, p = 0.909$; 95% CI = [-0.019 – 0.016]) or high ($+1 SD; b = 0.026, t(84) = 1.498, p = 0.138$; 95% CI = [-0.008 – 0.060]). In this population, 26.9% of subjects fell within the significance region.

The relationship between small world propensity and fluid intelligence was moderated by IL-18 ($F(1, 83) = 4.249, p = 0.042, \Delta R^2 = 0.040$; Figure 3.32) when IL-18 was very low ($> -1 SD; b = 0.042, t(83) = 1.989, p = 0.050$; 95% CI = [0.000 – 0.085]). In this population, 4.3% of subjects fell within the significance region. IL-18 also moderated the relationship between small

world propensity and general intelligence when small world propensity was high (+1 *SD*; $b = -0.025$, $t(84) = -2.443$, $p = 0.017$; 95% CI = [-0.045 – 0.005]) but not moderate ($b = -0.002$, $t(84) = -0.228$, $p = 0.820$; 95% CI = [-0.019 – 0.015]) or low (-1 *SD*; $b = 0.021$, $t(84) = 1.454$, $p = 0.150$; 95% CI = [-0.008 – 0.049]; Figure 3.33). In this population, 25.8% of subjects fell within the significance region.

For both fluid ($F(1, 83) = 4.487$, $p = .037$, $\Delta R^2 = 0.042$; Figure 3.34) and general ($F(1, 84) = 6.164$, $p = .015$, $\Delta R^2 = 0.052$; Figure 3.35) intelligence, VCAM-1 interacted with global efficiency. When global efficiency was very low, VCAM-1 moderated the relationship with fluid intelligence (> -1 *SD*; $b = -0.142$, $t(83) = 1.989$, $p = 0.050$; 95% CI = [-0.284 – 0.000]). In this population, 10.9% of subjects fell within the significance region. VCAM-1 moderated the relationship between global efficiency and general intelligence when global efficiency was high (+1 *SD*; $b = 0.184$, $t(84) = 2.704$, $p = 0.008$; 95% CI = [0.049 – 0.318]) but not moderate ($b = 0.068$, $t(84) = 1.486$, $p = 0.141$; 95% CI = [-0.023 – 0.159]) or low (-1 *SD*; $b = -0.048$, $t(84) = -0.758$, $p = 0.450$; 95% CI = [-0.172 – 0.077]). In this population, 36.6% of subjects fell within the significance region.

For both fluid ($F(1, 83) = 7.433$, $p = .008$, $\Delta R^2 = 0.065$; Figure 3.36) and general ($F(1, 84) = 6.191$, $p = .015$, $\Delta R^2 = 0.051$; Figure 3.37) intelligence, ferritin interacted with small world propensity. When fluid intelligence was the outcome, ferritin was a moderator when small world propensity was low (-1 *SD*; $b = 0.040$, $t(83) = 3.310$, $p = 0.001$; 95% CI = [0.016 – 0.064]) or moderate ($b = 0.020$, $t(83) = 2.052$, $p = 0.043$; 95% CI = [0.001 – 0.040]) but not when small world propensity was high (+1 *SD*; $b = 0.000$, $t(83) = 0.022$, $p = 0.982$; 95% CI = [-0.024 – 0.025]). For this interaction, 46.7% of subjects fell within the significance region. When general intelligence was the outcome, ferritin was a moderator when small world propensity was low (-1

SD; $b = 0.035$, $t(84) = 3.088$, $p = 0.003$; 95% CI = [0.013 – 0.058]) but not moderate ($b = 0.018$, $t(84) = 1.976$, $p = 0.052$; 95% CI = [> 0.000 – 0.037]) or high (+1 *SD*; $b = 0.001$, $t(84) = 0.108$, $p = .914$; 95% CI = [-0.022 – 0.024]). For this interaction, 44.1% of subjects fell within the significance region.

Additionally, when general intelligence was the outcome, factor VII ($F(1, 84) = 7.574$, $p = .007$, $\Delta R^2 = 0.064$; Figure 3.38) interacted with global efficiency. Factor VII was a moderator when global efficiency was low (-1 *SD*; $b = 0.019$, $t(84) = 2.209$, $p = .030$; 95% CI = [0.002 – 0.037]) but not moderate ($b = 0.001$, $t(84) = 0.155$, $p = .877$; 95% CI = [-0.012 – 0.013]) or high (+1 *SD*; $b = -0.017$, $t(84) = -1.820$, $p = .072$; 95% CI = [-0.036 – 0.002]). In this population, 20.4% of subjects fell within the significance region.

3.4.2.5 *Ventral Attention Network*

A series of moderation analyses between efficiency in the VAN and individual inflammation biomarkers and IBPs revealed many significant overall models after FDR correction when fluid intelligence, general intelligence, or immediate memory was the outcome. Small world propensity did not interact with any of the moderators significantly when fluid intelligence (see Appendix B, Table B.2q) or general intelligence (see Appendix B, Table B.2r) was the outcome. Models with immediate memory as the outcome did not have significant interaction terms with individual inflammation biomarkers or IBPs (see Appendix B, Table B.2s).

For both fluid (Table 3.23) and general (Table 3.24) intelligence, $\alpha 2$ -macroglobulin interacted with both local and global efficiency. When fluid intelligence was the outcome ($F(1, 83) = 10.633$, $p = .002$, $\Delta R^2 = 0.090$; Figure 3.39), $\alpha 2$ -macroglobulin interacted with local

efficiency when it was low (-1 SD ; $b = 6.561$, $t(83) = 2.513$, $p = .014$; 95% CI = [1.368 – 11.755]) or high ($+1\text{ SD}$; $b = -7.098$, $t(83) = -2.081$, $p = .040$; 95% CI = [-13.881 – -0.315]), but not when local efficiency was moderate ($b = -0.268$, $t(83) = -0.122$, $p = .903$; 95% CI = [-4.643 – 4.106]). These interactions influenced 19.6% and 13.0% of this population, respectively. When general intelligence was the outcome ($F(1, 84) = 6.751$, $p = .011$, $\Delta R^2 = 0.055$; Figure 3.40), $\alpha 2$ -macroglobulin was a moderator when local efficiency was low (-1 SD ; $b = 7.094$, $t(84) = 2.839$, $p = .006$; 95% CI = [2.125 – 12.063]) but not moderate ($b = 1.946$, $t(84) = 0.926$, $p = .357$; 95% CI = [-2.234 – 6.126]) or high ($+1\text{ SD}$; $b = -3.201$, $t(84) = -0.991$, $p = .325$; 95% CI = [-9.627 – 3.225]). In this population, 30.1% of subjects fell within the significance region.

When global efficiency was the focal predictor, $\alpha 2$ -macroglobulin moderated the relationship with fluid ($F(1, 83) = 7.876$, $p = .006$, $\Delta R^2 = 0.070$; Figure 3.41) and general ($F(1, 84) = 5.659$, $p = .020$, $\Delta R^2 = 0.046$; Figure 3.42) intelligence. When global efficiency was low (-1 SD ; $b = 5.781$, $t(83) = 2.212$, $p = .030$; 95% CI = [0.584 – 10.979]) but not moderate ($b = 0.041$, $t(83) = 0.018$, $p = .986$; 95% CI = [-4.433 – 4.515]) or high ($+1\text{ SD}$; $b = -5.700$, $t(83) = -1.099$, $p = .099$; 95% CI = [-12.492 – 1.091]) $\alpha 2$ -macroglobulin significantly moderated the relationship with fluid intelligence. In this population 15.2% of subjects fell within the significance region. Similarly, $\alpha 2$ -macroglobulin moderated the relationship with general intelligence when global efficiency was low (-1 SD ; $b = 6.559$, $t(84) = 2.666$, $p = .009$; 95% CI = [1.666 – 11.451]) but not moderate ($b = 2.030$, $t(84) = 0.960$, $p = .340$; 95% CI = [-2.178 – 6.238]) or high ($+1\text{ SD}$; $b = -2.498$, $t(84) = -0.784$, $p = .435$; 95% CI = [-8.833 – 3.838]). For this moderation, 24.7% of the population fell within the significance region.

Both ICAM-1 and IBP 5 interact with local efficiency to predict fluid and general intelligence. When fluid intelligence was the outcome, ICAM-1 was a conditional moderator (F

(1, 83) = 7.270, $p = .008$, $\Delta R^2 = 0.064$; Figure 3.43). This interaction was significant when ICAM-1 was moderate ($b = -72.329$, $t(83) = -2.617$, $p = .010$; 95% CI = [-127.298 – -17.360]) and high (+1 SD; $b = -133.098$, $t(83) = -3.245$, $p = .002$; 95% CI = [-214.670 – -51.525]), and 60.9% of this population fell within the significance region. When general intelligence was the outcome, ICAM-1 was a conditional moderator as well ($F(1, 84) = 3.960$, $p = .050$, $\Delta R^2 = 0.034$; Figure 3.44). Similarly, this interaction was significant when ICAM-1 was moderate ($b = -70.697$, $t(84) = -2.645$, $p = .010$; 95% CI = [-123.850 – -17.544]) and high (+1 SD; $b = -113.664$, $t(84) = -2.876$, $p = .005$; 95% CI = [-192.269 – -35.060]), and 63.4% of this population fell within the significance region.

When local efficiency was the focal predictor, IBP 5 was a conditional moderator in the relationship with fluid ($F(1, 79) = 9.356$, $p = .003$, $\Delta R^2 = 0.083$; Figure 3.45) and general intelligence ($F(1, 80) = 4.199$, $p = .044$, $\Delta R^2 = 0.035$; Figure 3.46). IBP 5 interacted with local efficiency to predict fluid intelligence when efficiency was low (-1 SD; $b = 4.080$, $t(79) = 3.103$, $p = .002$; 95% CI = [1.545 – 6.615]) but not moderate ($b = 0.717$, $t(79) = 0.614$, $p = .541$; 95% CI = [-1.609 – 3.044]) or high (+1 SD; $b = -2.645$, $t(79) = -1.408$, $p = .163$; 95% CI = [-6.384 – 1.093]). This interaction was significant in 29.5% of this population. Similarly, IBP 5 interacted with local efficiency to predict general intelligence when efficiency was low (-1 SD; $b = 4.138$, $t(80) = 3.371$, $p = .001$; 95% CI = [1.695 – 6.581]) but not moderate ($b = 1.983$, $t(80) = 1.754$, $p = .083$; 95% CI = [-0.267 – 4.232]) or high (+1 SD; $b = -0.173$, $t(80) = -0.096$, $p = .924$; 95% CI = [-3.766 – 3.421]). This interaction was significant in 39.3% of this population.

To predict both fluid ($F(1, 79) = 6.128$, $p = .015$, $\Delta R^2 = 0.059$; Figure 3.47) and general ($F(1, 80) = 5.355$, $p = .023$, $\Delta R^2 = 0.047$; Figure 3.48) intelligence, IBP 2 interacted with global efficiency. When fluid intelligence was the outcome, IBP 2 was a moderator when global

efficiency was high (+1 *SD*; $b = 5.702$, $t(79) = 2.370$, $p = .020$; 95% CI = [0.913 – 10.491]) but not moderate ($b = 2.346$, $t(79) = 1.752$, $p = .084$; 95% CI = [-0.319 – 5.012]) or low (-1 *SD*; $b = -1.010$, $t(79) = -0.832$, $p = .408$; 95% CI = [-3.427 – 1.406]). In this population, 44.3% of subjects fell within the significance region. Similarly, when general intelligence was the outcome IBP 2 was a moderator when global efficiency was high (+1 *SD*; $b = 4.719$, $t(80) = 2.058$, $p = .043$; 95% CI = [0.156 – 9.283]) but not moderate ($b = 1.765$, $t(80) = 1.374$, $p = .173$; 95% CI = [-0.791 – 4.322]) or low (-1 *SD*; $b = -1.189$, $t(80) = -1.042$, $p = .300$; 95% CI = [-3.459 – 1.081]). Here, 19.1% of subjects fell within the significance region.

When general intelligence was the outcome, MMP-3 interacted with both local ($F(1, 84) = 4.776$, $p = .032$, $\Delta R^2 = 0.041$; Figure 3.49) and global ($F(1, 84) = 4.189$, $p = .044$, $\Delta R^2 = 0.036$; Figure 3.50) efficiency. When local efficiency was the focal predictor, MMP-3 was a moderator at low (-1 *SD*; $b = -130.532$, $t(84) = -3.017$, $p = .003$; 95% CI = [-216.574 – -44.489]) and moderate ($b = -60.846$, $t(84) = -2.406$, $p = .018$; 95% CI = [-111.130 – -10.562]) levels. Similarly, MMP-3 interacted with global efficiency at low (-1 *SD*; $b = -114.667$, $t(84) = -2.867$, $p = .005$; 95% CI = [-194.194 – -35.139]) and moderate ($b = -57.897$, $t(84) = -2.557$, $p = .012$; 95% CI = [-102.927 – -12.868]) levels. For both moderations, 76.3% of subjects fell within the significance region.

Additionally, when fluid intelligence was the outcome, VCAM-1 ($F(1, 83) = 4.086$, $p = .046$, $\Delta R^2 = 0.037$; Figure 3.51) interacted with local efficiency and complement C3 ($F(1, 83) = 4.188$, $p = .044$, $\Delta R^2 = 0.037$; Figure 3.52) interacted with global efficiency. VCAM-1 interacted with local efficiency to predict fluid intelligence when VCAM-1 was at ($b = -60.212$, $t(84) = -2.195$, $p = .031$; 95% CI = [-114.761 – -5.663]) or above (+1 *SD*; $b = -121.207$, $t(84) = -2.661$, $p = .009$; 95% CI = [-211.793 – -30.620]) the mean, and 48.9% of this population fell within the

significance region. Complement C3 moderated the relationship between global efficiency and fluid intelligence when global efficiency was low ($-1\ SD$; $b = 21.221$, $t(83) = 2.855$, $p = .005$; 95% CI = [6.438 – 36.004]) but not moderate ($b = 10.844$, $t(83) = 1.919$, $p = .058$; 95% CI = [-0.396 – 22.084]) or high ($+1\ SD$; $b = 0.468$, $t(83) = 0.604$, $p = .952$; 95% CI = [-14.944 – 15.880]). In this population, 45.6% of subjects fell within the significance region.

3.4.3 *Inflammation Biomarkers and White Matter Structure*

Linear regression models were conducted to reveal relationships integrity of white matter tracts highly susceptible to aging and the facets of intelligence (DV) with the greatest number of significant moderations while accounting for covariates. Only inflammation biomarkers that previously acted as significant moderators were included, and all IBPs were included. Relevant demographic, neuropsychological assessment, and white matter tract integrity data are presented for inflammation biomarkers and IBPs in Table 3.25. Integrity in global white matter and the genu of the corpus callosum significantly predicted ($p < .05$) each fluid or general intelligence (Table 3.26).

A series of moderation analyses were conducted between white matter integrity and facets of intelligence from significant regression models and inflammation biomarkers and IBPs (M) as conceptualized in Figure 2.2. Despite some significant overall models, moderations with RD as the focal predictor had non-significant interaction terms globally (see Appendix B, Tables B.3a and B.3b) and in the genu of the corpus callosum (see Appendix B, Tables B.3c and B.3d). Fractional anisotropy did not interact with inflammation biomarkers globally (see Appendix B, Table B.3b) or in the genu (see Appendix B, Table B.3d) to predict general intelligence. In fact, white matter integrity in the genu did not interact with inflammatory biomarkers to predict

general intelligence at all (see Appendix B, Table B.3d). Finally, AxD in the genu did not interact with inflammation biomarkers to predict fluid intelligence (see Appendix B, Table B.3c).

When considering global white matter integrity, IL-18 moderated the relationship between FA and fluid intelligence ($F(1, 99) = 3.984, p = .049, \Delta R^2 = 0.032$; Table 3.27; Figure 3.53). This moderation was most significant when IL-18 was low ($-1 SD; b = 180.428, t(99) = 2.750, p = .007; 95\% CI = [50.253 - 310.602]$) and a Johnson-Neyman analysis revealed that this moderation was significant in 50.0% of this population.

Additionally, global white matter AxD interacted with factor VII and IBP 3 to predict both fluid (Table 3.27) and general (Table 3.28) intelligence. Factor VII conditionally moderated the relationship between global white matter AxD and fluid intelligence ($F(1, 99) = 7.436, p = .008, \Delta R^2 = 0.059$; Figure 3.54). This moderation was most significant when AxD was low ($-1 SD; b = 0.025, t(99) = 3.059, p = .003; 95\% CI = [0.009 - 0.042]$) compared to moderate ($b = 0.009, t(99) = 1.672, p = .098; 95\% CI = [-0.002 - 0.020]$) or high AxD ($+1 SD; b = -0.007, t(99) = -0.953, p = .343; 95\% CI = [-0.023 - 0.008]$). In this population, 38.9% of the subjects fell within the significance region. When general intelligence was the outcome, factor VII interacted with global white matter AxD as well ($F(1, 100) = 4.522, p = .036, \Delta R^2 = 0.033$; Figure 3.55). This moderation was also conditional, and the moderation was strongest when AxD was low ($-1 SD; b = 0.016, t(100) = 2.050, p = .043; 95\% CI = [0.000 - 0.031]$) compared to AxD that was moderate ($b = 0.004, t(100) = 0.732, p = .466; 95\% CI = [-0.006 - 0.014]$) or high ($+1 SD; b = -0.008, t(100) = -1.121, p = .265; 95\% CI = [-0.023 - 0.006]$). In this population, only 12.8% of subjects fell within the significance region.

Global white matter AxD also interacted with IBP 3 to predict both fluid ($F(1, 94) = 6.590, p = .012, \Delta R^2 = 0.056$; Figure 3.56) and general ($F(1, 95) = 5.968, p = .016, \Delta R^2 = 0.045$;

Figure 3.57) intelligence. The moderation predicting fluid intelligence was most significant when AxD was low ($-1\ SD$; $b = 4.868$, $t(94) = 3.016$, $p = .003$; 95% CI = [1.664 – 8.072]) compared to AxD that was moderate ($b = 1.986$, $t(94) = 1.752$, $p = .083$; 95% CI = [-0.264 – 4.237]) or high ($+1\ SD$; $b = -0.896$, $t(94) = -0.568$, $p = .571$; 95% CI = [-4.026 – 2.234]). This moderation was significant in 39.8% of the population. When predicting general intelligence, the moderation was strongest when IBP 3 was moderate ($b = -2340.792$, $t(95) = -2.340$, $p = .021$; 95% CI = [-115,284.97 – -9463.068]) or high ($+1\ SD$; $b = -62374.022$, $t(95) = -2.774$, $p = .007$; 95% CI = [-209,995.24 – -34819.259]). In this population, 58.6% of subjects fell within the significance region.

Global white matter AxD also interacted with $\alpha 2$ -macroglobulin ($F(1, 99) = 5.289$, $p = .024$, $\Delta R^2 = 0.043$; Figure 3.58), ferritin ($F(1, 99) = 7.598$, $p = .007$, $\Delta R^2 = 0.058$; Figure 3.59), IBP 4 ($F(1, 94) = 4.075$, $p = .046$, $\Delta R^2 = 0.035$; Figure 3.60), and IBP 5 ($F(1, 94) = 4.447$, $p = .038$, $\Delta R^2 = 0.037$; Figure 3.61) to predict fluid intelligence (Table 3.27). $\alpha 2$ -Macroglobulin conditionally moderated the relationship between AxD and fluid intelligence, which was significant when AxD was high ($+1\ SD$; $b = 7.998$, $t(99) = 2.717$, $p = .008$; 95% CI = [2.157 – 13.839]) but not moderate ($b = 2.326$, $t(99) = 1.186$, $p = .238$; 95% CI = [-1.566 – 6.219]) or low ($-1\ SD$; $b = -3.346$, $t(99) = -1.000$, $p = .320$; 95% CI = [-9.985 – 3.293]). In this population, 38.0% of the subjects fell within the significance region. Ferritin moderated the relationship when AxD was moderate ($b = 0.024$, $t(99) = 2.844$, $p = .005$; 95% CI = [0.007 – 0.041]) or high ($+1\ SD$; $b = 0.042$, $t(99) = 3.792$, $p = .000$; 95% CI = [0.020 – 0.063]), but not when AxD was low ($-1\ SD$; $b = 0.006$, $t(99) = 0.624$, $p = .534$; 95% CI = [-0.014 – 0.026]). Ferritin was a moderator in 73.1% of this population. Inflammation biomarker pattern 4 moderated the relationship between AxD and fluid intelligence when AxD was high ($+1\ SD$; $b = 4.886$, $t(94) =$

2.823, $p = .006$; 95% CI = [1.449 – 8.323]) but not moderate ($b = 2.247$, $t(94) = 1.901$, $p = .060$; 95% CI = [-0.010 – 4.594]) or high (-1 SD ; $b = -0.392$, $t(94) = -0.218$, $p = .828$; 95% CI = [-3.952 – 3.169]), and 53.4% of this population fell within the significance region. Last, the IBP 5 was a moderator when AxD was moderate ($b = 2.182$, $t(94) = 2.053$, $p = .043$; 95% CI = [0.071 – 4.293]) and high (+1 SD ; $b = 5.319$, $t(94) = 3.092$, $p = .003$; 95% CI = [1.903 – 8.736]) but not when AxD was low (-1 SD ; $b = -0.955$, $t(94) = -0.495$, $p = .622$; 95% CI = [-4.789 – 2.878]). This moderation was significant in 56.3% of the population.

Finally, global white matter AxD interacted with ICAM-1 to predict general intelligence ($F(1, 100) = 3.953$, $p = .050$, $\Delta R^2 = 0.029$; Figure 3.62). This moderation was most significant when ICAM-1 was high (+1 SD ; $b = -92452.498$, $t(100) = -2.370$, $p = .020$; 95% CI = [-169833.31 – -15071.689]) and in this population 33.9% of the subjects fell within the significance region.

In the genu of the corpus callosum, IL-18 moderated the relationship between FA and fluid intelligence ($F(1, 99) = 4.080$, $p = .046$, $\Delta R^2 = 0.034$; Table 3.29; Figure 3.63). This moderation was most significant when IL-18 was low (-1 SD ; $b = 102.979$, $t(99) = 2.697$, $p = .008$; 95% CI = [27.208 – 178.749]) and a Johnson-Neyman analysis revealed that this moderation was significant in 47.2% of this population.

3.5 Discussion

3.5.1 Summary of Findings

This series of studies was performed to investigate the following fundamental question and constituent hypotheses:

Can relationships between peripheral xanthophyll carotenoids and markers of brain health be characterized using a systematic framework of moderation analyses?

- 1. Do inflammation biomarkers influence relationships between grey matter volume and facets of intelligence?*
- 2. Do inflammation biomarkers influence relationships between efficiency of intrinsic connectivity networks and facets of intelligence?*
- 3. Do inflammation biomarkers influence relationships between white matter microstructure and facets of intelligence?*

A series of exploratory, cross-sectional studies in a population of healthy, older adults revealed that inflammation biomarkers did indeed moderate relationships between markers of brain health and facets of intelligence at the structural, functional, and microstructural level.

3.5.2 *Do inflammation biomarkers influence relationships between grey matter volume of cortical regions and facets of intelligence?*

Yes, in this population of healthy, older adults inflammation biomarkers moderated independent relationships between volumes of several cortical regions and fluid intelligence.

These ROIs include the caudal anterior cingulate, entorhinal, precuneus, superior temporal, and supramarginal cortices. Additional relationships moderated by inflammation biomarkers include those between volume in the caudal anterior cingulate and general intelligence, frontal pole and auditory memory, lingual gyrus and task switching, and the posterior cingulate and immediate memory.

First, to determine relationships between markers of brain health in our population of healthy, older adults a correlation matrix revealed which facets of intelligence may associate with the grey matter ROIs (Table 3.1). Linear regression models performed with each ROI (IV), correlated facets of intelligence (DVs; auditory memory, delayed memory, fluid intelligence, general intelligence, immediate memory, task switching, and visual working memory), and five covariates (age, BMI, education, income, sex) revealed significant relationships between ROIs and auditory memory, delayed memory, fluid intelligence, general intelligence, and immediate memory (Table 3.5). Second, a correlation matrix revealed which facets of intelligence may associate with inflammation biomarkers (Table 3.2), and those with significant correlations were included in the list of possible moderators for that particular DV. Significant regression models were followed by a series of moderation analyses repeated with each individual inflammation biomarker and IBP (Table 3.3) as moderators (see section 3.3.5). All reported results remained significant after correcting for multiple comparisons.

The body of literature investigating relationships between peripheral inflammation biomarkers and brain volume is small but increases in some inflammation biomarkers have been associated with smaller whole-brain grey matter volume and the strength of that association varied across biomarkers (Gu et. al., 2017). To my knowledge, this is the first study to systematically explore associations between multiple inflammation biomarkers and regional grey

matter volume. Notably, most significant moderations in this study predicted fluid intelligence over the other facets of intelligence. Considering that physical health fully mediates the relationship between age and fluid intelligence (Bergman & Almkvist, 2013), it is possible that one component of that mediation is the interaction between inflammation biomarkers and cortical structure. With this in mind and due to the novel and exploratory nature of these studies, the discussion will focus on moderations that predict fluid intelligence.

This study found that in a population of healthy, older adults inflammation biomarkers moderated relationships between cortical volume in multiple ROIs and fluid intelligence. As a pattern (IBP 2), inflammation interacted with superior temporal (Figure 3.13), caudal anterior cingulate (Figure 3.3) and supramarginal gyrus (Figure 3.17) volumes to predict fluid intelligence. This biomarker pattern is most notably comprised of BDNF, RANTES, VEGF, and MMP-3. Though they differ in function, each of these biomarkers has been studied in relation to the aging brain.

Brain-derived neurotrophic factor is understood to affect neuroplasticity through synaptic regulation of long-term potentiation and depression, and during aging changes in neuronal plasticity are associated with cognitive decline (Lu, Nagappan, & Lu, 2014). Additionally, BDNF may aid survival and prevent apoptosis in neurons by protecting against inflammation (Kerschensteiner et. al., 1999; Tamatani et. al., 1998). In the periphery, lower serum BDNF level is associated with poorer cognitive performance, specifically in measures of delayed memory and processing speed suggesting that peripheral BDNF level could be a neurobiological correlate of cognitive function (Komulainen et. al., 2008; Shimada et. al., 2014). Vascular endothelial growth factor is also involved in neuroprotection and has been indicated in BBB maintenance, apoptosis hindrance, and microglial activation (Provias & Jeynes, 2014; Zachary, 2005).

Elevated prefrontal VEGF expression in decedent tissues is associated with worse cognitive outcomes and lower assessment scores (Mahoney et. al., 2019), whereas AD brains have decreased VEGF expression in the superior temporal and hippocampal regions when compared with normative brains (Provias & Jeynes, 2014). In the periphery, decreased serum VEGF correlated with AD diagnosis when compared to controls (Mateo et. al., 2006), and within the CNS elevated VEGF in cerebrospinal fluid associates with better aging outcomes on episodic memory and executive function (Hohman, Bell, & Jefferson, 2015).

Both RANTES and MMP-3 are more novel neurological biomarkers and studies investigating connections to brain health in humans are limited. Within the CNS, it is believed that the chemokine RANTES facilitates movement of peripheral monocytes through the BBB in response to inflammation, however this has only been demonstrated *in vitro* (Ubogu, Callahan, Tucky, & Ransohoff, 2006a, 2006b). However, in patients with traumatic brain injury, plasma RANTES levels were greater than those in CSF or decedent brain tissue and were correlated with mortality, indicating that peripheral levels are detectable and may be indicative of brain health (Albert et. al., 2017). Matrix Metalloproteinase-3 is part of an enzyme family that targets endothelial tight junctions, extracellular matrix, and basal lamina resulting in BBB disruption and increased permeability (Rosenberg, 2009). Although their relationship to cognitive function in healthy aging is largely uncharacterized, MMP-3 is activated in CSF during inflammation and enzymes in this family have been implicated in vascular cognitive impairment, AD, and Parkinson's disease (Rosenberg, 2017). Interestingly, these markers are all indicated in the inflammation or repair following ischemia (Iadecola & Anrather, 2011) and are induced (RANTES, MMP-3) or regulated (BDNF, VEGF) by NF- κ B signaling during inflammation (Liu

et. al., 2017). With this evidence in mind, it is possible that IBP 2 is capturing the complex signaling interactions involved with BBB damage and repair associated with aging.

The relationship between regional volume and fluid intelligence was moderated by individual inflammation biomarkers as well. Complement C3 interacted with both entorhinal cortex (Figure 3.6) and supramarginal gyrus (Figure 3.16) volumes; both IL-8 (Figure 3.14) and ICAM-1 (Figure 3.15) also interacted with supramarginal gyrus volume. Finally, precuneus volume interacted with IL-8 (Figure 3.12), and VCAM-1 interacted with caudal anterior cingulate volume (Figure 3.2).

Both ICAM-1 and VCAM-1 are adhesion molecules and IL-8 is an inflammatory cytokine affected by NF- κ B signaling, whereas Complement C3 is a component of the complement cascade, a major actor in the innate immune system. Levels of ICAM-1 and VCAM-1 are thought to express levels of endothelial damage and NVU impairment, resulting in aberrant BBB permeability (Yoon et. al., 2017; Zlokovic, 2011). Circulating levels of adhesion molecules are related to cognitive impairment (Tchalla et. al., 2016) and poor cognitive performance on tests of executive function, immediate memory, and processing speed (Yoon et. al., 2017). Additionally, IL-8 is an inflammatory mediator involved in endothelial dysfunction at the level of the NVU and is expressed at increased levels in AD (Zlokovic, 2011). This cytokine is related to poorer performance on measures of general cognitive impairment, memory, and cognitive speed (Baune et. al., 2008). Complement C3 is not as well studied using cognitive neuroscience methods within psychoneuroimmunology, but *in vitro* studies suggest that dysregulated interactions between neurons and glia caused by aberrant NF- κ B/C3 signaling contribute to synaptic dysfunction during AD (Lian et. al., 2014). In patients with mild cognitive impairment, C3 levels are related to speed of cognitive decline (Toledo et. al., 2014), and in mice

C3 deficiency caused enhanced spatial learning and cognitive performance (Mastellos, 2014; Perez-Alcazar et. al., 2014). Together, these studies suggest that multiple inflammation biomarkers, both individually and as a pattern, may contribute to cognitive impairment associated with both pathological and healthy brain aging. Further, it is possible that these markers contribute to cognitive performance in aging by interfering with NVU integrity and BBB permeability, however mechanistic studies are necessary to investigate this hypothesis.

Each of these moderations is most significant when ROI volume is large. Interestingly, presence of a specific VEGF polymorphism is related to global grey matter volume (Takeuchi et. al., 2017) but relationships between the other biomarkers and cortical grey matter volume are unclear outside of their relationship to AD progression. Regionally, there is some evidence supporting the relationship between grey matter volume and cognitive performance. Most notably, caudal anterior cingulate (Brodmann area 32) volume predicts higher performance on tasks measuring fluid intelligence after a multi-modal intervention, suggesting that caudal anterior cingulate volume could be an important characteristic when considering the neural architecture of and individual differences in fluid intelligence (Daugherty et. al., 2020). Larger anterior cingulate (Brodmann areas 24, 32, 33) volumes also predict behavioral therapy outcomes in major depressive disorder (Frodl et. al., 2008; Fujino et. al., 2015), and taken together these studies indicate that this region may be important to consider when investigating cognitive response to modifiable lifestyle factors, such as peripheral inflammation.

Within the parietal lobe, the supramarginal gyrus (Brodmann area 40) and the precuneus (Brodmann area 7) are implicated in the Parieto-Frontal Integration Theory (P-FIT) model of intelligence (Jung & Haier, 2007) and in the Network Neuroscience Theory of Intelligence (Barbey, 2018) as components of both the frontoparietal and default mode networks (Yeo et. al.,

2011). The supramarginal gyrus is implicated in information integration during processing, and the volume in this region is associated with general intelligence as well as verbal and spatial intelligence (Colom et. al., 2009). The precuneus is also implicated in fluid reasoning tasks (Prabhakaran et. al., 1997), although it is most implicated in episodic memory (Cavanna & Trimble, 2006; Nyberg, 2017). Interestingly, episodic memory appears to be more vulnerable to systemic inflammation compared to language, executive function, or processing speed (Walker et. al., 2019).

Finally, the superior temporal (Brodmann area 22) and entorhinal cortex (Brodmann areas 28, 34) are located in the rostral anterior temporal lobe and both are associated with fluid intelligence. Though often associated with multisensory integration, damage to the superior temporal results in spatial neglect (Karnath, 2011), volume in this region is related to intelligence (Basten, Hilger, & Fiebach, 2015), and it is activated during fluid intelligence tasks (Luo et. al., 2003). As part of the medial temporal lobe system, the entorhinal cortex is important for memory function as it mediates hippocampal signaling (Reagh et. al., 2018), and this area is particularly susceptible to age-related changes structurally and functionally (Khan, et. al., 2013). Further, longitudinal atrophy in the entorhinal cortex is linked to lower fluid intelligence scores in adults (Raz et. al., 2008).

The moderation results from the present study provide evidence that the relationship between grey matter volume and fluid intelligence is moderated by specific inflammation markers, both individually and as a pattern. Some regional volumes, like that of the caudal anterior cingulate or supramarginal gyrus, interacted with multiple inflammation biomarkers while others, like the entorhinal cortex, precuneus, or superior temporal, interacted with singular biomarkers. Specifically, IBP 2 (a pattern predominantly comprised of BDNF, VEGF, RANTES,

and MMP-3) and VCAM-1 interacted with caudal anterior cingulate volume; IBP 2, ICAM-1, IL-8, and complement C3 interacted with supramarginal volume; complement C3 interacted with entorhinal volume; IL-8 interacted with precuneus volume, and IBP 2 interacted with superior temporal volume. These biomarkers are implicated in NF- κ B signaling and in NVU construction, both of which affect permeability and integrity of the BBB (Liu et. al., 2017). Inflammatory responses involving NF- κ B in particular are a major component of inflamm-aging (Salminen et. al., 2008).

In combination, evidence from the literature and findings from the present study suggest that inflammatory responses involved with NF- κ B signaling moderate associations between regional grey matter volume and fluid intelligence. It is possible that these inflammation biomarkers influence fluid intelligence via BBB disruption, however further studies are necessary to elucidate any mechanistic explanation. These findings identify biomarkers that may be targets for brain aging or precision medicine studies seeking to attenuate cognitive dysfunction associated with inflamm-aging. Additionally, these moderations were most significant when volumes were large which suggests that these ROIs may also be targets to ameliorate deficits during inflamm-aging or may indicate subgroups for precision medicine studies.

3.5.3 Do inflammation biomarkers influence relationships between efficiency of intrinsic connectivity networks and facets of intelligence?

Yes, in this population of healthy older adults inflammation biomarkers moderated independent relationships between efficiency measures in the FPN, LN, SMN, DAN, and VAN

and fluid intelligence. Relationships between efficiency measures in the FPN, DAN, and VAN and general intelligence were also independently moderated by inflammation biomarkers.

First, to determine relationships between markers of brain health in our population of healthy, older adults linear regression models performed with ICNs containing each ROI with at least one significant moderation (IV), correlated facets of intelligence (DVs; auditory memory, fluid intelligence, general intelligence, immediate memory, and task switching), and five covariates (age, BMI, education, income, sex) revealed significant relationships between network efficiency and all facets (Tables 3.15 and 3.16). Significant regression models were followed by a series of moderation analyses repeated with each individual inflammation biomarker and IBP (Table 3.3) as moderators. All reported results remained significant after correcting for multiple comparisons.

To my knowledge, this is the first study to systematically explore associations between inflammation biomarkers and neural efficiency in ICNs using rsfMRI and graph theory metrics. There is some evidence of association between DMN connectivity and systemic inflammation in patients with AD and mild cognitive impairment (Balthazar et. al., 2015) as well as in cognitively intact middle-aged adults (Marsland et. al., 2017). More recently a whole-brain connectivity analysis in rheumatoid patients indicated that higher levels of systemic inflammation correlated with connectivity between the inferior parietal lobule and medial prefrontal cortex (Schrepf et. al., 2018). Connectivity changes between these regions and the DMN, DAN, and FPN were more prominent in those with higher levels of peripheral inflammation and may be recruited to serve a compensatory function. The present study found that inflammation biomarkers moderated associations between network efficiency in two of these

networks and intelligence in a population of healthy, older adults, and these results will be the focus of the following discussion.

In the FPN, α 2-macroglobulin and IBP 5 each moderated the relationship between small world propensity and fluid intelligence (Figures 3.18 and 3.19), as well as the relationship between small world propensity and general intelligence (Figures 3.22 and 3.23). Associations between local (Figure 3.20) and global (Figure 3.21) efficiency and general intelligence were also moderated by α 2-macroglobulin, but since small world propensity is characterized by optimal balance between local and global efficiency (Muldoon, Bridgeford, & Bassett, 2016) only interactions with small world propensity will be the focus of this discussion. Also, because α 2-macroglobulin is the major factor in IBP 5 this biomarker will be the focus for interpreting relevant results.

α 2-Macroglobulin is an acute phase protease inhibitor that acts on MMPs and can be stimulated by IL-6, a cytokine commonly associated with systemic inflammation and NF- κ signaling (Cucullo et. al., 2003; Gao et. al., 2002). Importantly, this biomarker is increased in the periphery after BBB injury *in vitro* and *in vivo* and may protect against MMP-mediated degradation of the endothelial extracellular matrix within the NVU (Cucullo et. al., 2003). In human studies, α 2-macroglobulin is implicated in AD pathology (Blacker et. al., 1998; Tooyama et. al., 1993; Varma et. al., 2016), preclinical AD and early neuronal injury (Varma et. al., 2016), BBB disruption in neuropsychiatric systemic lupus erythematosus (Asano et. al., 2017), is related to BDNF in less severe mild cognitive impairment outcomes (Dursun et. al., 2015). Another study using a machine-learning approach identified α 2-macroglobulin as one of a five-marker panel optimized for diagnosing AD (Eke et. al., 2018). The influence of α 2-macroglobulin in healthy brain aging, however, remains unclear. One longitudinal study of nondemented, older

twins found that a polymorphism in the $\alpha 2$ -macroglobulin gene related to delayed memory impairment, however presence of this polymorphism was rare and the relationship between this biomarker and healthy brain aging in the general population remains uncharacterized (Reynolds et. al., 2006). To my knowledge, the relationship between this biomarker and specific facets of intelligence or network efficiency is largely unstudied.

The present investigation found that $\alpha 2$ -macroglobulin influenced associations between small world topology and measures of intelligence. The emerging network neuroscience theory of human intelligence directly links intelligence to small world architecture (Barbey, 2018) and results from this study suggest that this relationship is moderated by inflammation. Altered small-world topology has been linked to AD (Stam et. al., 2007) and cognitive decline in aging (Zuo et. al., 2017). Considering the strong implication of the FPN in higher-order cognitive function (Barbey et. al., 2012; Marek & Dosenbach, 2018; Santarnecchi et. al., 2017), it logically follows that small-world propensity in the FPN would associate with fluid and general intelligence in this population. $\alpha 2$ -Macroglobulin is strongly associated with AD (Blacker et. al., 1998; Tooyama et. al., 1993; Varma et. al., 2016) and altered serum levels occur after proinflammatory changes and BBB dysregulation (Cucullo et. al., 2003), suggesting that aberrant immune signaling in response to BBB disruption may inhibit information transfer in small-world networks. Due to the cross-sectional and observational nature of this study, connection to BBB integrity is speculative, however, and requires mechanistic studies for support. That said, the present study identified $\alpha 2$ -macroglobulin as a potential target for ameliorating age-related cognitive decline associated with small world architecture in the FPN.

In the DAN, IL-18 and ferritin each moderated the relationship between small world propensity and fluid intelligence (Figures 3.31 and 3.35), as well as the relationship between

small world propensity and general intelligence (Figures 3.33 and 3.37). Associations between global efficiency and fluid (Figure 3.30) and general (Figure 3.31) intelligence were also moderated by IL-18, but since small world propensity is characterized by optimal balance between local and global efficiency (Muldoon, Bridgeford, & Bassett, 2016) only interactions between IL-18 and small world propensity are discussed.

Additionally, VCAM-1 interacted with global efficiency to predict fluid (Figure 3.34) and general (Figure 3.34) intelligence, and Factor VII moderated the relationship between global efficiency and general intelligence (Figure 3.38). As mentioned in the previous section, VCAM-1 is an adhesion molecule related to endothelial damage and BBB permeability (Yoon et. al., 2017; Zlokovic, 2011), and circulating VCAM-1 has been associated with cognitive impairment (Tchalla et. al., 2016). Factor VII is a protein involved in blood clotting and circulating levels of this protein are related to IL-6 and CRP in hypercholesterolemic patients, suggesting that factor VII is involved in systemic inflammation (Porreca et. al., 2002). As a marker for vascular risk, factor VII has been related to cognitive impairment in healthy aging when accompanied by elevation in at least one other risk factor (Gillett et. al., 2018), AD (Gupta et. al., 2005; Mari et. al., 1996), and most predominantly with vascular dementia (Gallacher et. al., 2010; Gupta et. al., 2005; Mari et. al., 1996; Quinn et. al., 2011). Influence of these biomarkers in healthy aging is largely uncharacterized, but observations from this study indicate that a significant interaction is present. Both biomarkers interacted only with global efficiency, suggesting that the influence of VCAM-1 and factor VII on intelligence may be dependent on path length within the DAN. However, due to the cross-sectional nature of this study claims about dependency or directionality cannot be made, and further investigation is necessary to understand the relationship between global efficiency and these biomarkers.

Interleukin-18 is a proinflammatory cytokine involved in NF- κ B signaling during an inflammatory response and mediates various sickness behaviors, including altered cognitive performance (Dantzer et. al., 2008; Dantzer & Kelley, 2007). Animal studies provide evidence that IL-18 influences synaptic plasticity and cognitive function by interacting with NMDA receptors thereby reducing long-term potentiation (Cumiskey, Pickering, & O'Connor, 2007; Cumiskey et. al., 2007; Curran, Murray, & O'Connor, 2003; Curran & O'Connor, 2001; del Rey et. al., 2013). It is also believed that IL-18 mediates vascular changes during inflamm-aging (Fahey & Doyle, 2019; Rodriguez-Menocal et. al., 2014), though it is not yet characterized whether this response is pro- or anti-angiogenetic. Though mostly studied in animal models, in humans IL-18 level is increased in multiple sclerosis and early AD (Motta et. al., 2007; Nicoletti et. a., 2001; Ojala et. al., 2009), as well as during healthy aging (Gangemi et. al., 2003). Though IL-18 has been implicated in cognitive impairment after traumatic brain injury and in AD (Bossù et. al., 2008; Della et. al., 2014), the relationship between IL-18 and cognitive function and other markers of brain health in healthy aging remains unclear.

Ferritin is a protein that stores and controls the release of iron throughout the body, including in the brain where iron accumulates during aging (Halgren & Sourander, 1958). This accumulation increases oxidative stress by increasing ROS production, thereby contributing to neurodegeneration (Schipper, 2004). Iron accumulation in the brain has been linked to lower general intelligence (Penke et. al., 2012), executive dysfunction, and decreased psychomotor speed (Ghadery et. al., 2015). In the periphery, serum ferritin reliably indicates iron load in tissues (Cook, 1999; Wang et. al., 2010). Since it is an acute phase protein, serum ferritin levels can also be an indicator of inflammatory state, as its release is mediated by IL-6 signaling (Streetz et. al., 2001). Though uncharacterized in older adults, serum ferritin was recently related

to general cognitive function in toddlers (Parkin et. al., 2020), suggesting a need to investigate this relationship in other parts of the lifespan as well.

The present study found that serum IL-18 and ferritin independently influenced associations between small world topology and measures of intelligence in healthy, older adults. The DAN is associated with executive function and intelligence (Beineberg et. al., 2018; Santarnecchi et. al., 2017), which supports the finding in this study that small world propensity in the DAN correlated with fluid and general intelligence. Increased levels of IL-18 and iron are both related to poorer cognitive performance and serum levels of both biomarkers also indicate an inflammatory state, suggesting they may be related to age-related cognitive decline associated with inflamm-aging. Notably, IL-18 is involved in NF- κ B cytokine signaling. Taken together, observations from this study and evidence from the psychoneuroimmunology literature suggest that the pro-inflammatory state characteristic of inflamm-aging may inhibit information transfer in small-world networks, thereby contributing to age-related cognitive changes. Specifically, these observations identified IL-18 and ferritin as potential targets for ameliorating age-related cognitive decline associated with small world architecture in the DAN.

Curiously, the nature of interaction between biomarkers and small world propensity varied between these networks. In the FPN, α 2-macroglobulin interacted most significantly when small world propensity was high. In the DAN, ferritin interacted most significantly when small world propensity was low, and IL-18 moderation varied by outcome. These observations suggest a nuanced role for inflammation biomarkers in cognitive aging relative to differences in topological architecture. Age-related changes in fluid intelligence are thought to result from changes in network topology and signaling dynamics within the brain (Barbey, 2018; Yankner,

Lu, & Loerch, 2008) and it is possible that inflammation biomarkers influence these changes, though mechanistic studies are needed to understand directionality underlying such influences.

3.5.4 Do inflammation biomarkers influence relationships between white matter microstructure and facets of intelligence?

Yes, in this population of healthy, older adults inflammation biomarkers moderated relationships between both axial diffusion and fractional anisotropy of global white matter and fluid intelligence. Inflammation biomarkers also moderated the relationship between axial diffusion of global white matter and general intelligence. Finally, one inflammation biomarker moderated the relationship between fractional anisotropy in the genu of the corpus callosum and fluid intelligence.

To determine relationships between markers of brain health in our population of healthy, older adults linear regression models were performed with diffusion measures for global white matter and the genu of the corpus callosum (IVs), fluid and general intelligence (DVs), and five covariates (age, BMI, education, income, sex). Regression models revealed all significant relationships (Table 3.26) and were followed by a series of moderation analyses repeated with each inflammation biomarker with a significant moderation in the previous section and each IBP (Table 3.3) as moderators. All reported results remained significant after correcting for multiple comparisons.

To my knowledge, this is the first study to systematically explore associations between multiple inflammation biomarkers and white matter integrity in healthy, older adults using DTI. Previously, one study showed that systemic inflammation during middle age is related to reduced whole brain FA later in life (Walker et. al., 2017). Other studies have shown associations

between white matter integrity and inflammation biomarkers in patients with chronic disease. Peripheral cytokines have been linked to decreased FA in multiple white matter tracts in patients with bipolar disorder (Benedetti et. al., 2016), major depressive disorder (Sugimoto et. al., 2018), AD (Swardfager et. al., 2017), and schizophrenia (Fu et. al., 2019; Prasad et. al., 2015). Associations between inflammation biomarkers and white matter integrity in healthy brain aging is largely unexplored within the cognitive neuroscience and psychoneuroimmunology literature, but the findings reported in this study contribute to this integrated field.

The present study found no associations between RD for global white matter or the genu of the corpus callosum and inflammation biomarkers. Biomarkers interacted with global white matter AxD to predict both fluid and general intelligence. Specifically, the relationship between global AxD and fluid intelligence was moderated by α 2-macroglobulin (Figure 3.58), factor VII (Figure 3.54), ferritin (Figure 3.59), IBP 3 (Figure 3.56), IBP 4 (Figure 3.60), and IBP 5 (Figure 3.61). The relationship between global AxD and general intelligence was moderated by ICAM-1 (Figure 3.62), factor VII (Figure 3.55), and IBP 3 (Figure 3.58). As was previously in this chapter, α 2-macroglobulin is the major component of IBP 5 so both will be explained as α 2-macroglobulin. The major components of IBP 3 are factor VII, ICAM-1, and stem cell factor, and IBP 4 is most significantly comprised of complement C3, fibrinogen, haptoglobin, and α 1-antitrypsin. Noticeably, the inflammation biomarkers influencing the relationship between AxD and fluid intelligence have significant overlap with those influencing general intelligence, though it seems a greater variety of biomarkers influence fluid intelligence.

For both facets of intelligence, factor VII had the most influence when AxD was low. The same was observed when IBP 3 interacted with AxD to predict fluid intelligence. When α 2-macroglobulin, ferritin, or IBP 4 was the moderator the interaction was most significant when

AxD was high. Though changes in AxD are considered reflective of axonal damage, it is unclear how regional AxD changes with age (Barrick et. al., 2010). Without a well-characterized relationship between age and AxD, these findings are difficult to interpret in the context of brain health. However, these findings do show that inflammation biomarkers, both individually and as a pattern, contribute to the relationship between white matter integrity and intelligence during normal aging. Some biomarkers relevant to white matter integrity were not relevant to associations with grey matter structure or network efficiency, primarily those comprising IBP 4. Briefly, complement C3, α 1-antitrypsin, fibrinogen, and haptoglobin are all acute phase proteins that are released from the liver in response to the innate inflammatory response. As discussed previously, a major contributor to inflamm-aging is the NF- κ B inflammatory signaling pathway and cytokines released in this cascade stimulate acute phase protein production and release. Taken together, the inflammation biomarkers associated with white matter integrity are also implicated in systemic inflammation characteristic of inflamm-aging. These observations demonstrate novel associations between white matter microstructure, chronic inflammation, and cognitive performance in the aging brain.

In addition, IL-18 moderated the relationship between white matter integrity and fluid intelligence globally (Figure 3.53) and in the genu of the corpus callosum (Figure 3.63). Both associations were most significant when IL-18 level was below the mean. There is evidence to support an association between IL-18 and white matter structure, however this is demonstrated in just one study. In older adults, white matter injury was related to an inflammatory composite score comprised of inflammation biomarkers driven by IL-18 activity (Altendahl et. al., 2020). Importantly, white matter integrity is associated with fluid intelligence throughout the lifespan (Chen et. al., 2020) and in older adults changes in white matter microstructure over time

correspond to changes in fluid intelligence (Ritchie et. al., 2015). Evidence that longitudinal changes in FA correspond to changes in fluid intelligence supports the idea that lower FA indicates less efficient information transfer thus contributing to age-related cognitive decline. Together, these observations suggest that IL-18 activity may contribute to age-related decline in fluid intelligence by interfering with signaling across white matter fibers and suggest IL-18 may be a target for intervention studies of or precision medicine approaches to the aging brain.

3.6 *Strengths, Limitations, and Conclusions*

The collection of studies within this chapter contribute to the field of psychoneuroimmunology by providing evidence that peripheral inflammation biomarkers influence brain health via interactions with cortical structure, network efficiency, and neural integrity. The multi-modal imaging paradigm of this collection of studies contributes substantially to an underdeveloped cognitive neuroscience branch in this field of study. Together, observations in this dissertation provide converging evidence that inflammation biomarkers, individually and as a pattern, moderate relationships between brain health and cognitive performance, particularly fluid and general intelligence. Significant inflammation biomarkers contribute to existing inflamm-aging literature as they largely fit into two categories: (1) BBB dysfunction and (2) systemic inflammation. The current research supports potential for specific biomarkers as targets in addressing healthy brain aging through intervention studies or precision medicine approaches.

Importantly, these studies are limited by the observational and cross-sectional nature of the data and do not allow inferences to be drawn regarding causality, directionality, or mechanisms of action. Also, the participants in these studies were Caucasian and mostly

educated, which does not provide a representative sample and therefore limits the generalizability of these observations to other populations. Additionally, genetic data was not available for participants, which limit our understanding of these results since the inflammatory response is heavily reliant on gene expression and transcription factors. Finally, the majority of relevant studies from the literature use preclinical animal models or are conducted in observational studies focused on a diseased state. Though animal models are extremely useful in identifying and characterizing mechanisms of action for biomarkers, they are less useful in understanding complex cognitive functions. Reliable interpretations of complex cognitive function data cannot be extrapolated from animal models or from patients in a diseased state known to significantly impact complex cognitive abilities, so replication in healthy controls is necessary to fully contextualize findings from the present studies. Future studies that address these limitations will be important to understand how inflammation biomarkers influence brain health in aging.

This collection of studies sought to fill some of the gaps of knowledge that exist within the field of psychoneuroimmunology by characterizing relationships between peripheral inflammation biomarkers and different measures of brain health. The data suggest that inflammation biomarkers moderate relationships between cortical volume, network efficiency, and neural integrity and intelligence in healthy, older adults. The most significant contributions of this are: (1) inflammation not influence brain health uniformly, but instead acts in a nuanced way, (2) there exists converging evidence across biomarkers, facets of intelligence, and measures of brain health supporting a role for inflammation biomarkers in brain aging, (3) influential biomarkers are largely associated with BBB disruption or systemic inflammation attributable to

acute phase proteins, and (4) specific biomarkers are potential targets when for developing intervention studies for or a precision medicine approach to age-related cognitive decline.

3.7 *Figures and Tables*

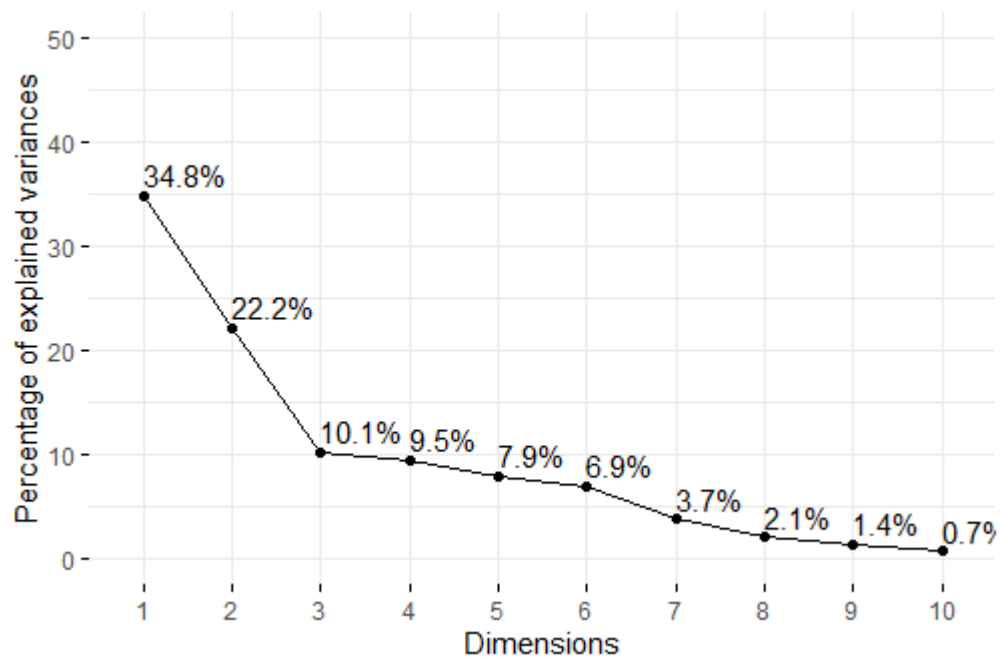


Figure 3.1 | Scree plot from the principle component analysis determining IBP composition. Six dimensions accounted for 5% or greater variance and determined the six component IBPs.

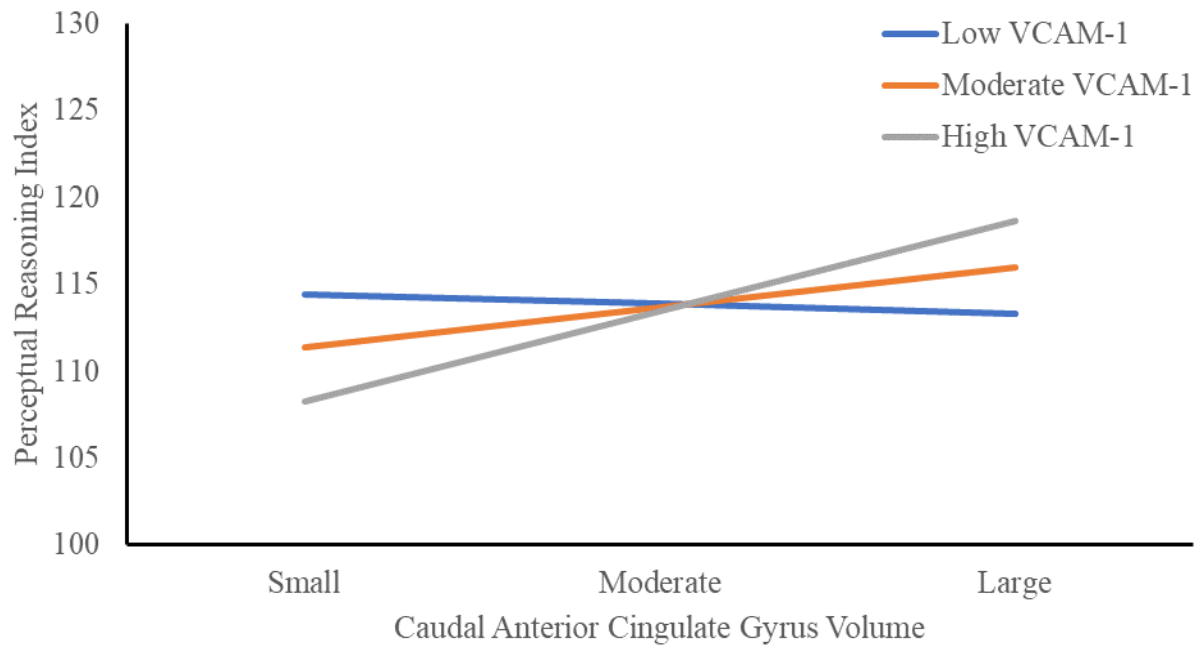


Figure 3.2 | VCAM-1 status conditionally moderates the relationship between caudal anterior cingulate volume and fluid intelligence. When volume is small, VCAM-1 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

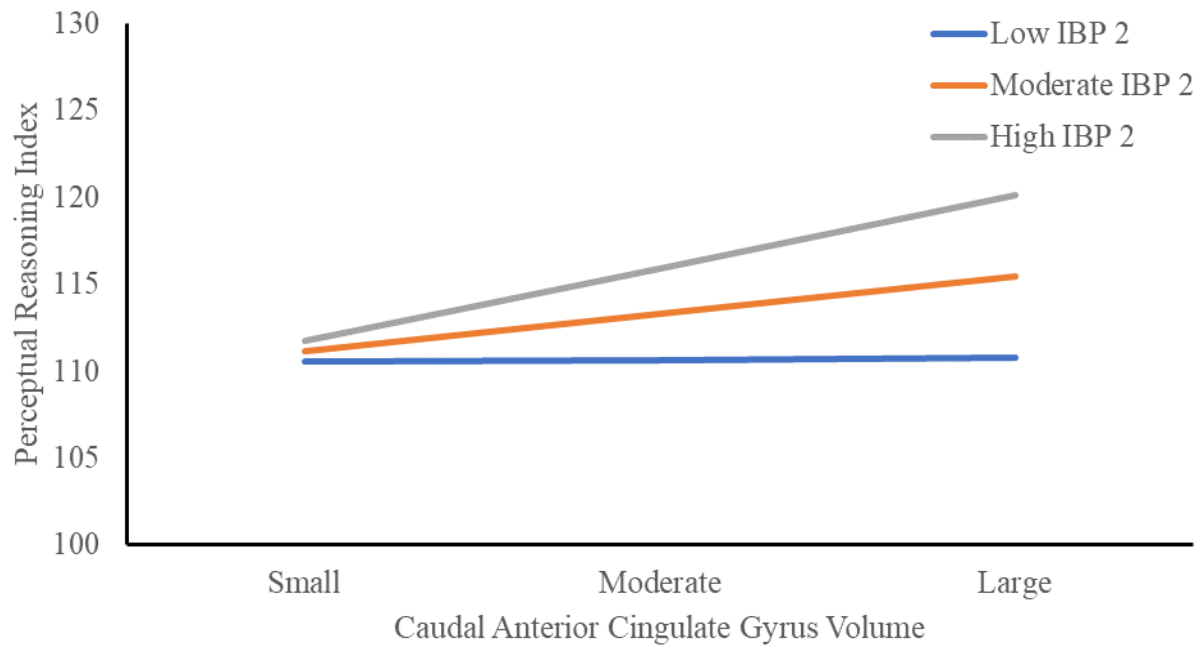


Figure 3.3 | IBP 2 status conditionally moderates the relationship between caudal anterior cingulate volume and fluid intelligence. When volume is moderate or large, IBP 2 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

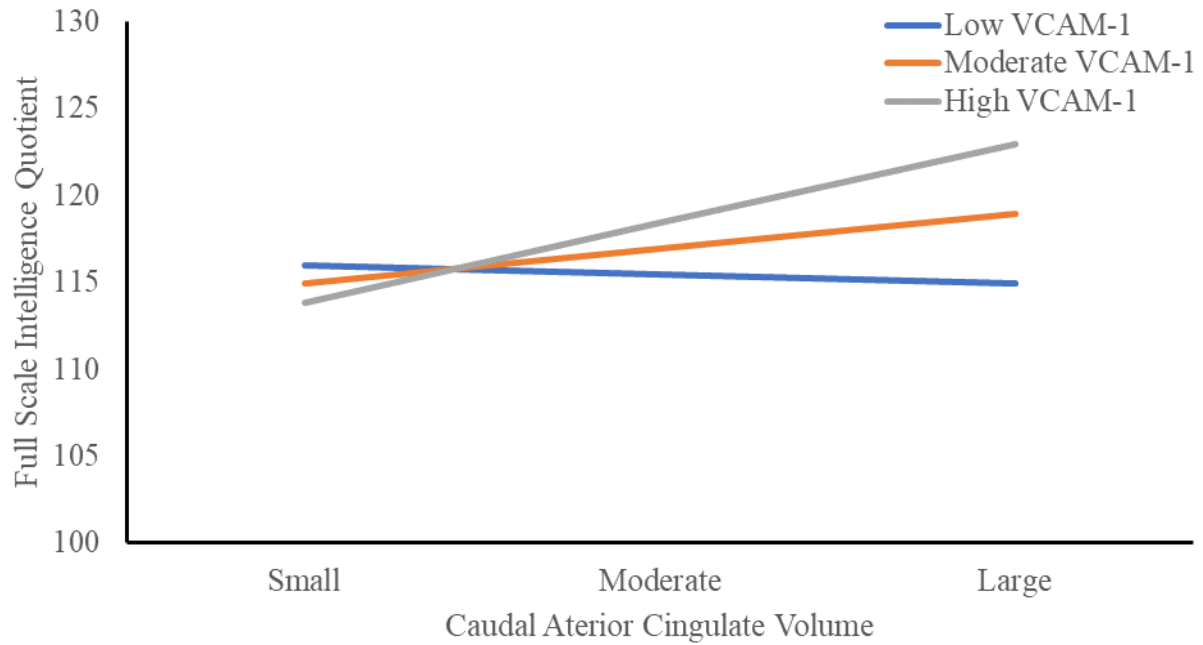


Figure 3.4 | VCAM-1 status conditionally moderates the relationship between caudal anterior cingulate volume and general intelligence. When volume is large, VCAM-1 significantly influences general intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

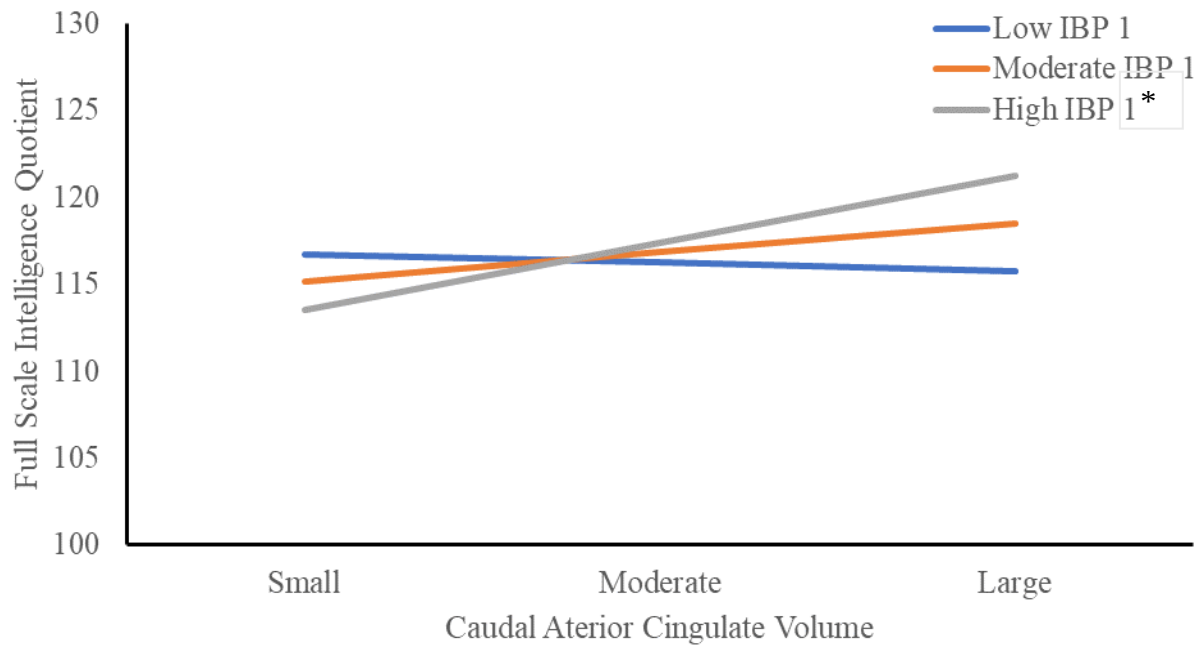


Figure 3.5 | IBP 1 conditionally moderates the relationship between caudal anterior cingulate volume and general intelligence. When IBP 1 is high, it significantly moderates the relationship between volume and general intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean. $*p < .05$

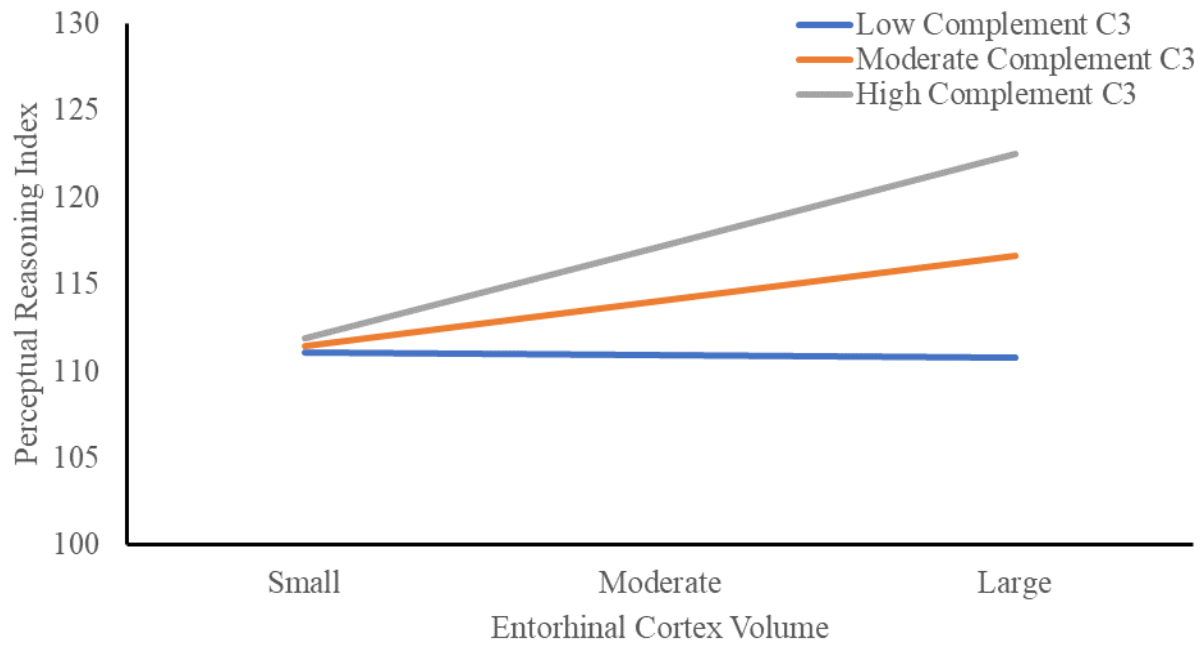


Figure 3.6 | Complement C3 conditionally moderates the relationship between entorhinal cortex volume and fluid intelligence. When volume is moderate or large, complement C3 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

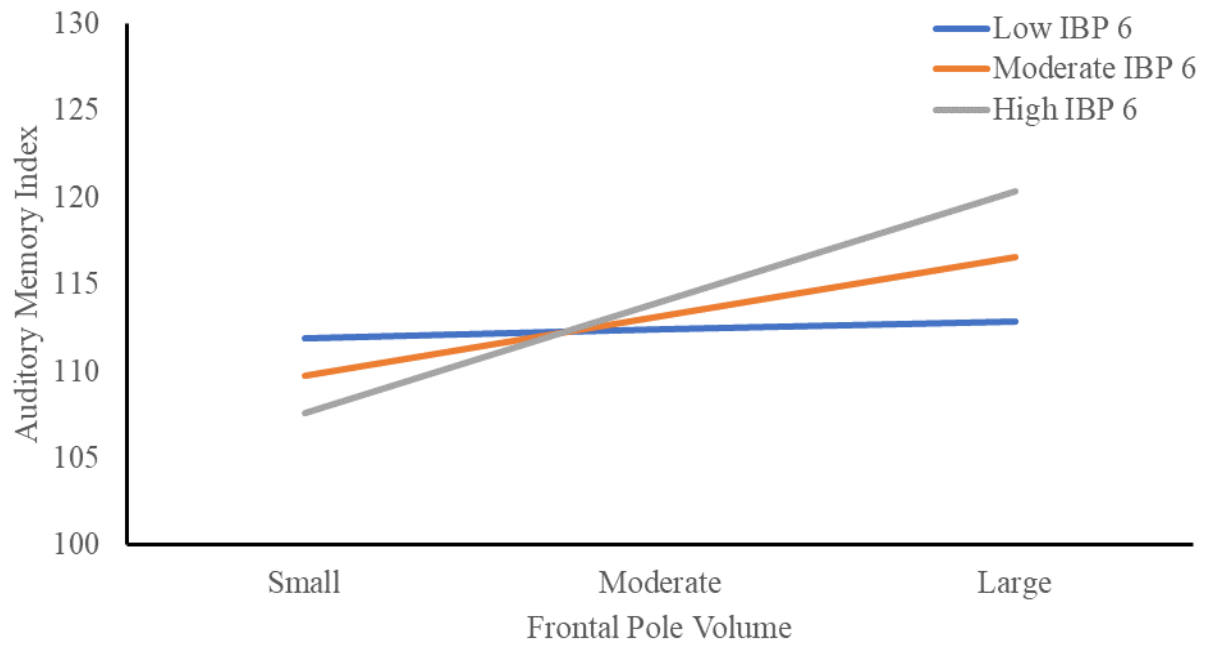


Figure 3.7 | IBP 6 conditionally moderates the relationship between frontal pole volume and auditory memory. When volume is large, IBP 6 significantly influences auditory memory. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

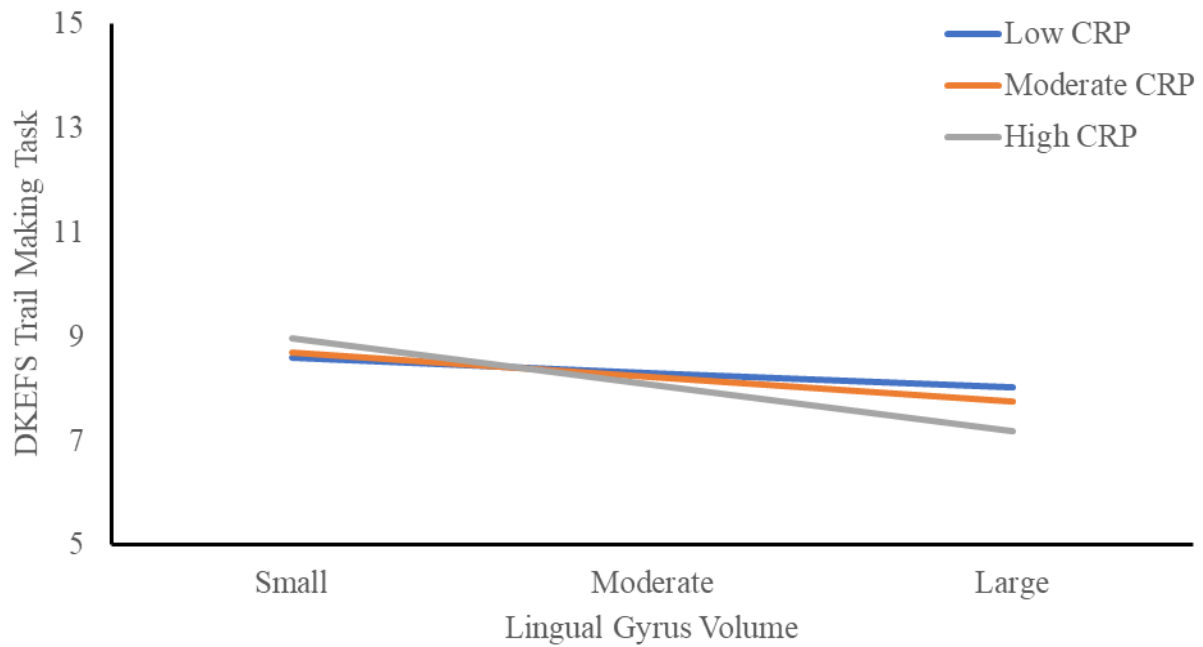


Figure 3.8 | CRP conditionally moderates the relationship between lingual gyrus volume and task switching. When CRP is high, it significantly moderates the relationship between volume and task switching. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean. $*p < .05$

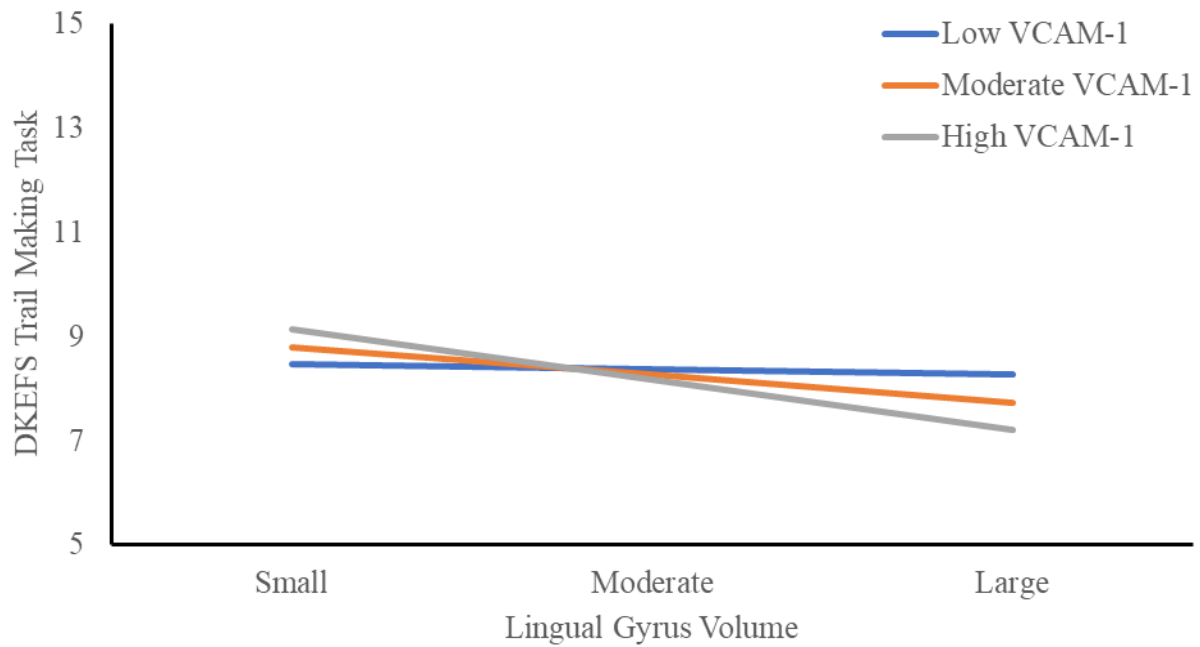


Figure 3.9 | VCAM-1 conditionally moderates the relationship between lingual gyrus volume and task switching. When volume is large, VCAM-1 significantly influences task switching. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

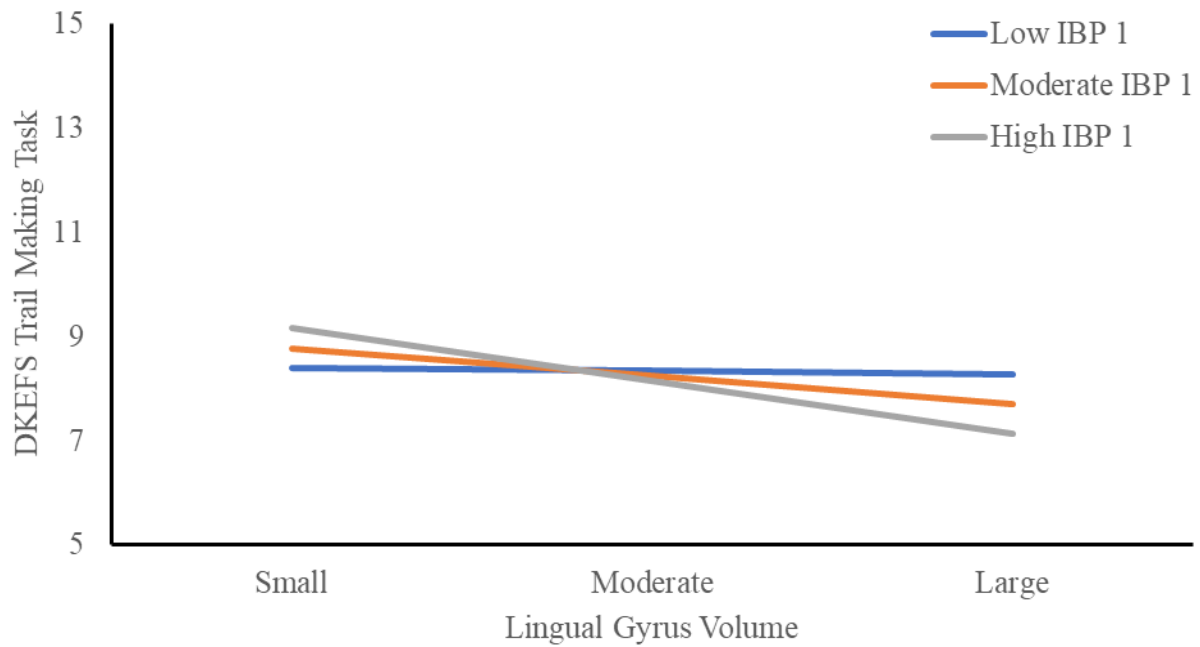


Figure 3.10 | IBP 1 conditionally moderates the relationship between lingual gyrus volume and task switching. When volume is large, IBP 1 significantly influences task switching. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

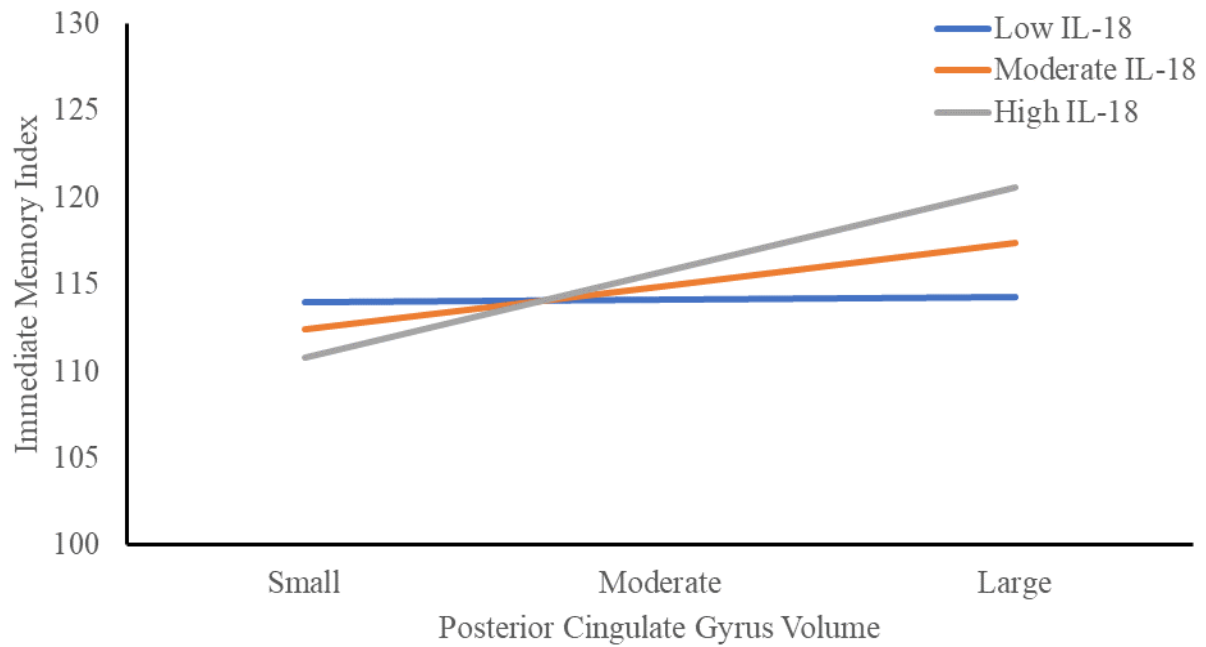


Figure 3.11 | IL-18 conditionally moderates the relationship between posterior cingulate volume and immediate memory. When IL-18 is moderate or high, it significantly moderates the relationship between volume and immediate memory. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean. $*p < .05$

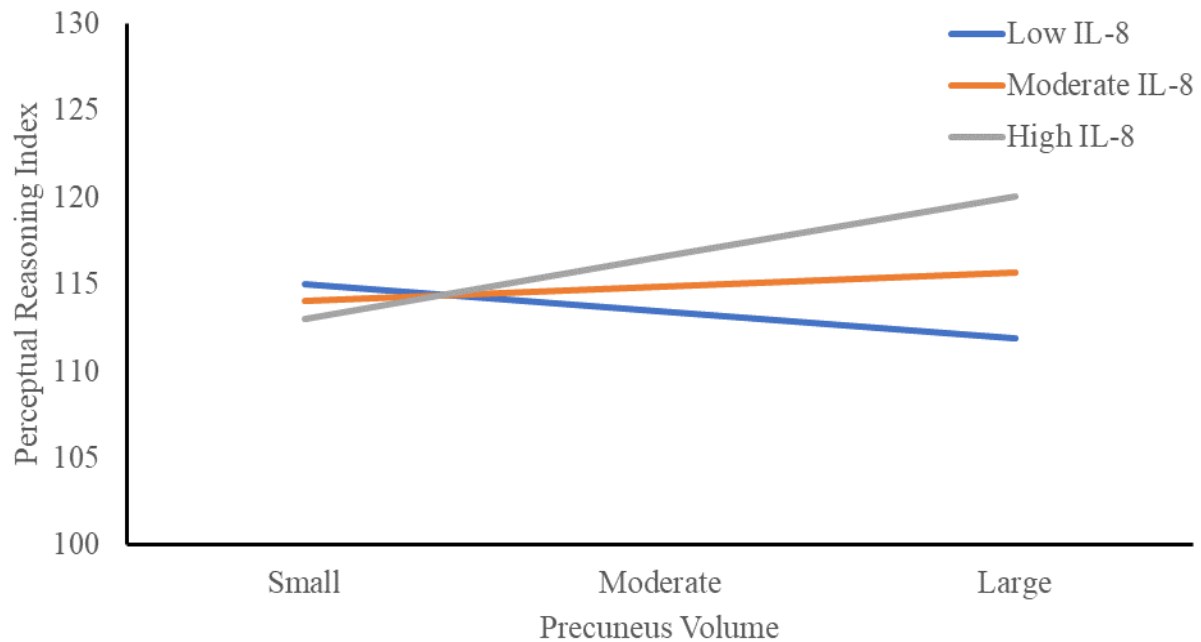


Figure 3.12 | IL-18 conditionally moderates the relationship between precuneus volume and fluid intelligence. When IL-18 is very high, it significantly moderates the relationship between volume and fluid intelligence. Small volume is defined as one *SD* below the mean; large volume is defined as one *SD* above the mean; very high status is defined as >1 *SD* above the mean.

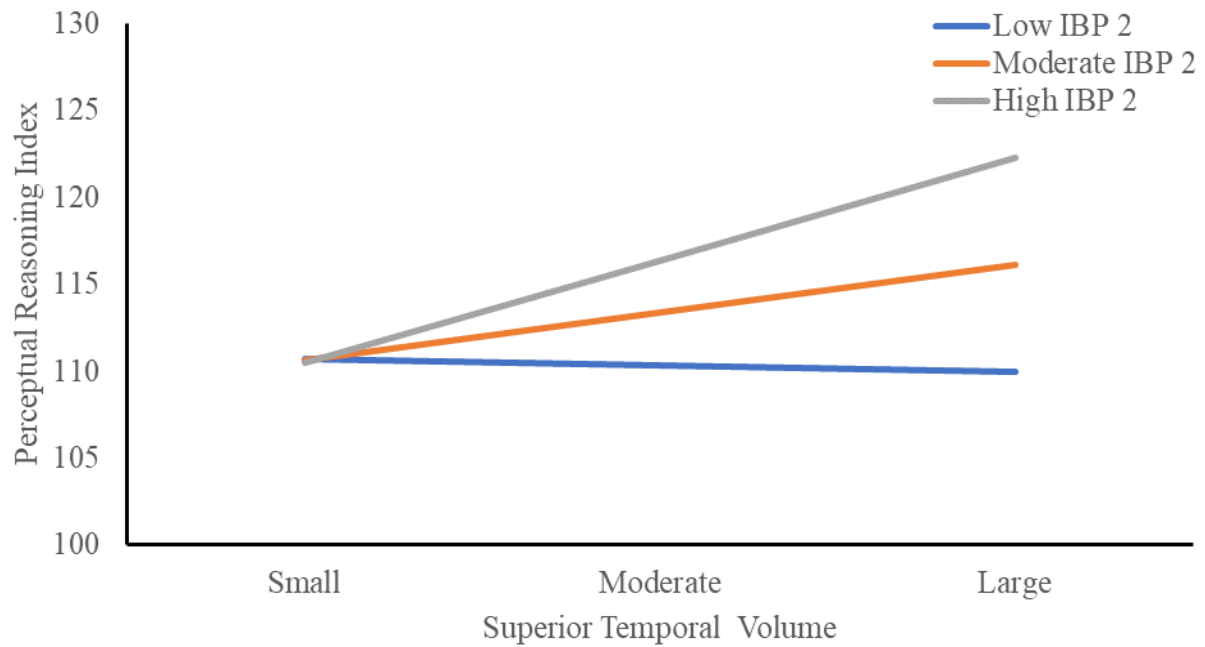


Figure 3.13 | IBP 2 conditionally moderates the relationship between superior temporal volume and fluid intelligence. When volume is moderate or large, IBP 2 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

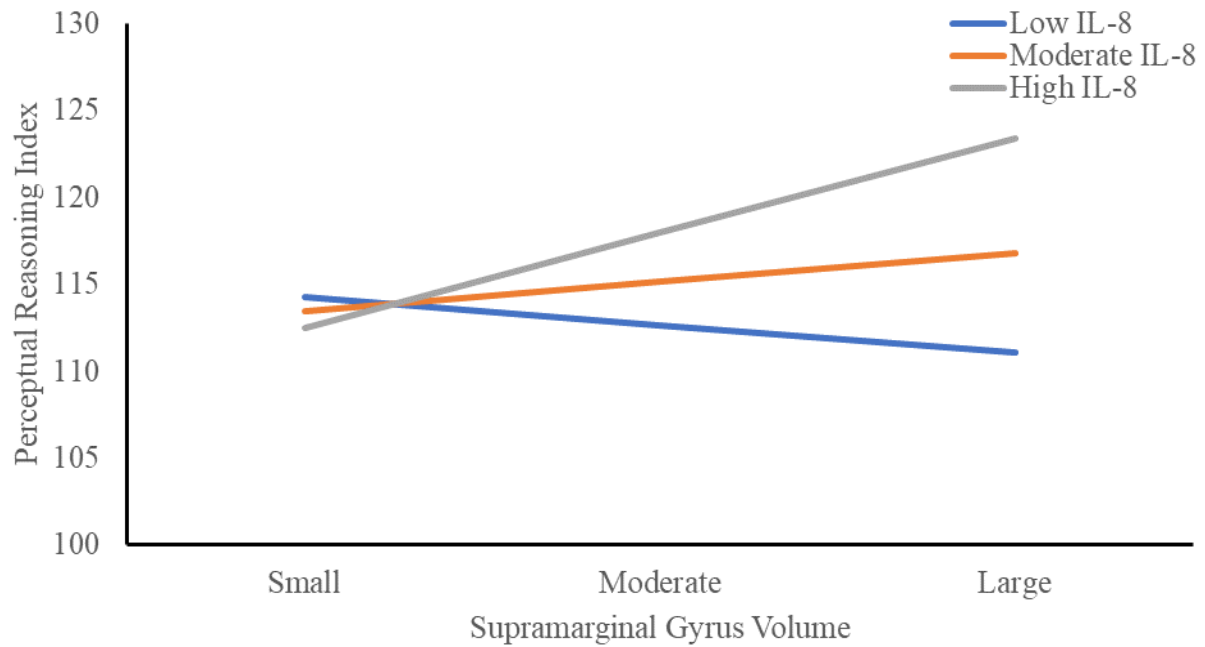


Figure 3.14 | IL-8 conditionally moderates the relationship between supramarginal gyrus volume and fluid intelligence. When volume is large, IL-8 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

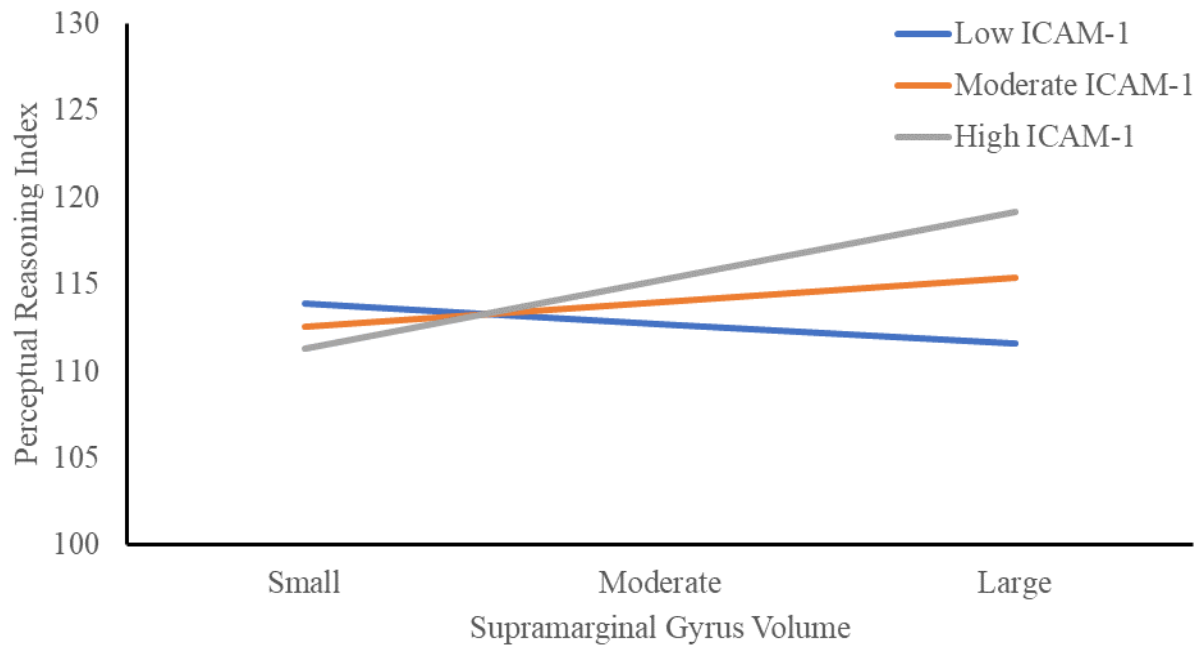


Figure 3.15 | ICAM-1 conditionally moderates the relationship between supramarginal gyrus volume and fluid intelligence. When volume is large, ICAM-1 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

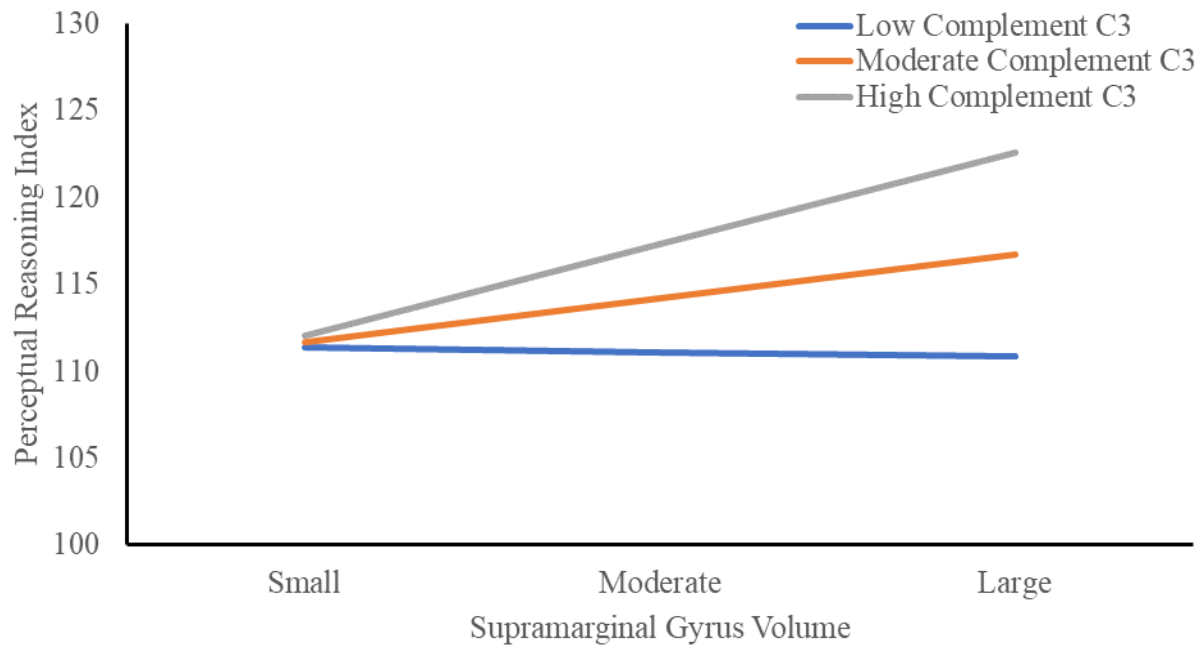


Figure 3.16 | Complement C3 conditionally moderates the relationship between supramarginal gyrus volume and fluid intelligence. When volume is moderate or large, complement C3 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

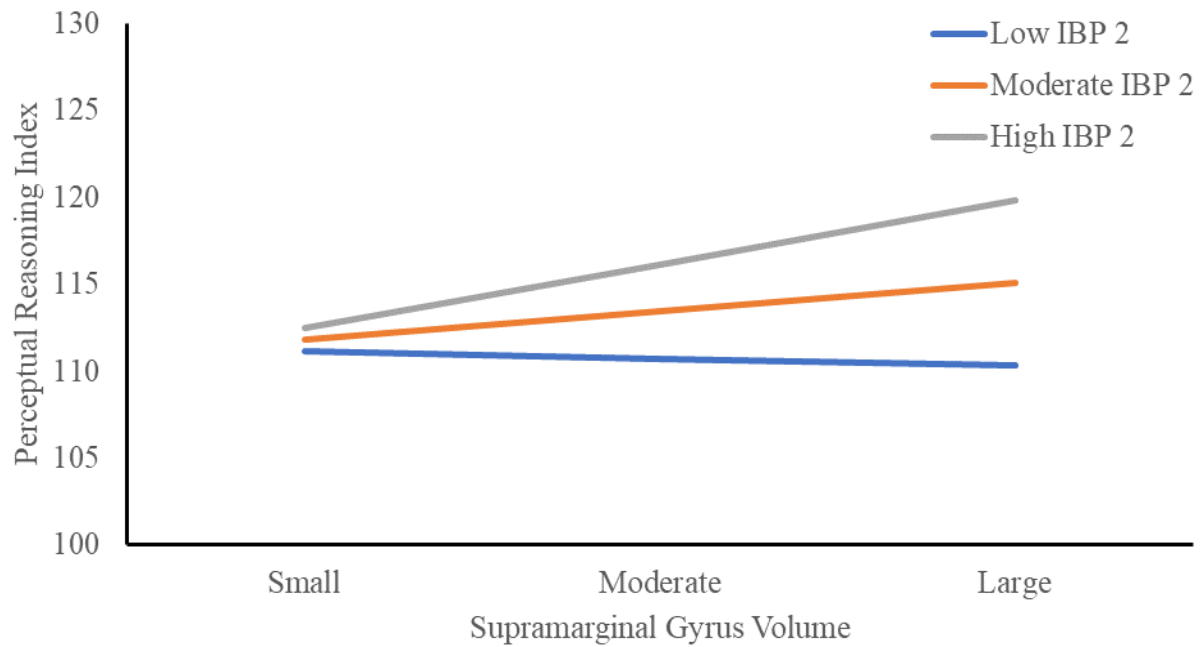


Figure 3.17 | IBP 2 conditionally moderates the relationship between supramarginal gyrus volume and fluid intelligence. When volume is moderate or large, IBP 2 significantly influences fluid intelligence. Low status and small volume are defined as one *SD* below the mean; high status and large volume are defined as one *SD* above the mean.

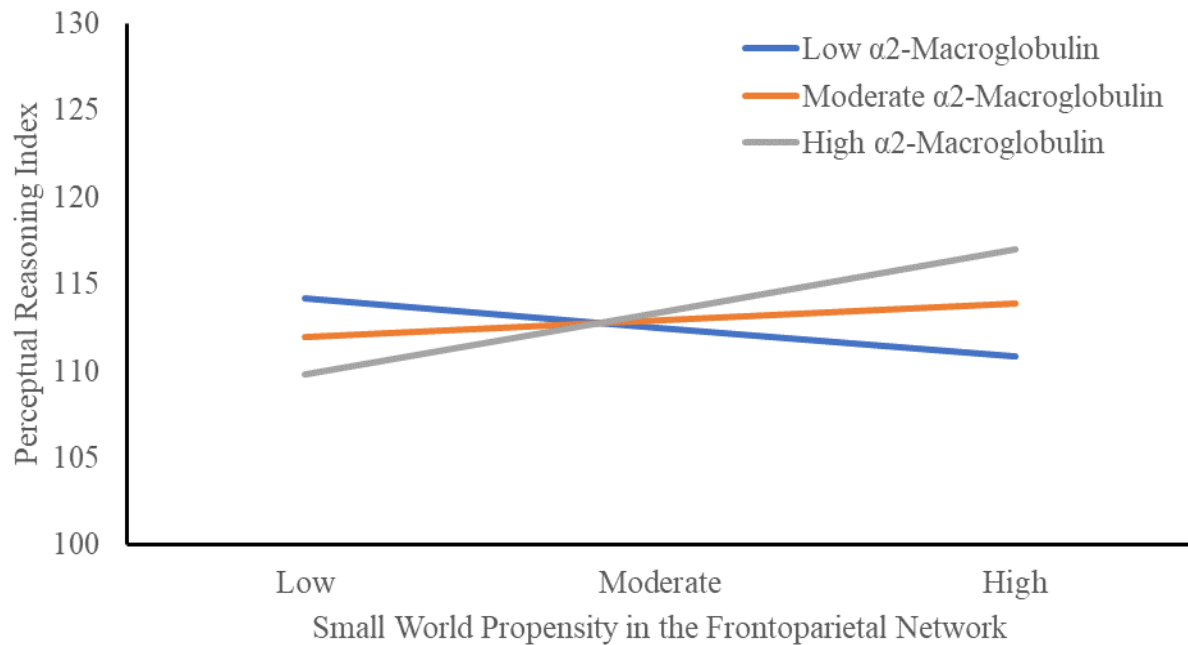


Figure 3.18 | $\alpha 2$ -Macroglobulin conditionally moderates the relationship between small world propensity in the FPN and fluid intelligence. When small world propensity is very high, $\alpha 2$ -macroglobulin significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean; very high efficiency is defined as >1 *SD* above the mean.

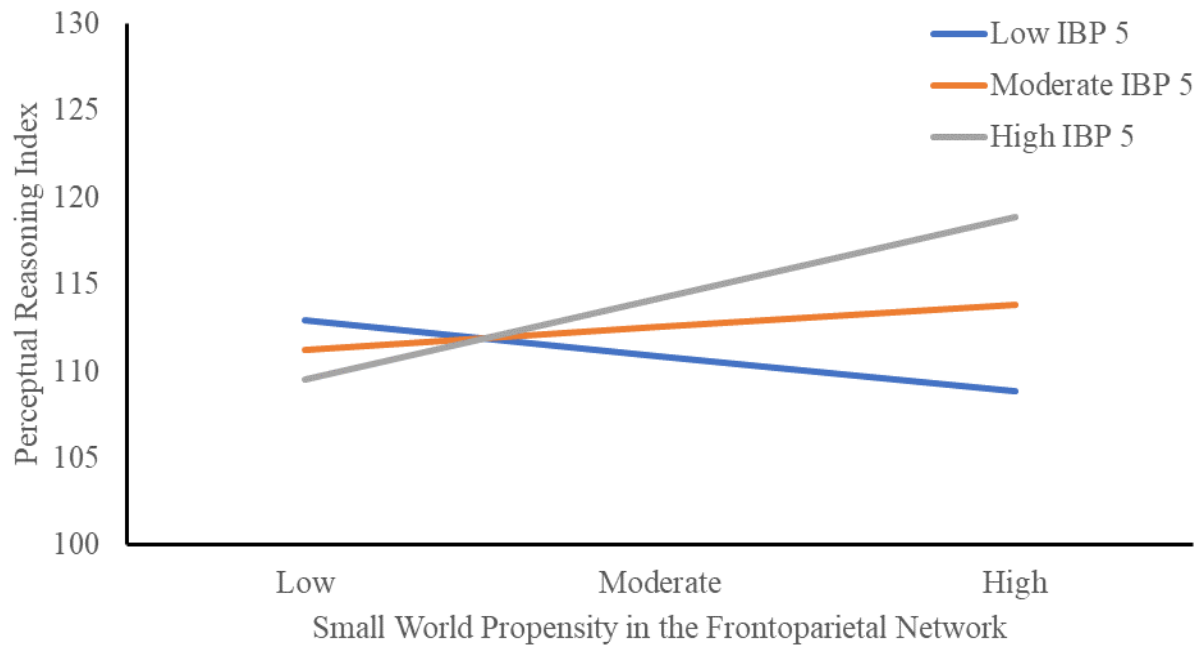


Figure 3.19 | IBP 5 conditionally moderates the relationship between small world propensity in the FPN and fluid intelligence. When small world propensity is high, IBP 5 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

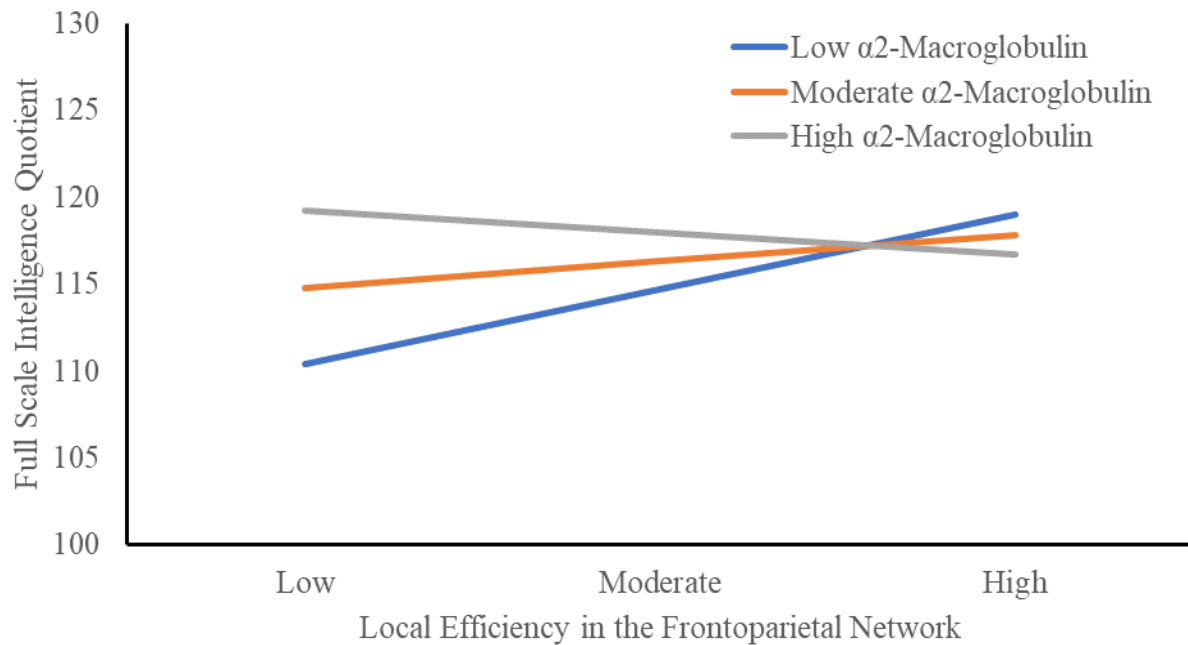


Figure 3.20 | $\alpha 2$ -Macroglobulin conditionally moderates the relationship between local efficiency in the FPN and general intelligence. When local efficiency is low, $\alpha 2$ -macroglobulin significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

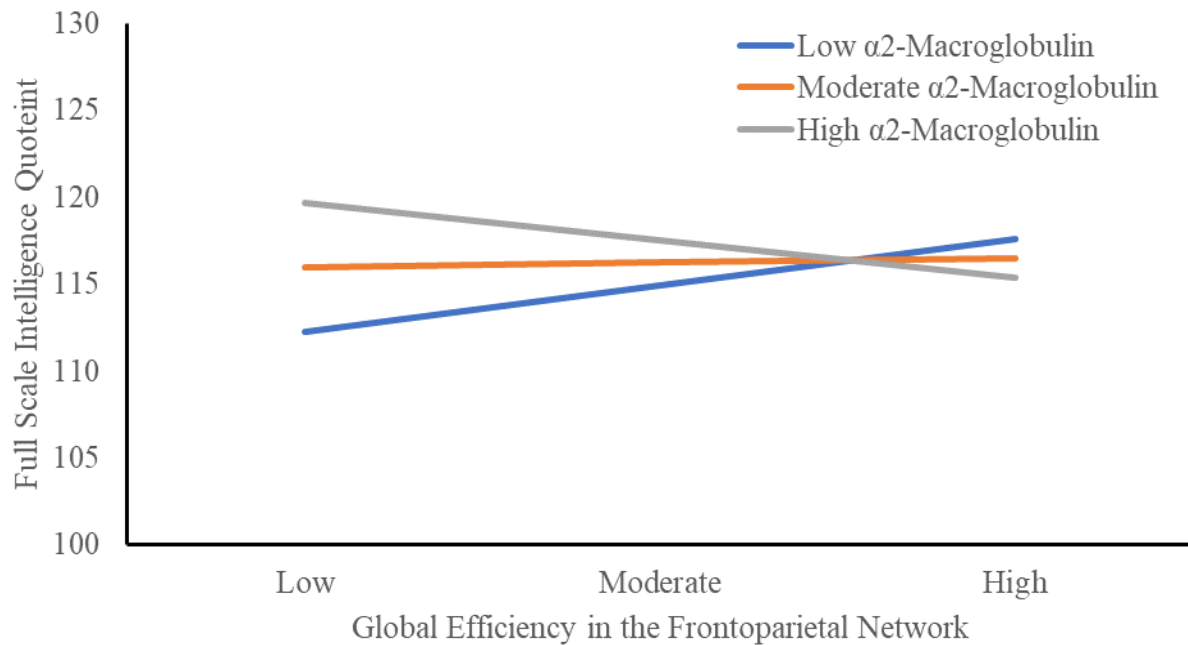


Figure 3.21 | $\alpha 2$ -Macroglobulin conditionally moderates the relationship between global efficiency in the FPN and general intelligence. When global efficiency low, $\alpha 2$ -macroglobulin significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

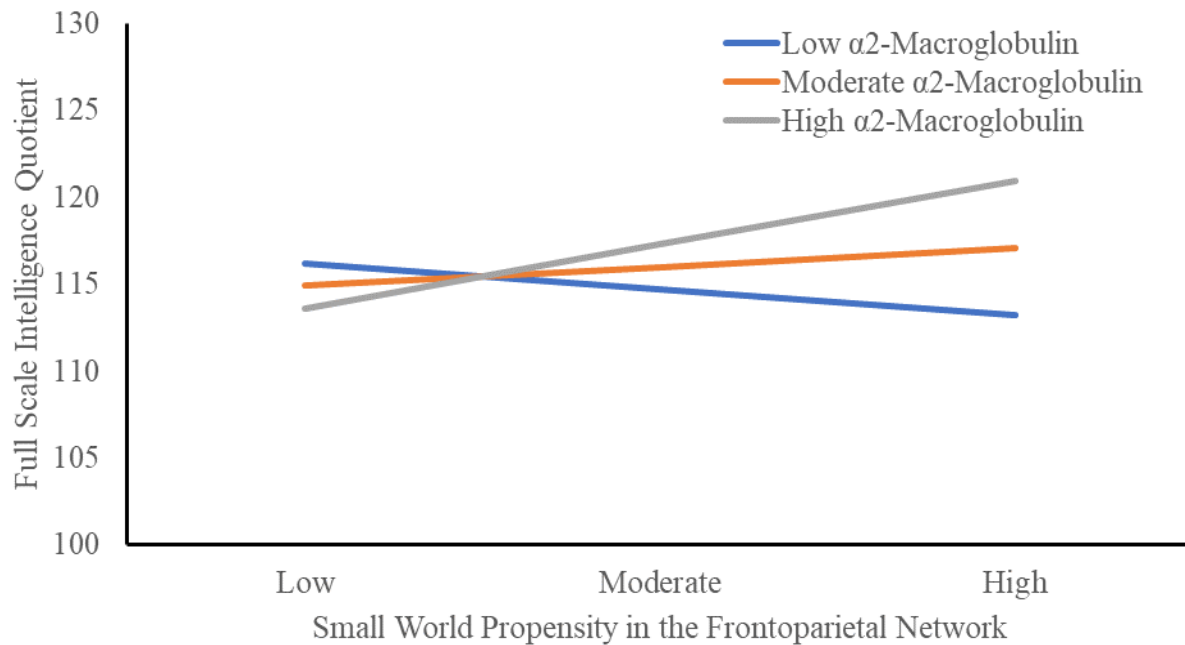


Figure 3.22 | $\alpha 2$ -Macroglobulin conditionally moderates the relationship between small world propensity in the FPN and general intelligence. When small world propensity is high, $\alpha 2$ -macroglobulin significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

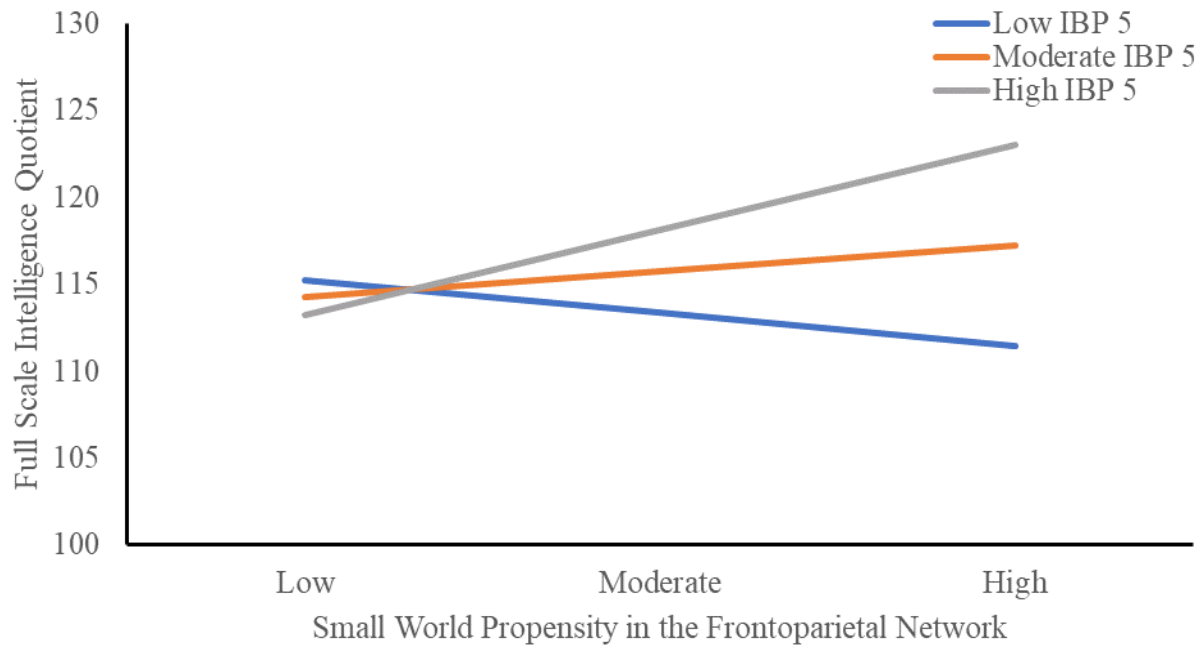


Figure 3.23 | IBP 5 conditionally moderates the relationship between small world propensity in the FPN and general intelligence. When small world propensity is moderate or high, IBP 5 significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

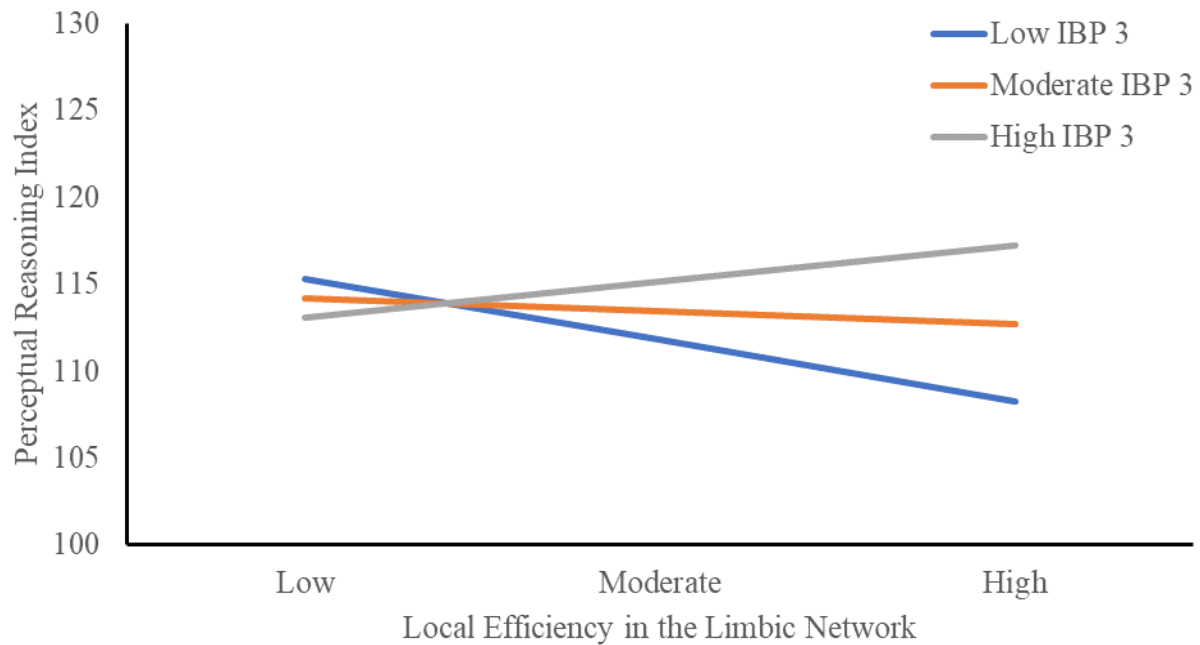


Figure 3.24 | IBP 3 conditionally moderates the relationship between local efficiency in the LN and fluid intelligence. When local efficiency is high, IBP 3 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

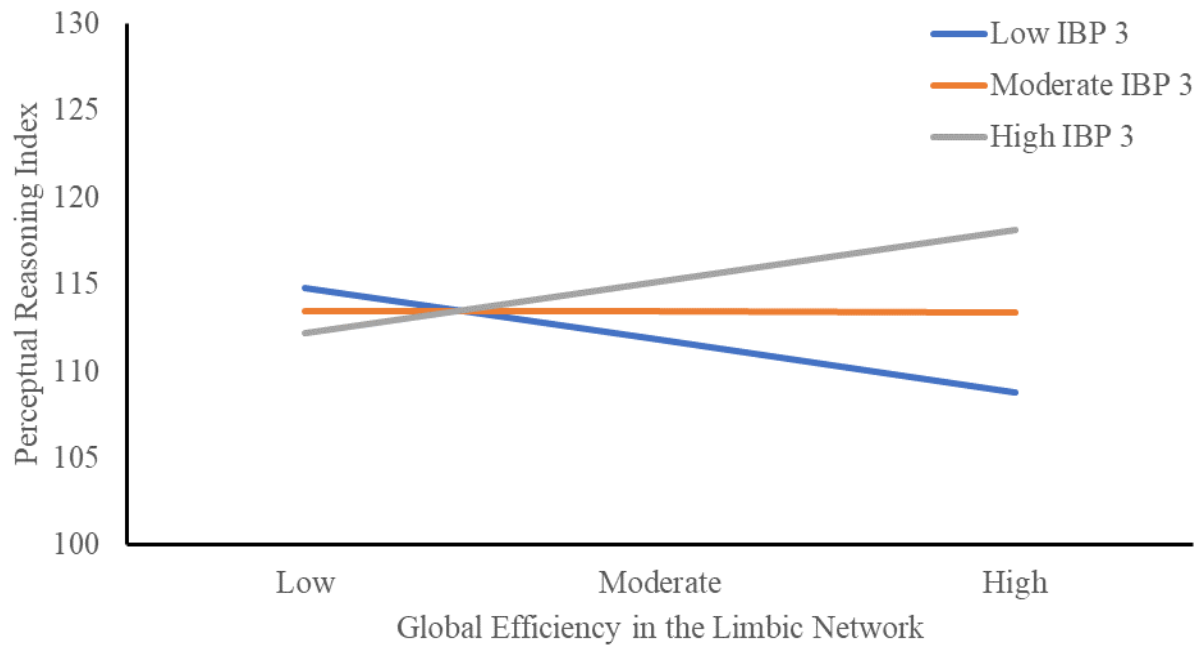


Figure 3.25 | IBP 3 conditionally moderates the relationship between global efficiency in the LN and fluid intelligence. When global efficiency is high, IBP 3 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

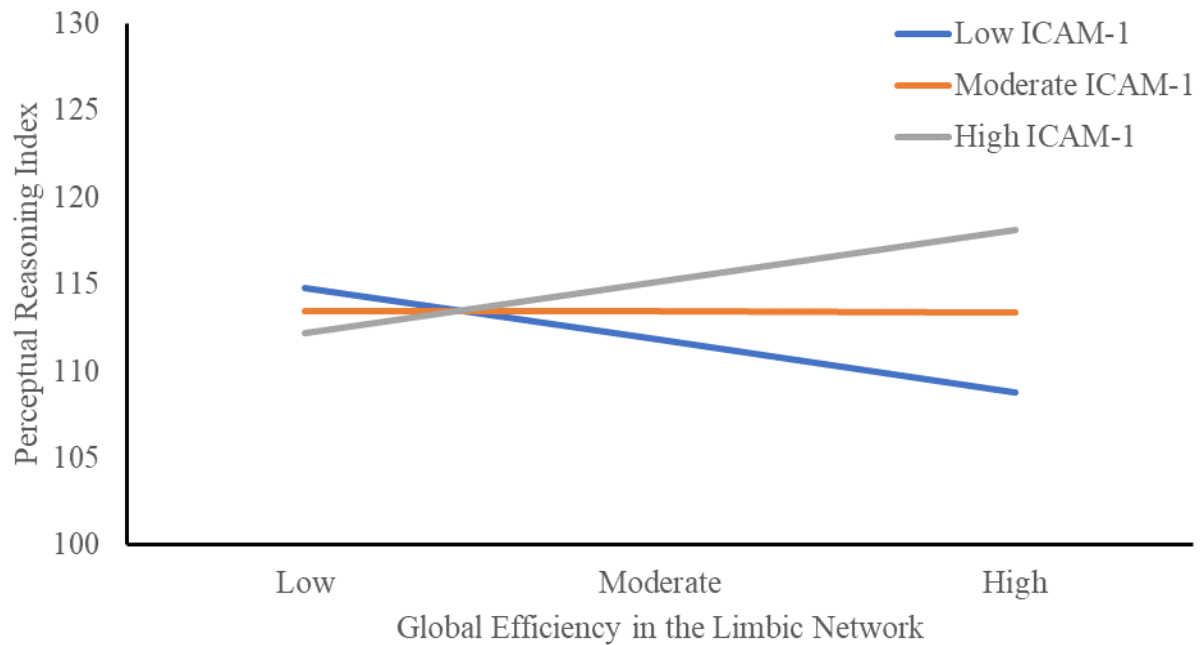


Figure 3.26 | ICAM-1 conditionally moderates the relationship between global efficiency in the LN and fluid intelligence. When global efficiency is high, ICAM-1 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

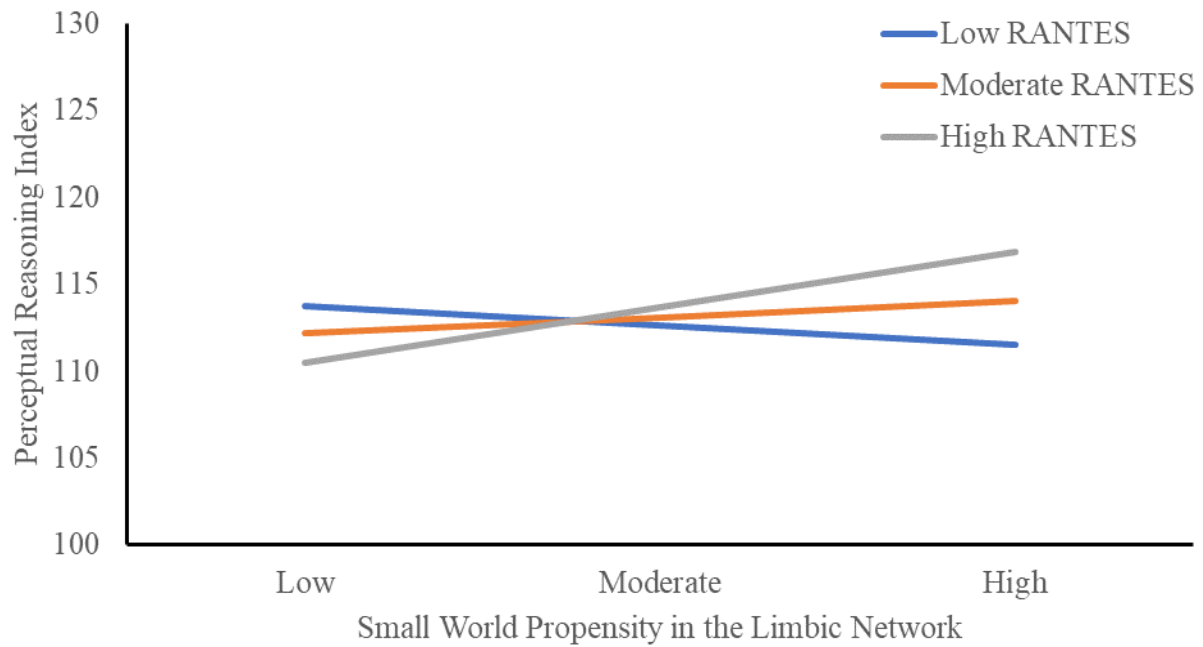


Figure 3.27 | RANTES conditionally moderates the relationship between small world propensity in the LN and fluid intelligence. When small world propensity is high, RANTES significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

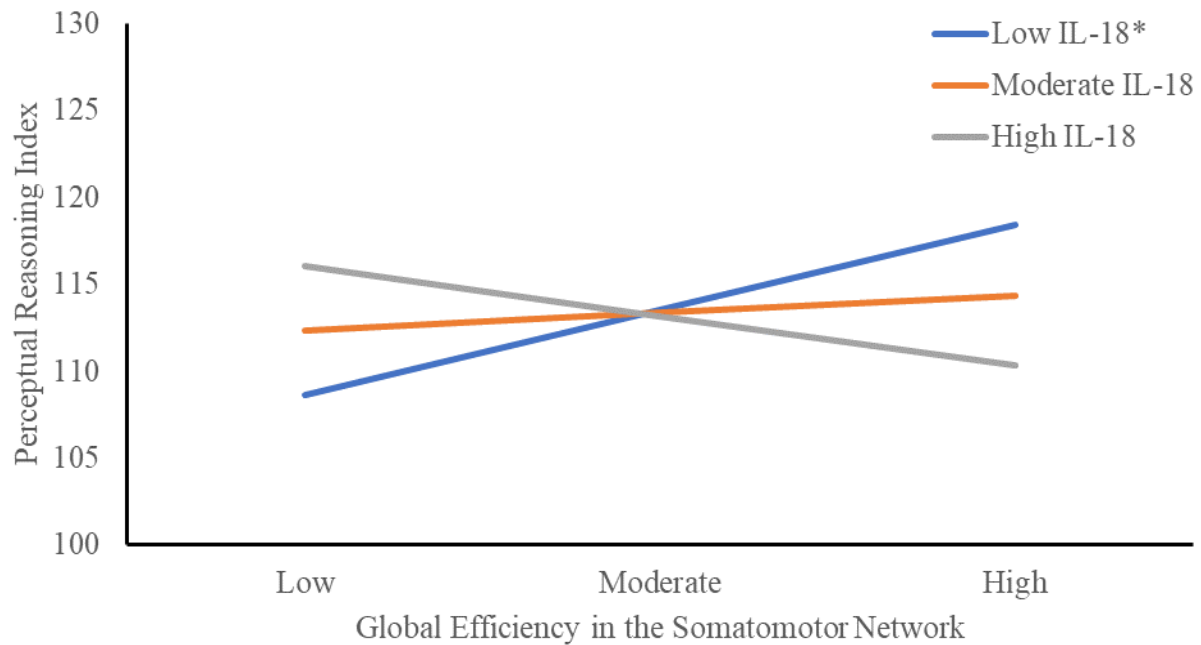


Figure 3.28 | IL-18 conditionally moderates the relationship between global efficiency in the SMN and fluid intelligence. When IL-18 is low, it significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean. $*p = <.05$

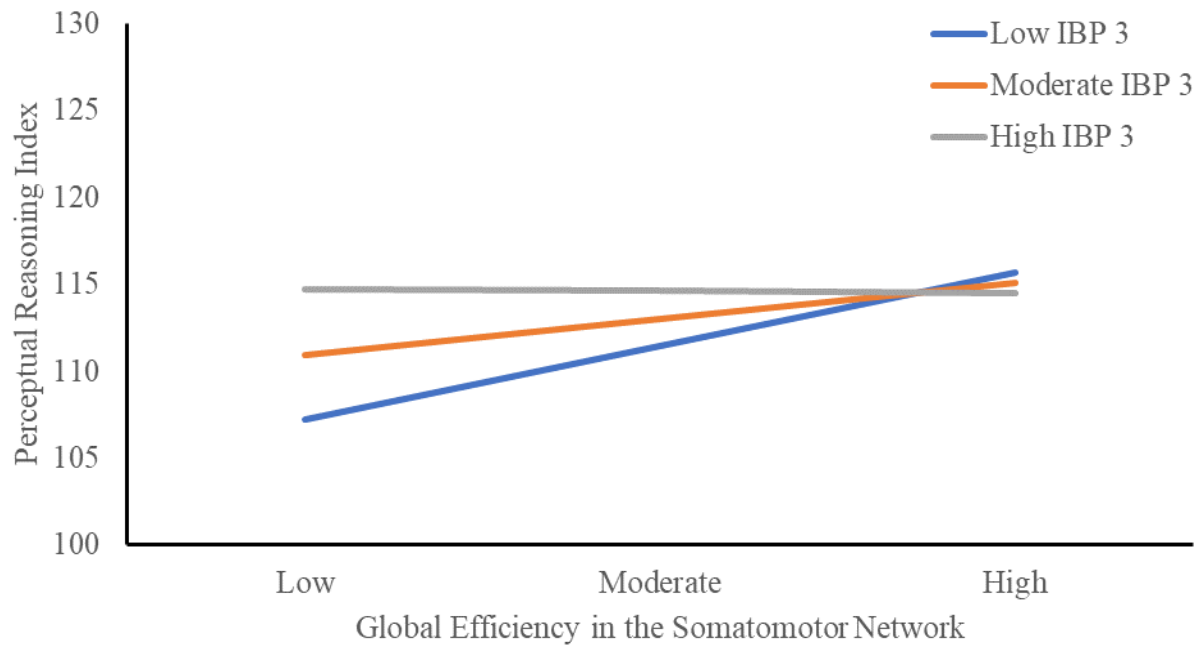


Figure 3.29 | IBP 3 conditionally moderates the relationship between global efficiency in the SMN and fluid intelligence. When global efficiency is low, IBP 3 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

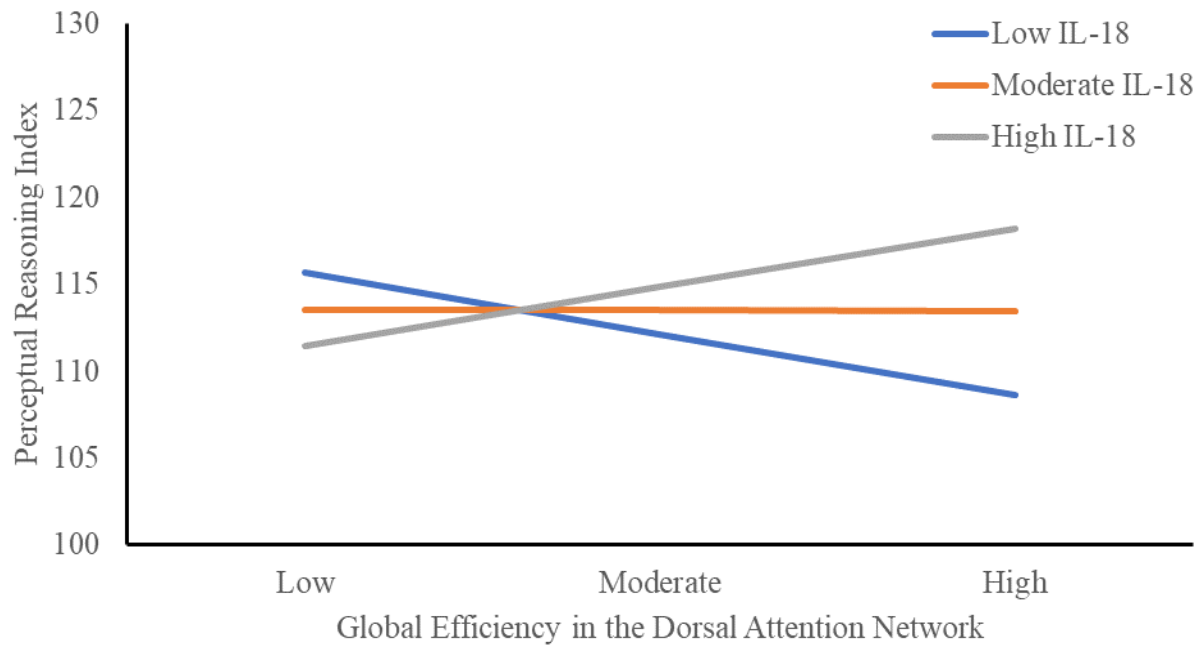


Figure 3.30 | IL-18 conditionally moderates the relationship between global efficiency in the DAN and fluid intelligence. When global efficiency is very high, IL-18 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status is defined as one *SD* above the mean; very high efficiency is defined as >1 *SD* above the mean.

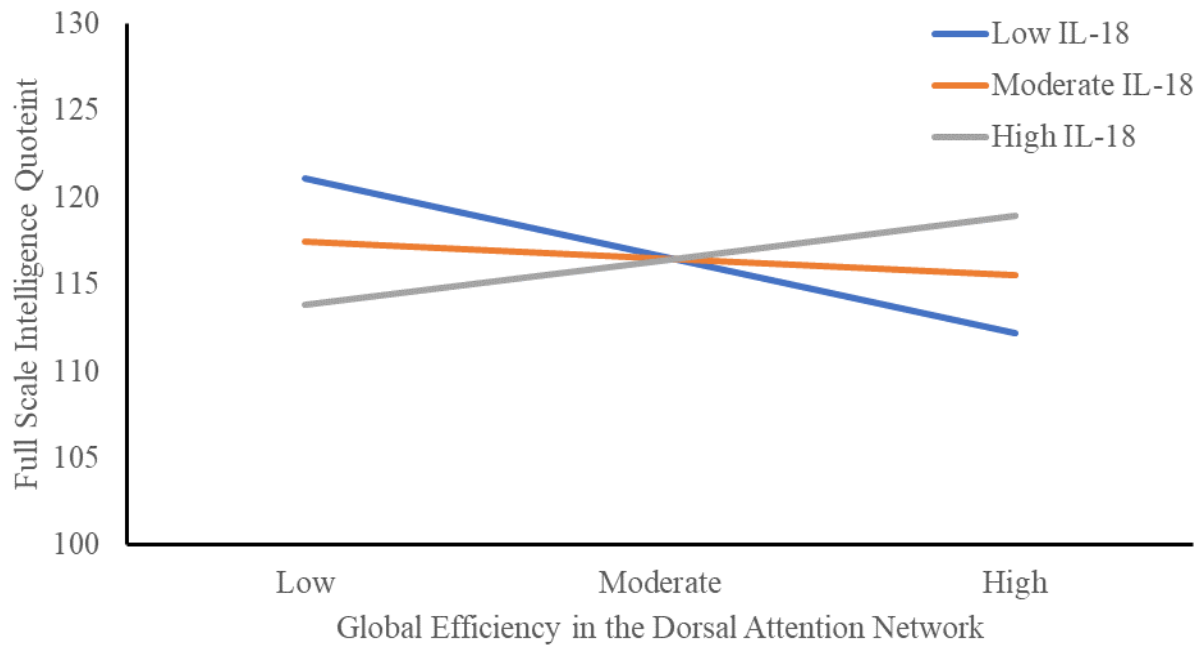


Figure 3.31 | IL-18 conditionally moderates the relationship between global efficiency in the DAN and general intelligence. When global efficiency is low, IL-18 significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

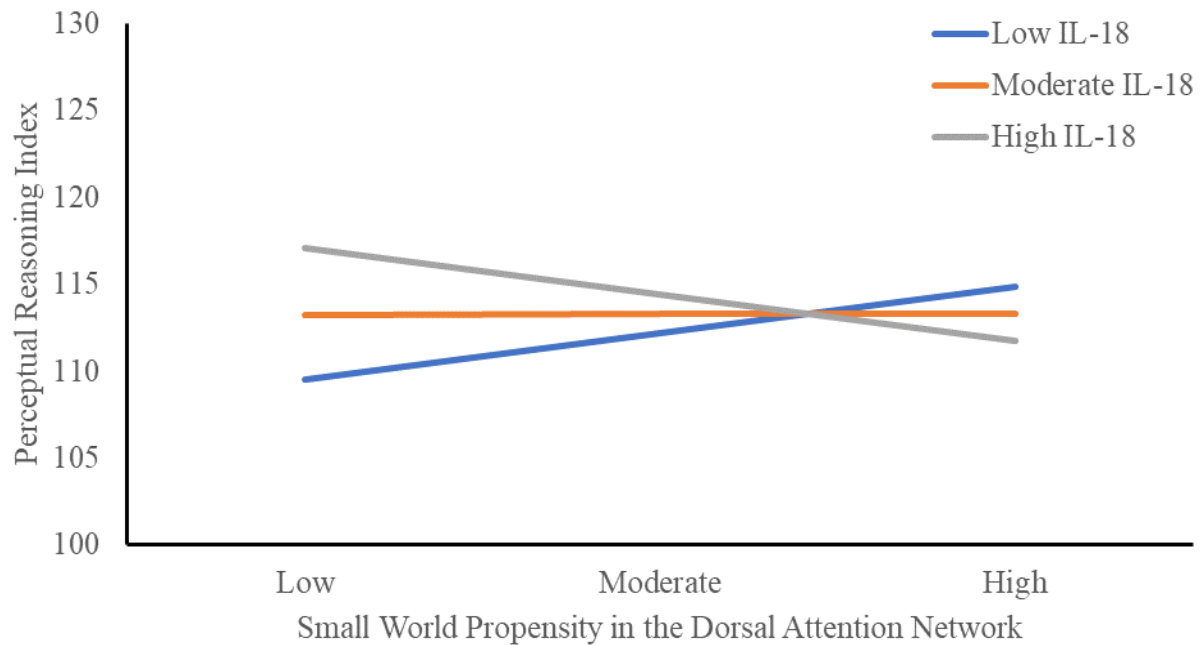


Figure 3.32 | IL-18 conditionally moderates the relationship between small world propensity in the DAN and fluid intelligence. When global efficiency is very low, IL-18 significantly influences fluid intelligence. Very low efficiency is defined as >1 *SD* below the mean; low status is defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

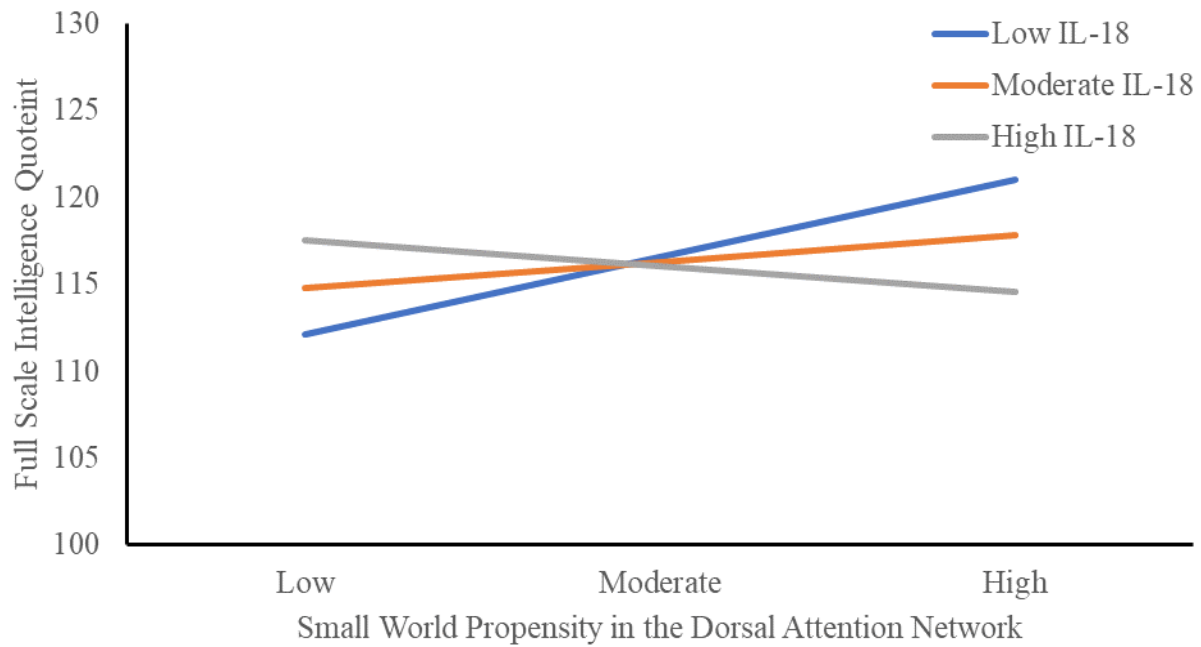


Figure 3.33 | IL-18 conditionally moderates the relationship between small world propensity in the DAN and general intelligence. When global efficiency is high, IL-18 significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

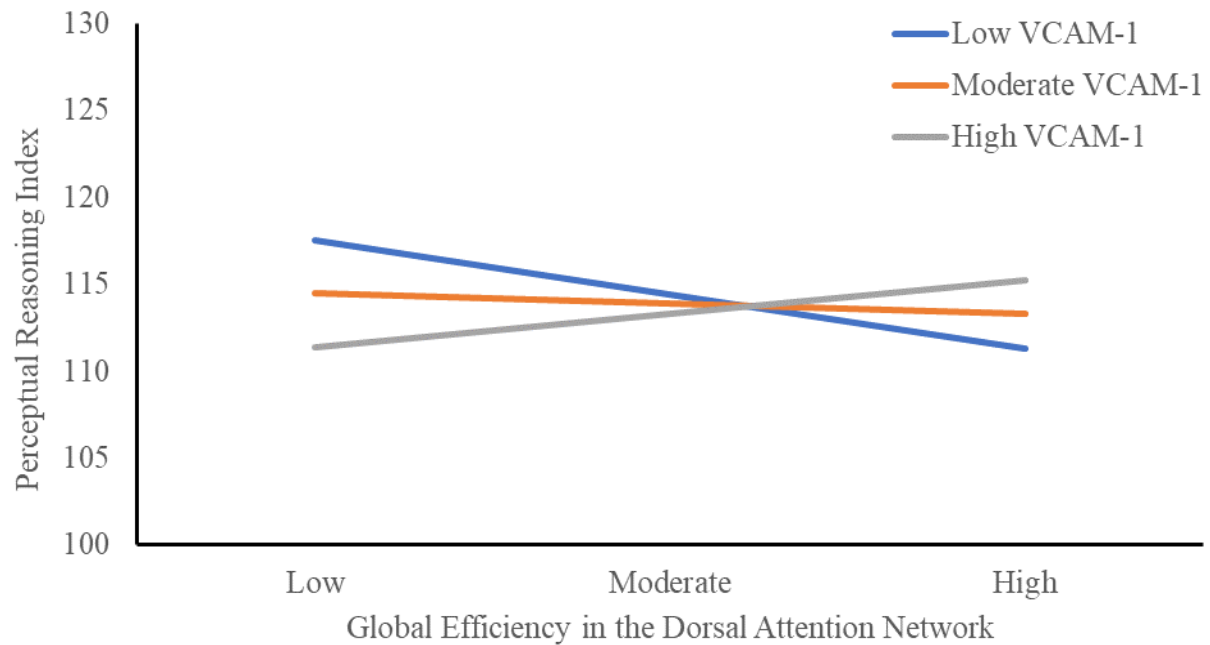


Figure 3.34 | VCAM-1 conditionally moderates the relationship between global efficiency in the DAN and crystallized intelligence. When global efficiency is very low, VCAM-1 significantly influences crystallized intelligence. Very low efficiency is defined as >1 *SD* below the mean; low status is defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

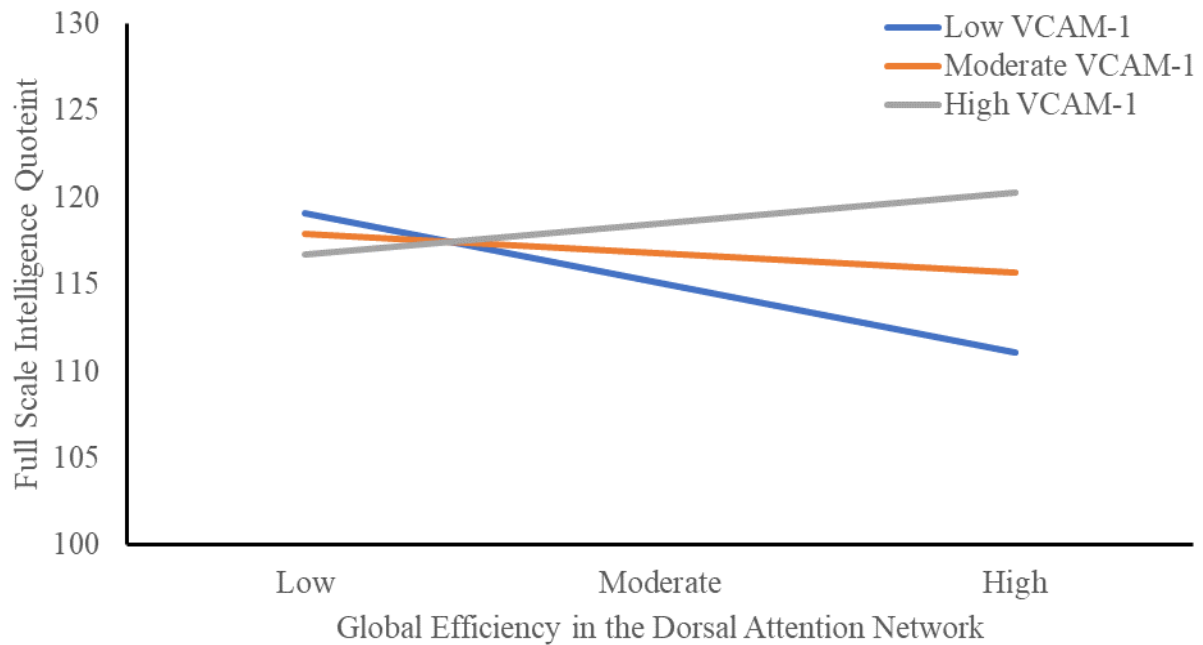


Figure 3.35 | VCAM-1 conditionally moderates the relationship between global efficiency in the DAN and general intelligence. When global efficiency is high, VCAM-1 significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

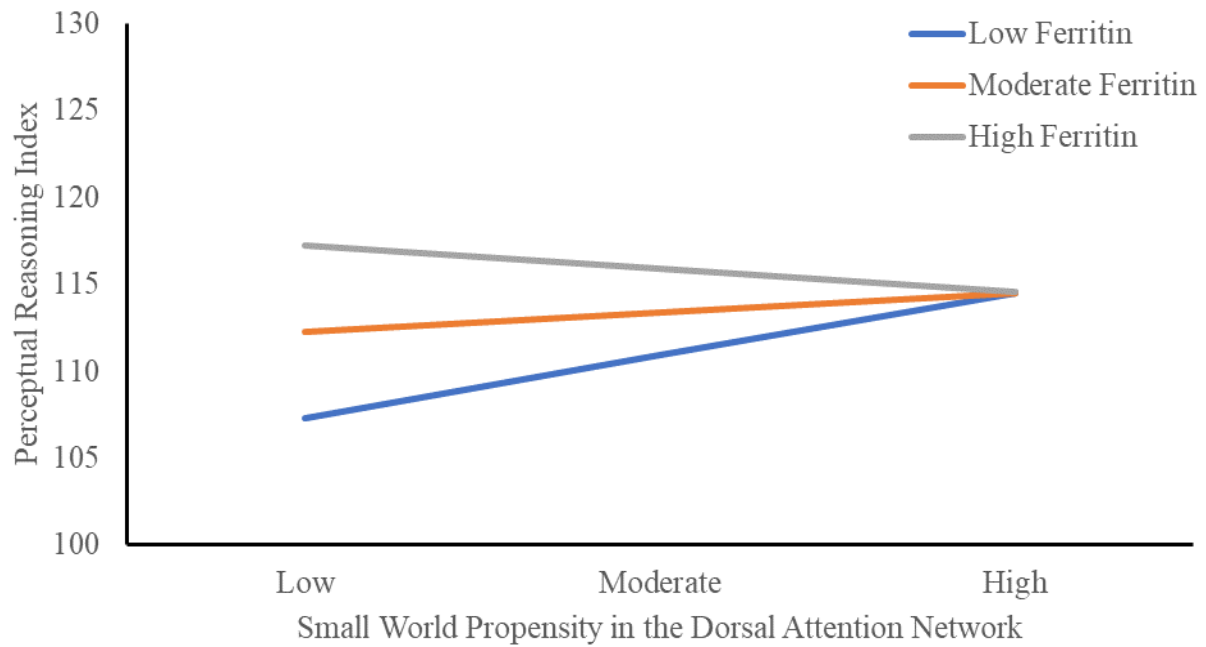


Figure 3.36 | Ferritin conditionally moderates the relationship between small world propensity in the DAN and fluid intelligence. When small world propensity is low or moderate, ferritin significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

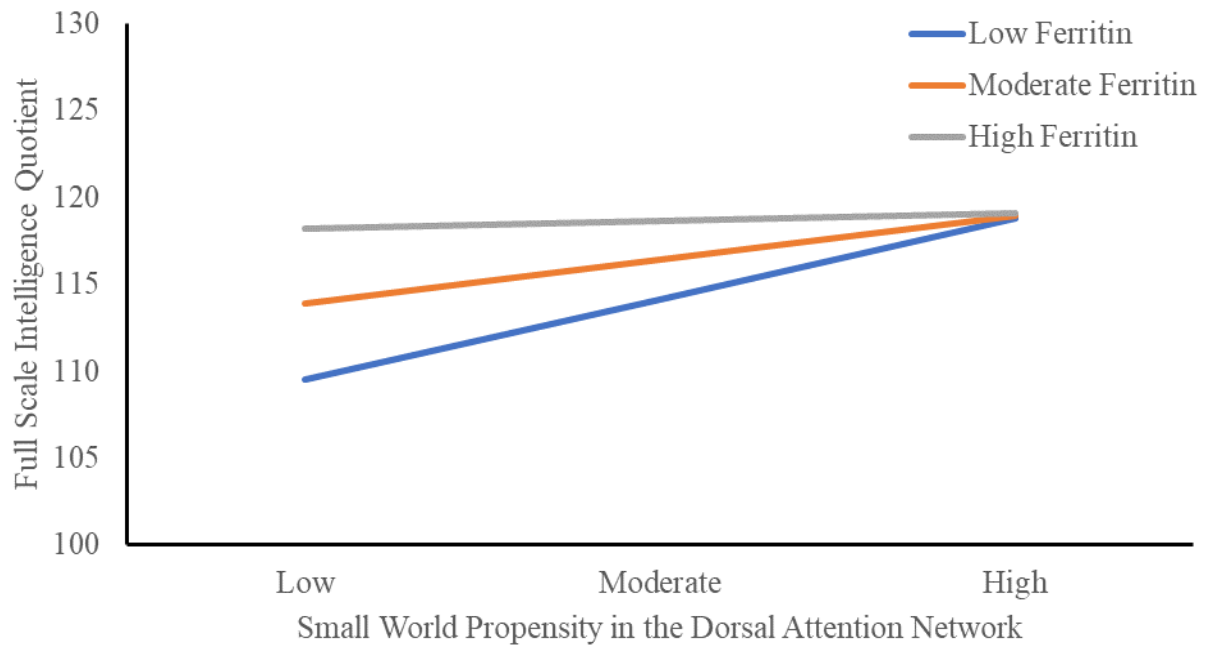


Figure 3.37 | Ferritin conditionally moderates the relationship between small world propensity in the DAN and general intelligence. When small world propensity low, ferritin significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

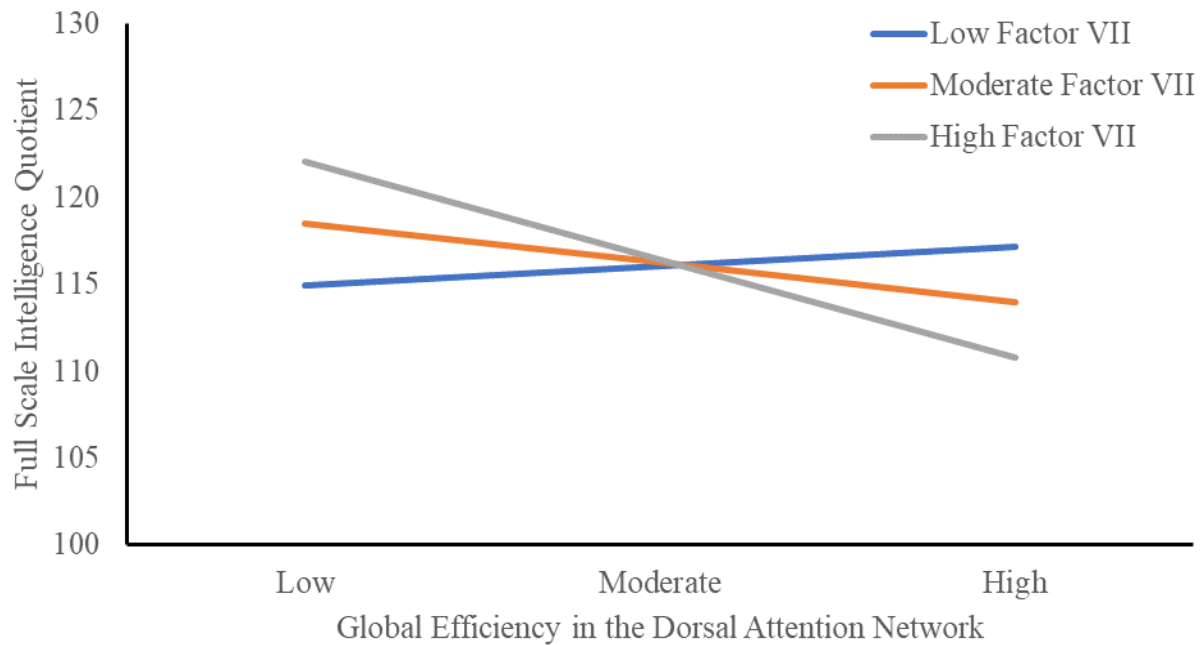


Figure 3.38 | Factor VII conditionally moderates the relationship between global efficiency in the DAN and general intelligence. When global efficiency is low, factor VII significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

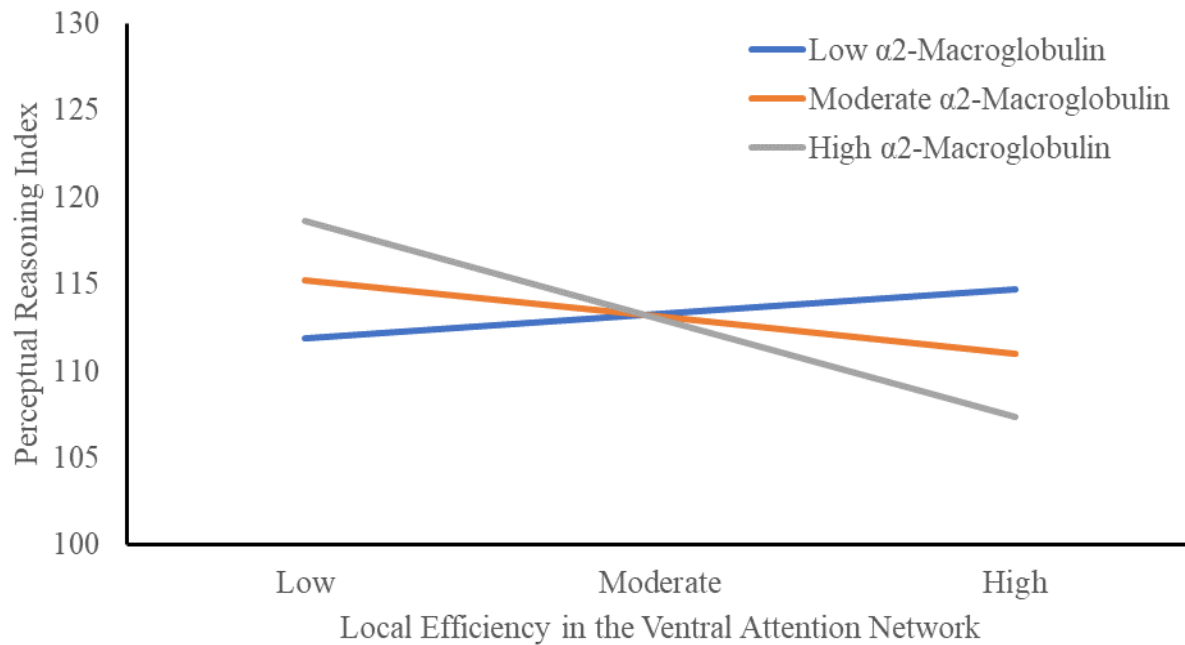


Figure 3.39 | α 2-Macroglobulin conditionally moderates the relationship between local efficiency in the VAN and fluid intelligence. When local efficiency is low or high, α 2-macroglobulin significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

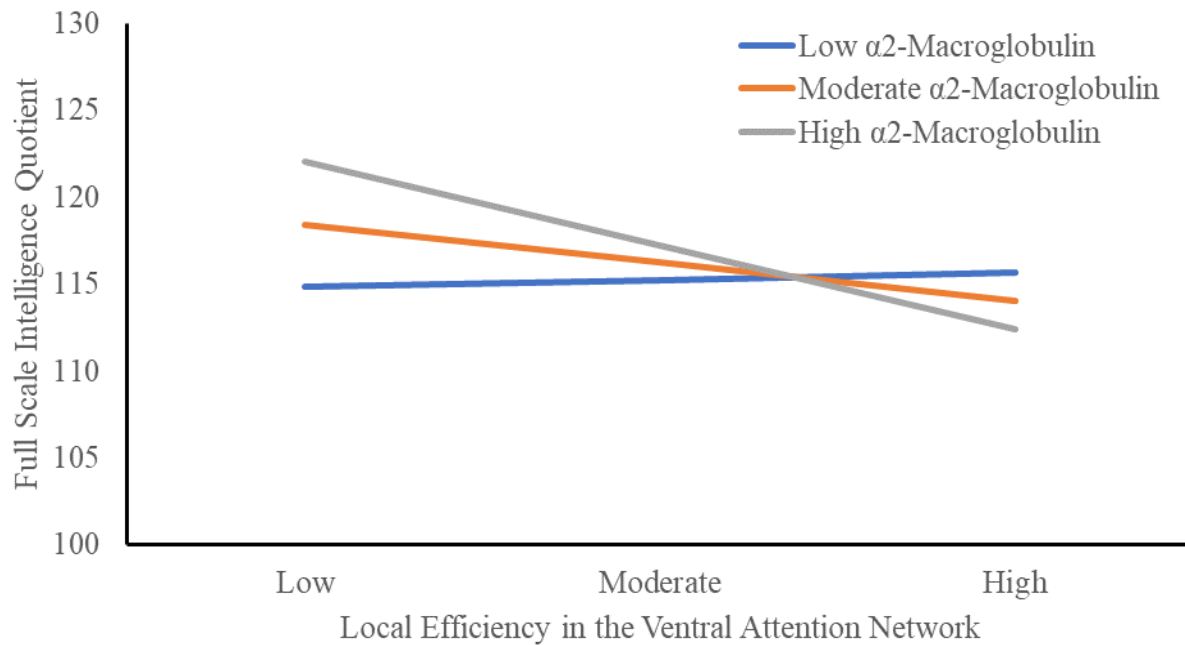


Figure 3.40 | $\alpha 2$ -Macroglobulin conditionally moderates the relationship between local efficiency in the VAN and general intelligence. When local efficiency is low, $\alpha 2$ -macroglobulin significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

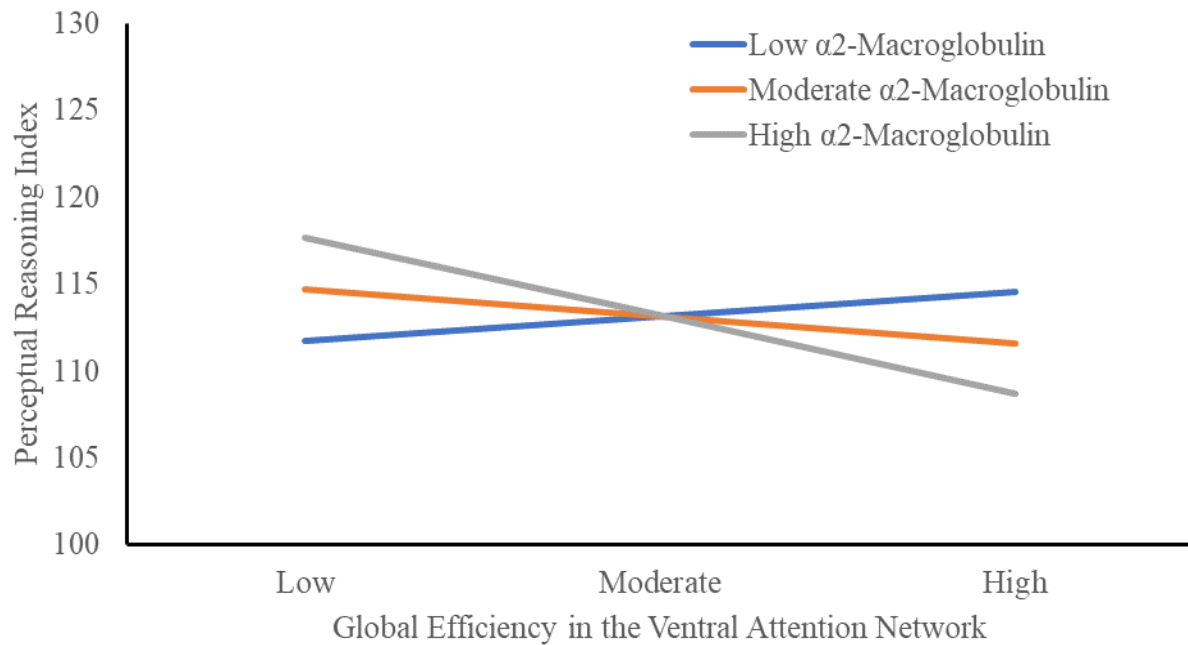


Figure 3.41 | $\alpha 2$ -Macroglobulin conditionally moderates the relationship between global efficiency in the VAN and fluid intelligence. When global efficiency is low, $\alpha 2$ -macroglobulin significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

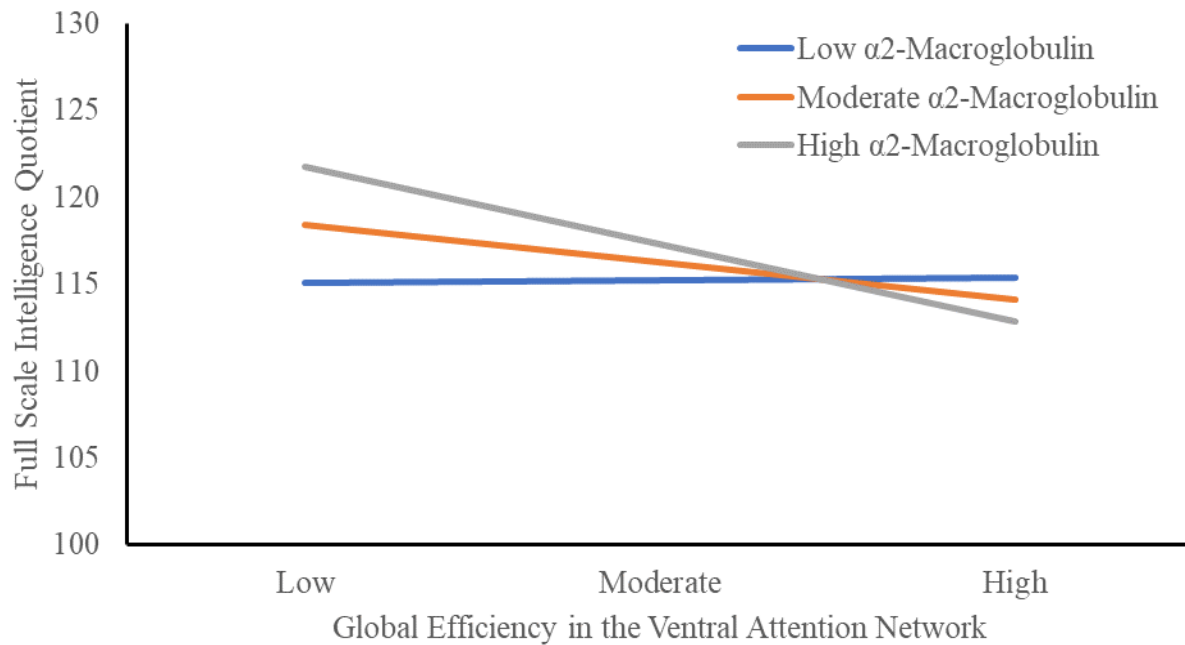


Figure 3.42 | $\alpha 2$ -Macroglobulin conditionally moderates the relationship between global efficiency in the VAN and general intelligence. When global efficiency is low, $\alpha 2$ -macroglobulin significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

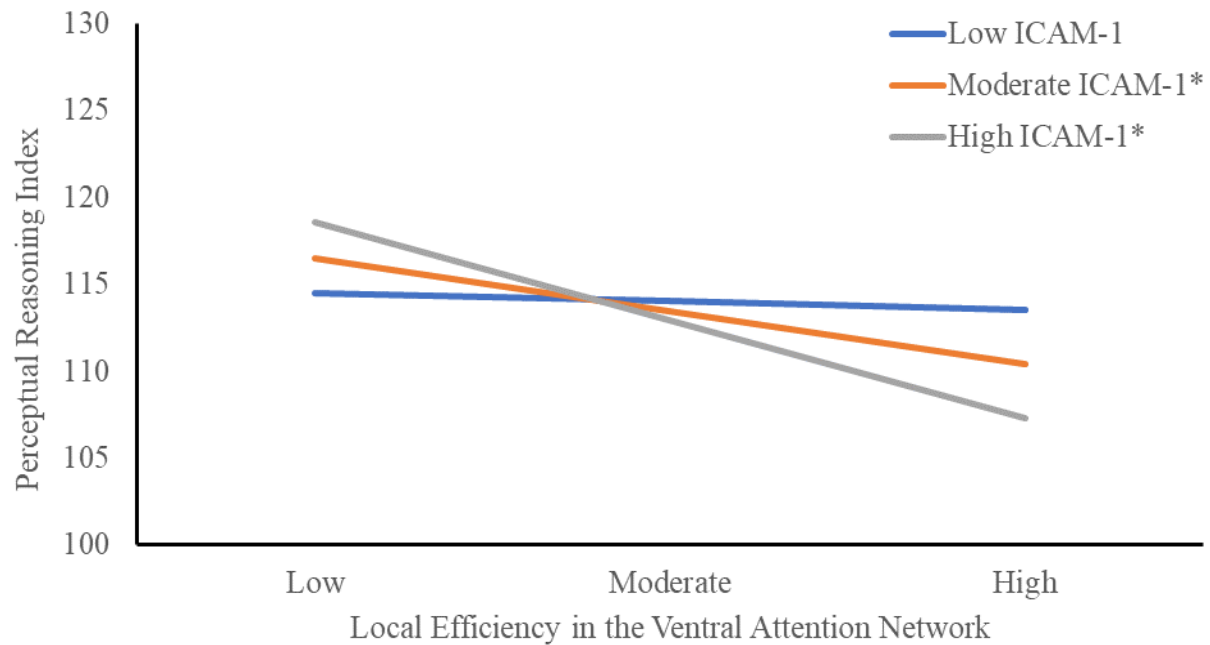


Figure 3.43 | ICAM-1 conditionally moderates the relationship between local efficiency in the VAN and fluid intelligence. When ICAM-1 is moderate or high, ICAM-1 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean. $*p = < .05$

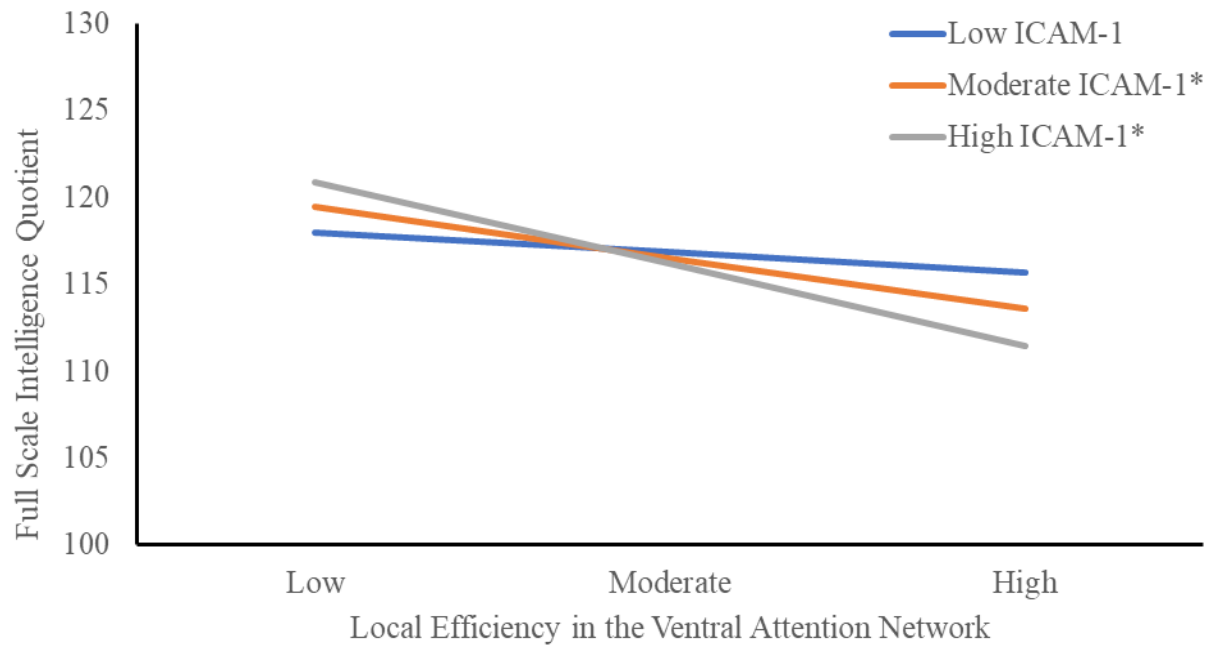


Figure 3.44 | ICAM-1 conditionally moderates the relationship between local efficiency in the VAN and general intelligence. When ICAM-1 is moderate or high, ICAM-1 significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean. $*p = < .05$

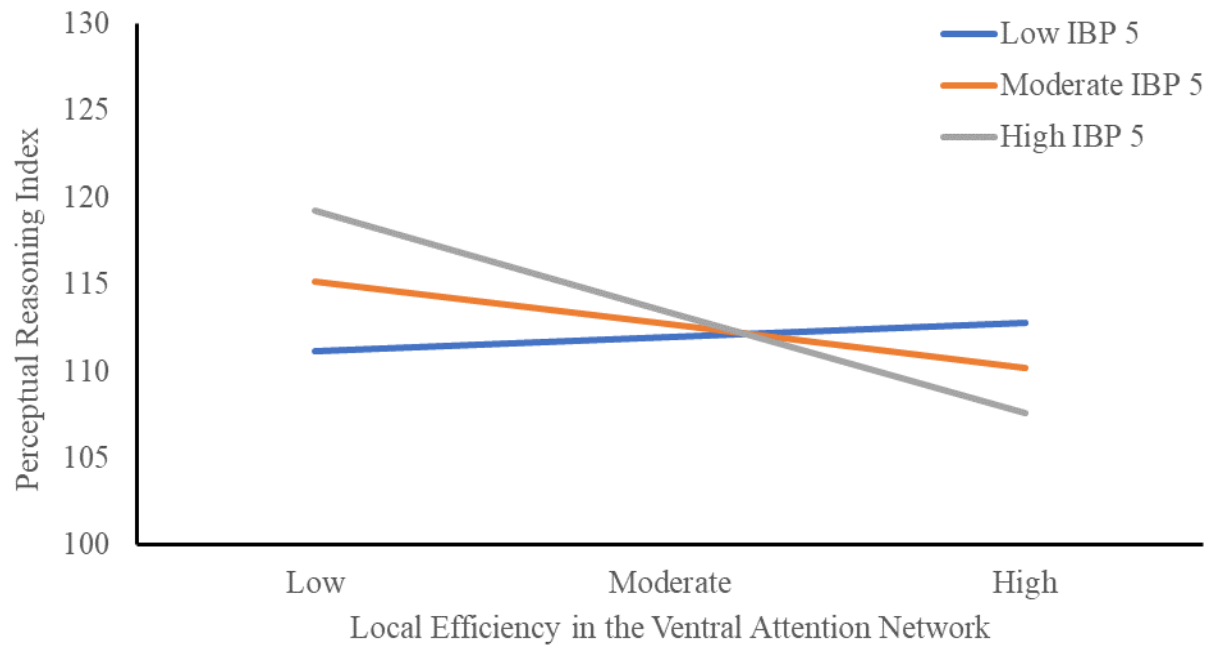


Figure 3.45 | IBP 5 conditionally moderates the relationship between local efficiency in the VAN and fluid intelligence. When local efficiency is low, IBP 5 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

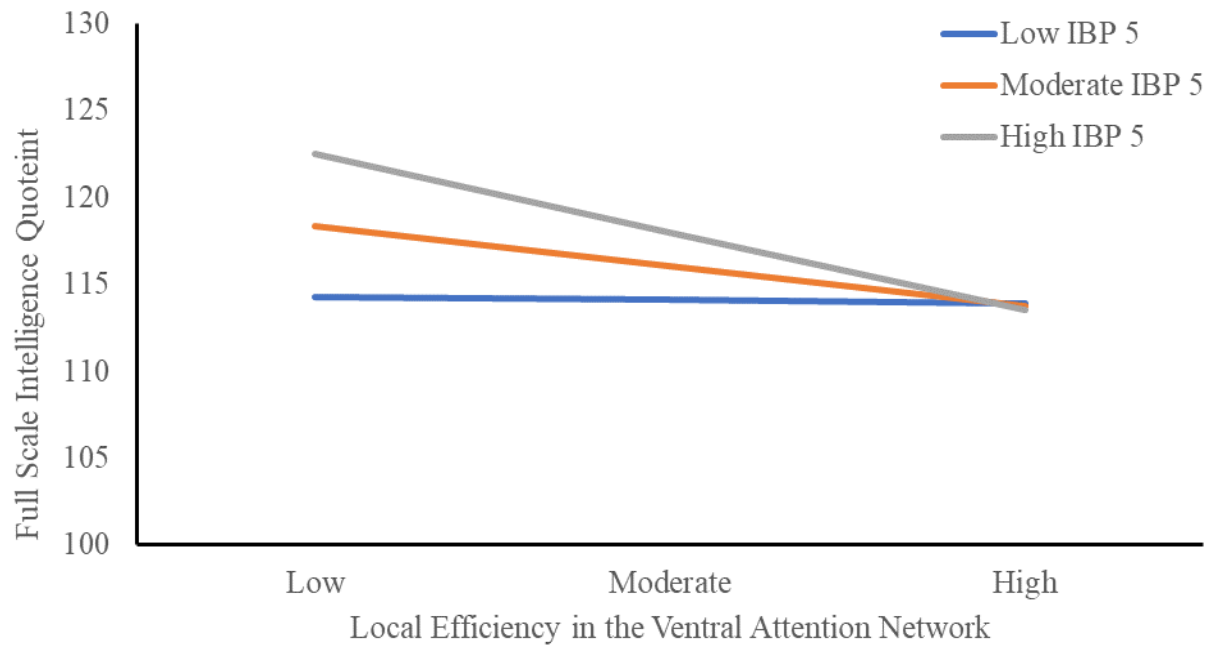


Figure 3.46 | IBP 5 conditionally moderates the relationship between local efficiency in the VAN and general intelligence. When local efficiency is low, IBP 5 significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

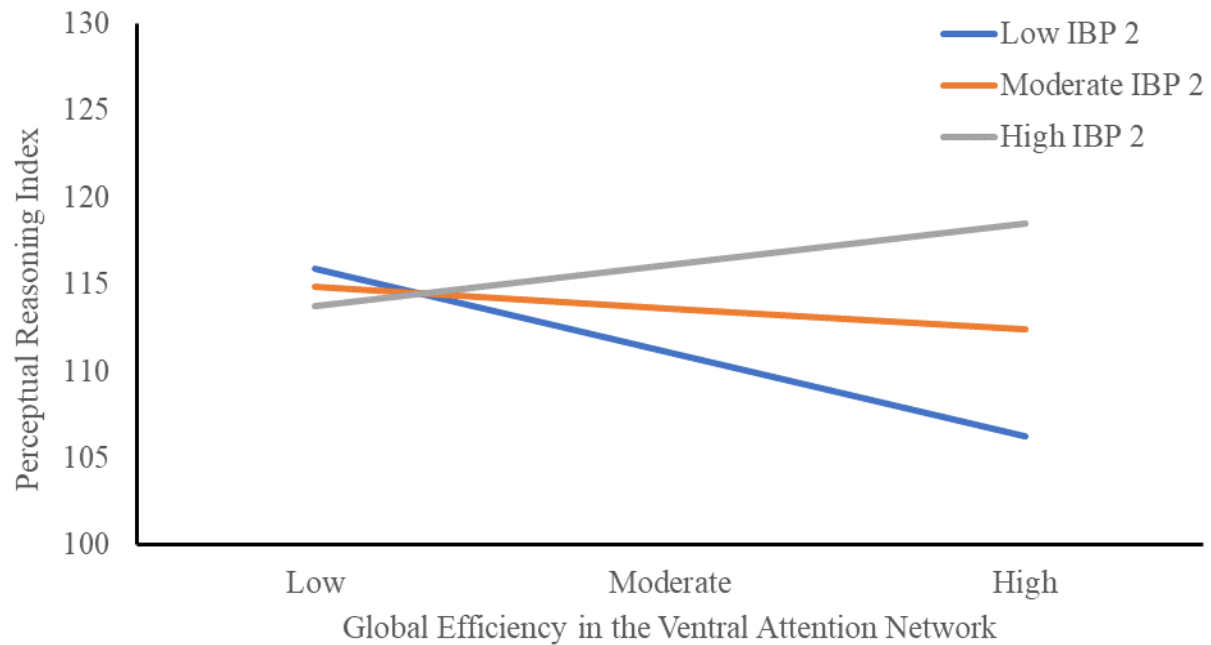


Figure 3.47 | IBP 2 conditionally moderates the relationship between global efficiency in the VAN and fluid intelligence. When global efficiency is high, IBP 2 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

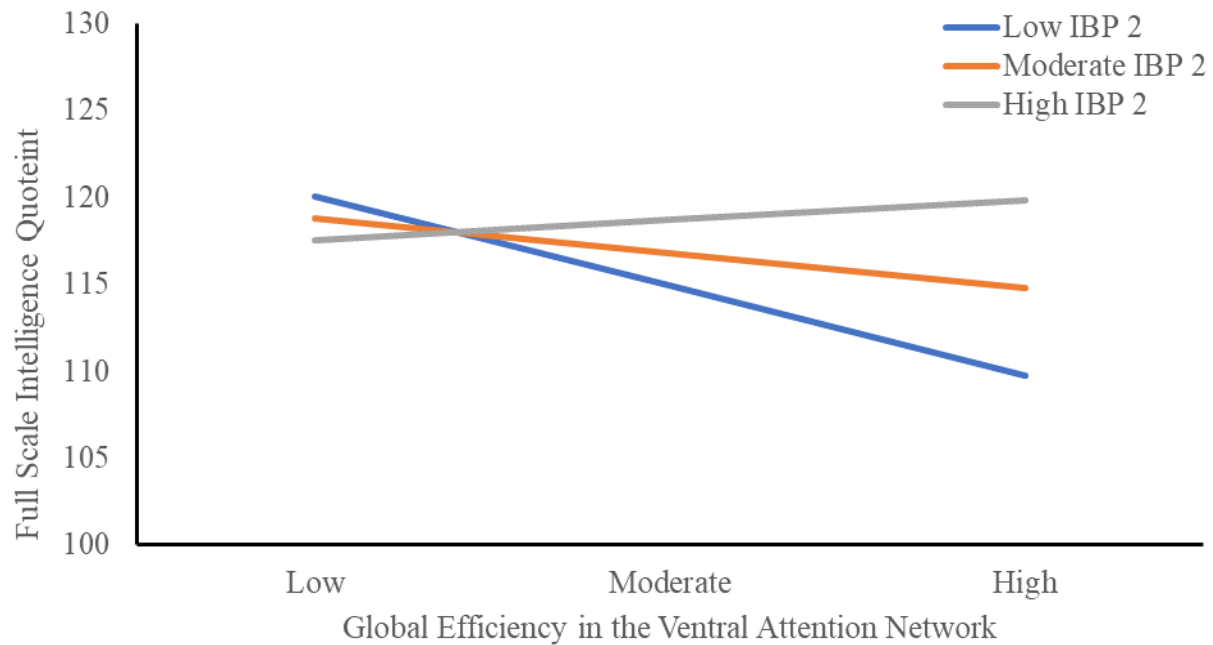


Figure 3.48 | IBP 2 conditionally moderates the relationship between global efficiency in the VAN and general intelligence. When global efficiency is high, IBP 2 significantly influences general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

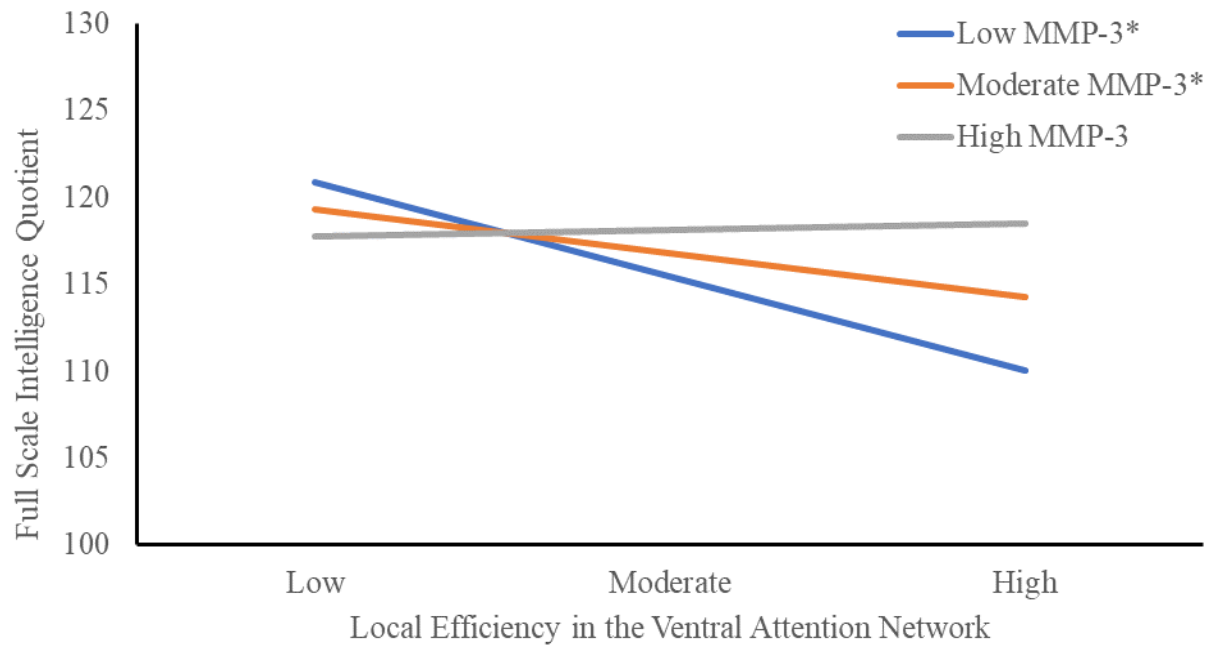


Figure 3.49 | MMP-3 conditionally moderates the relationship between local efficiency in the VAN and general intelligence. Low and moderate MMP-3 significantly influence general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean. $*p < .05$

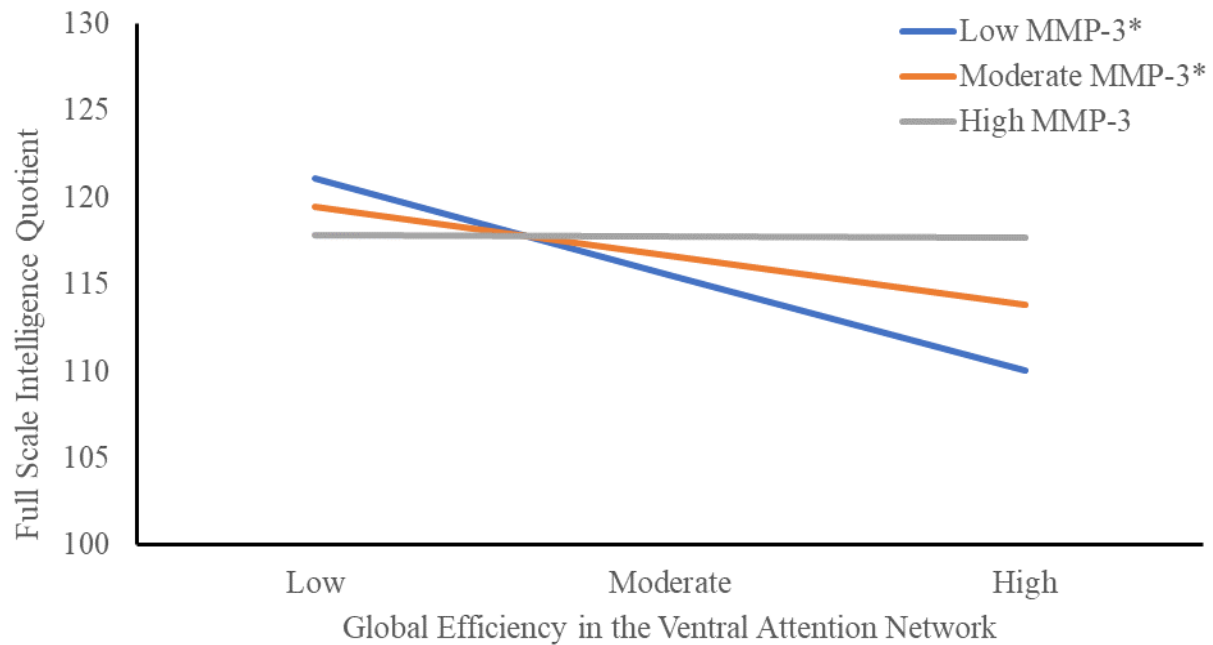


Figure 3.50 | MMP-3 conditionally moderates the relationship between global efficiency in the VAN and general intelligence. Low and moderate MMP-3 significantly influence general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean. $*p < .05$

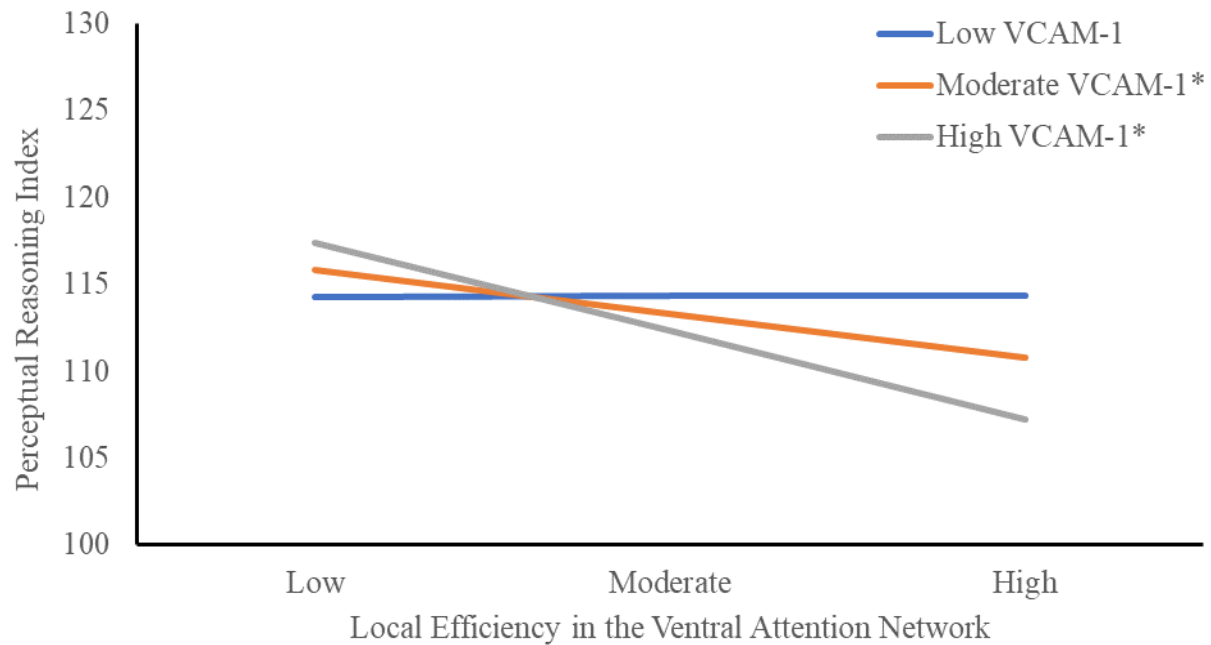


Figure 3.51 | VCAM-1 conditionally moderates the relationship between local efficiency in the VAN and fluid intelligence. Moderate and high VCAM-1 significantly influence general intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean. * $p < .05$

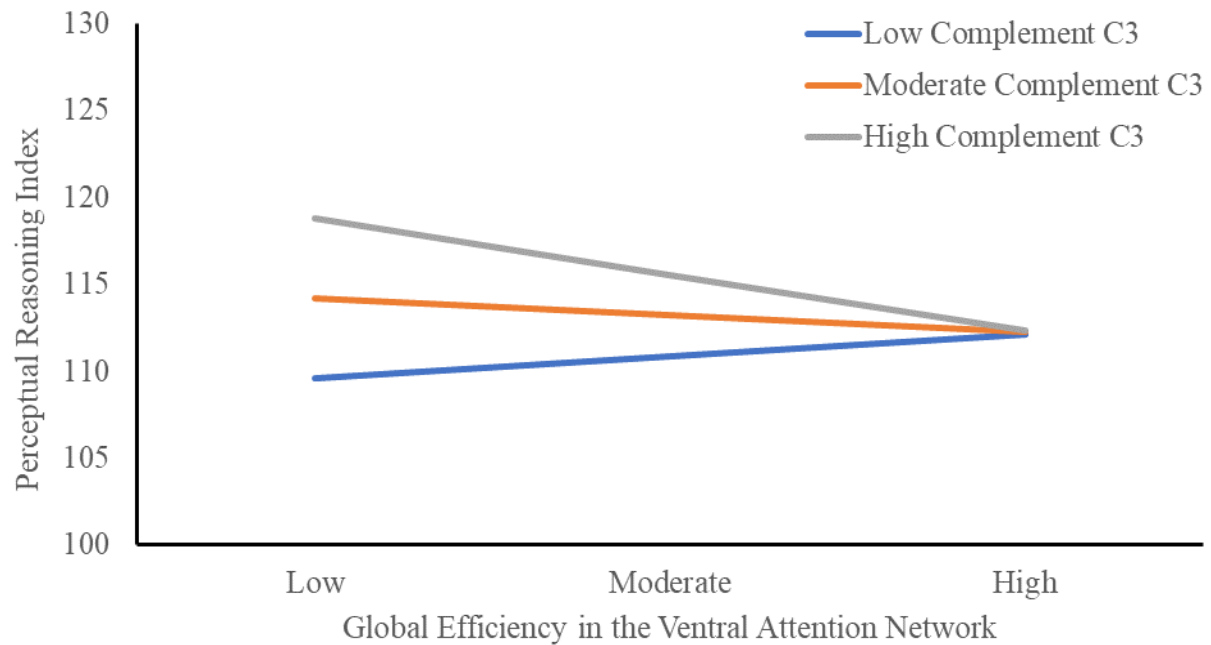


Figure 3.52 | Complement C3 conditionally moderates the relationship between global efficiency in the VAN and fluid intelligence. When global efficiency is low or moderate, Complement C3 significantly influences fluid intelligence. Low status and efficiency are defined as one *SD* below the mean; high status and efficiency are defined as one *SD* above the mean.

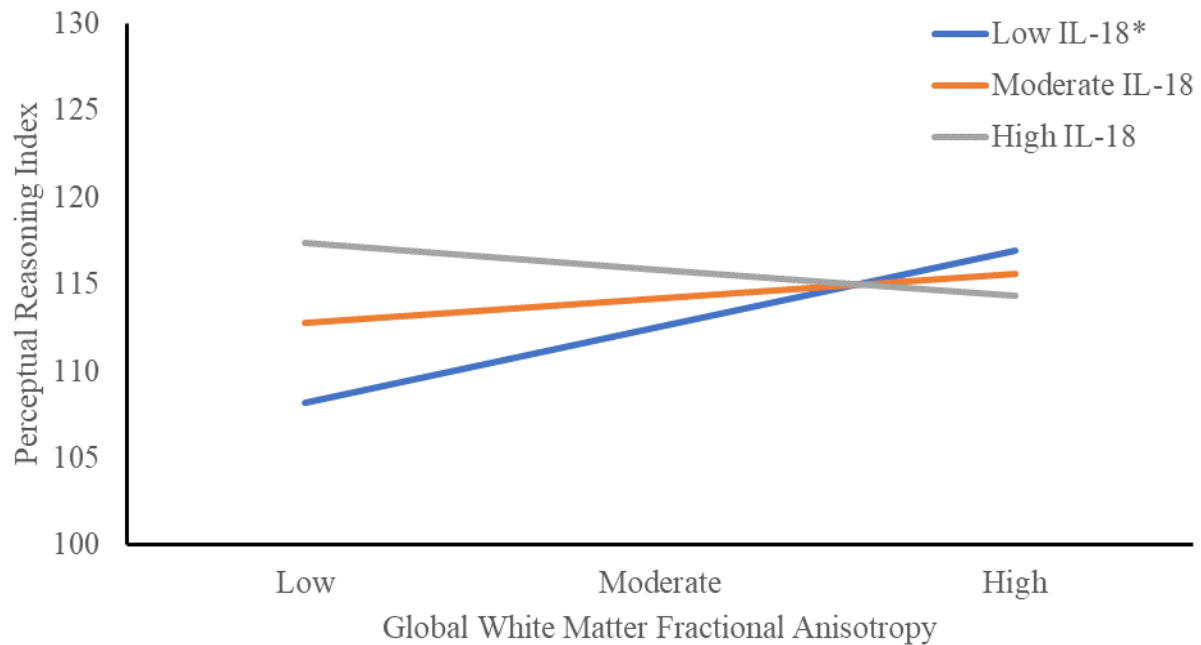


Figure 3.53 | IL-18 conditionally moderates the relationship between global white matter fractional anisotropy and fluid intelligence. When IL-18 is below the mean, it significantly influences fluid intelligence. Low status and FA are defined as one *SD* below the mean; high status and FA are defined as one *SD* above the mean. $*p < .05$

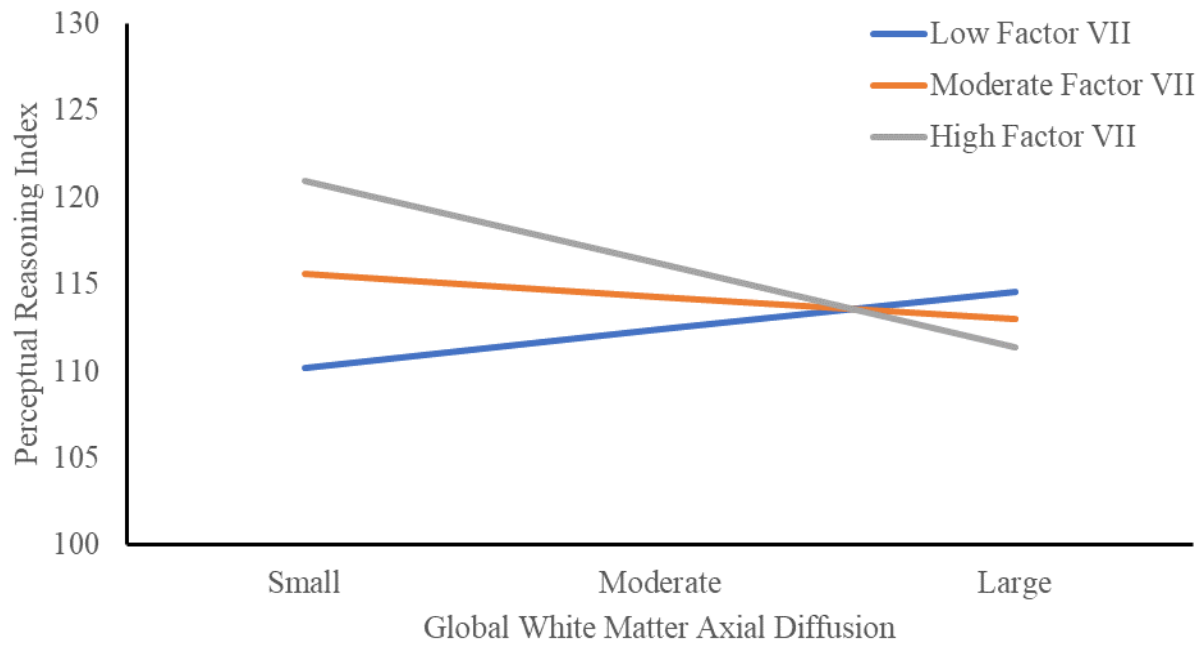


Figure 3.54 | Factor VII conditionally moderates the relationship between global white matter axial diffusion and fluid intelligence. When AD is low, Complement C3 significantly influences fluid intelligence. Low status and integrity are defined as one *SD* below the mean; high status and integrity are defined as one *SD* above the mean.

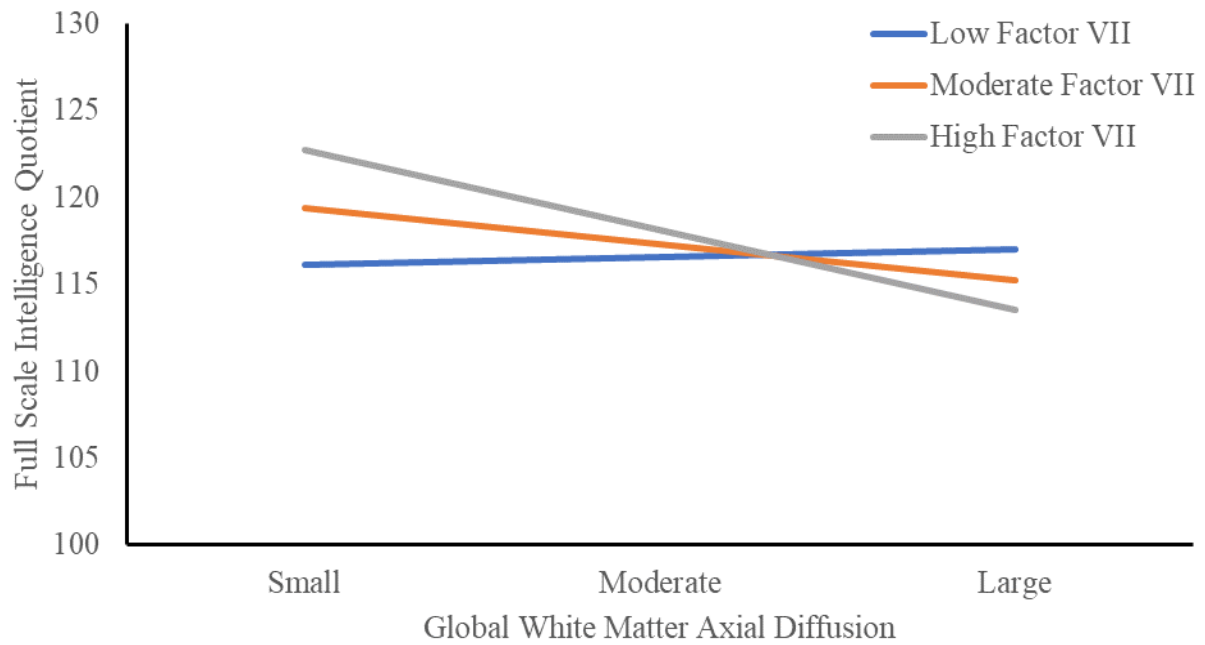


Figure 3.55 | Factor VII conditionally moderates the relationship between global white matter axial diffusion and general intelligence. When AD is low, factor VII significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

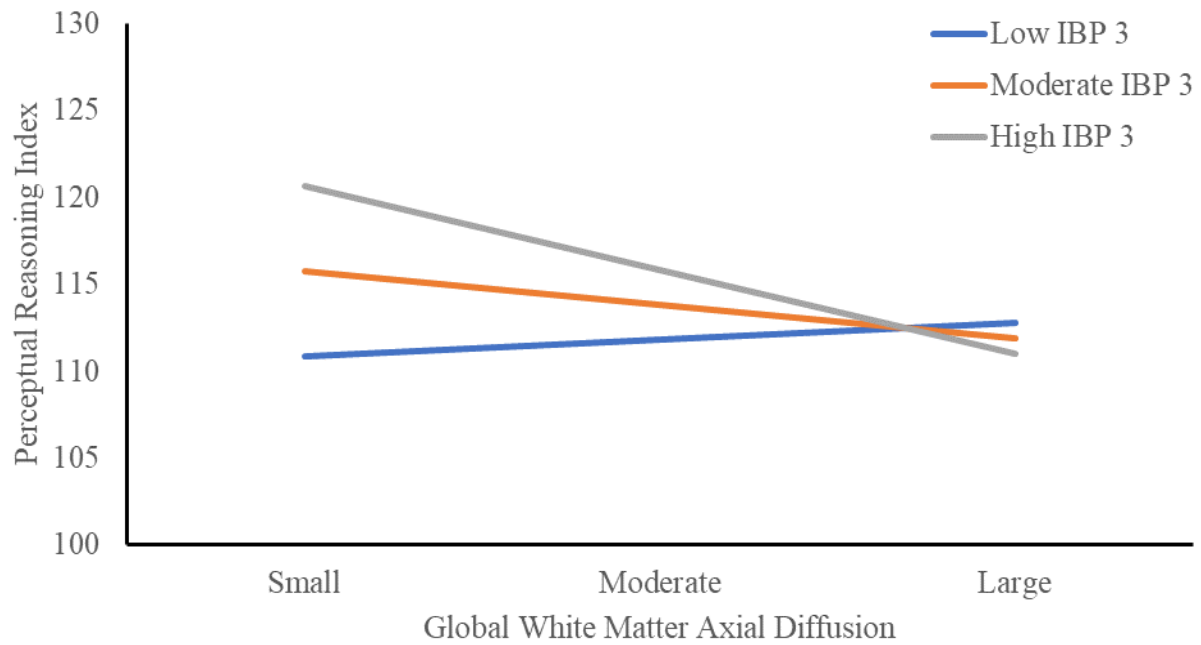


Figure 3.56 | IBP 3 conditionally moderates the relationship between global white matter axial diffusion and fluid intelligence. When AD is low, IBP 3 significantly influences fluid intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean.

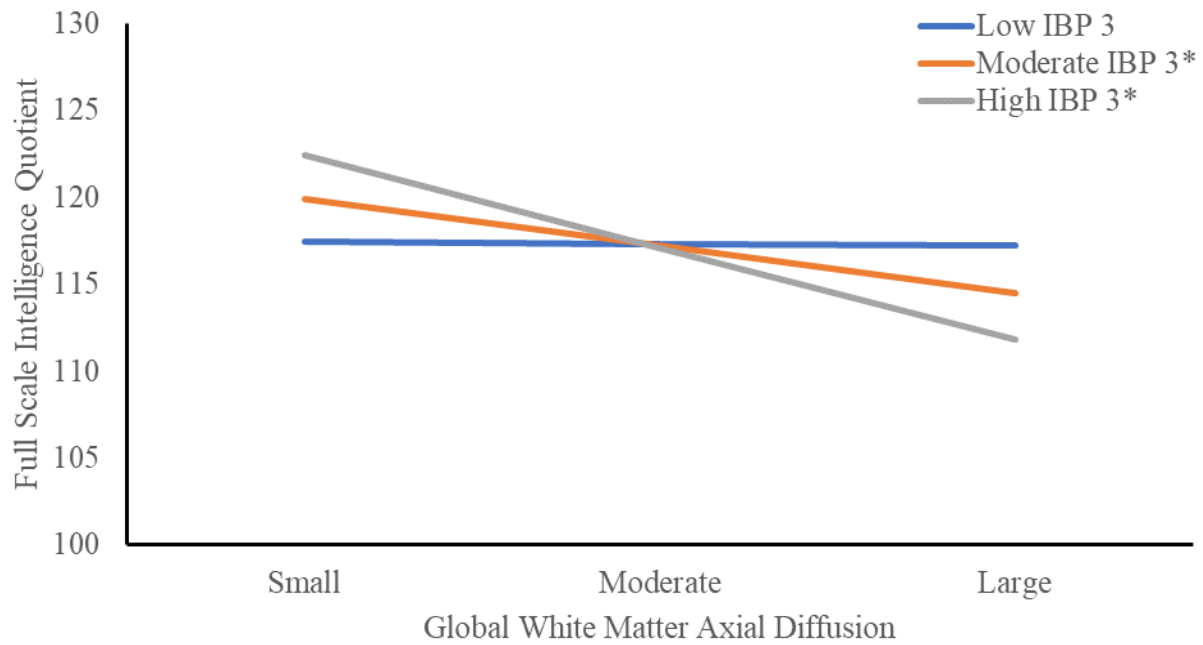


Figure 3.57 | IBP 3 conditionally moderates the relationship between global white matter axial diffusion and general intelligence. When IBP 3 is at or above the mean, it significantly influences general intelligence. Low status and AD are defined as one *SD* below the mean; high status and AD are defined as one *SD* above the mean. * $p < .05$

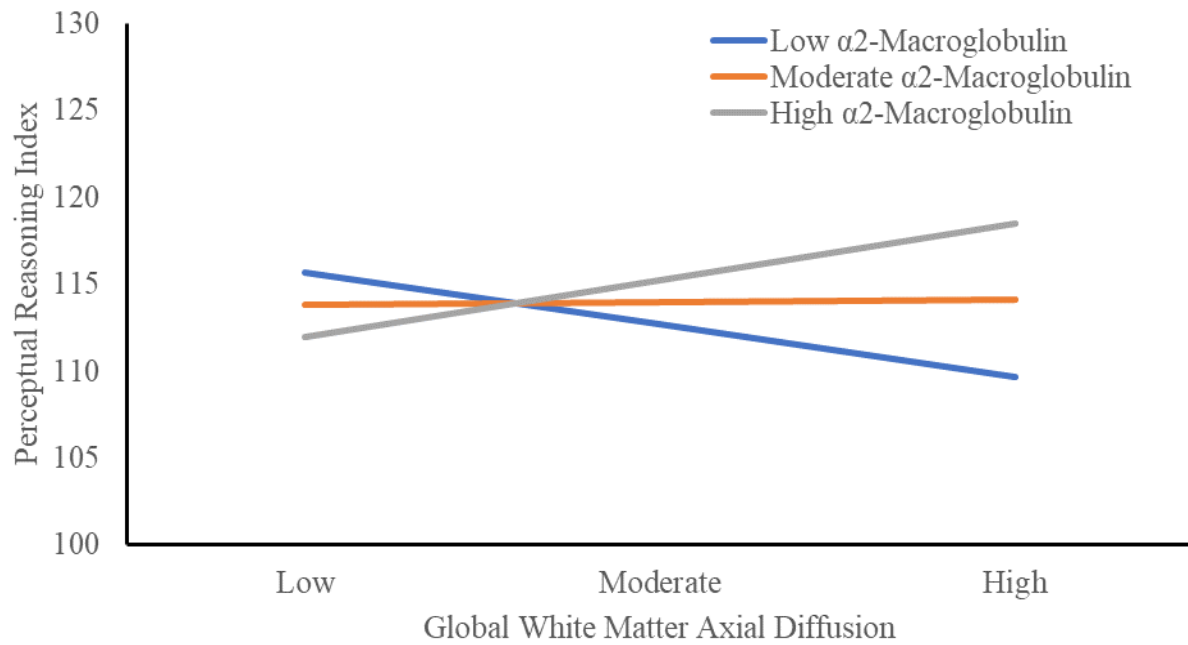


Figure 3.58 | α 2-Macroglobulin conditionally moderates the relationship between global white matter axial diffusion and fluid intelligence. When AxD is high, α 2-macroglobulin significantly influences fluid intelligence. Low status and AxD are defined as one *SD* below the mean; high status and AxD are defined as one *SD* above the mean.

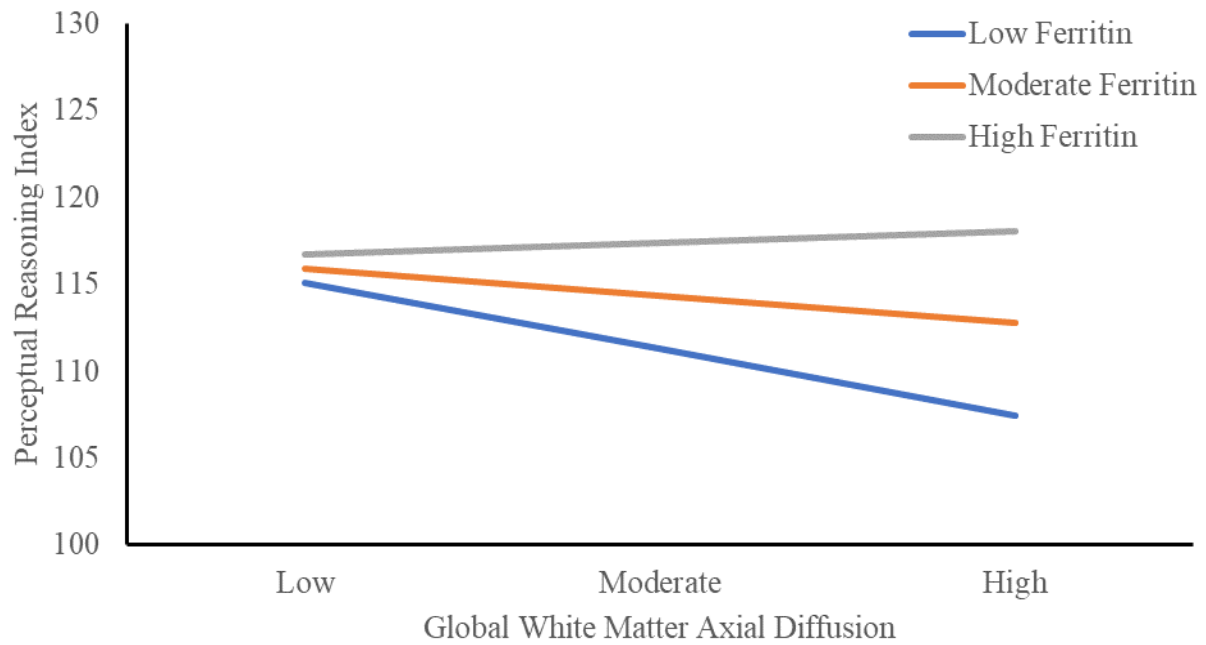


Figure 3.59 | Ferritin conditionally moderates the relationship between global white matter axial diffusion and fluid intelligence. When AxD is moderate or high, ferritin significantly influences fluid intelligence. Low status and AxD are defined as one *SD* below the mean; high status and AxD are defined as one *SD* above the mean.

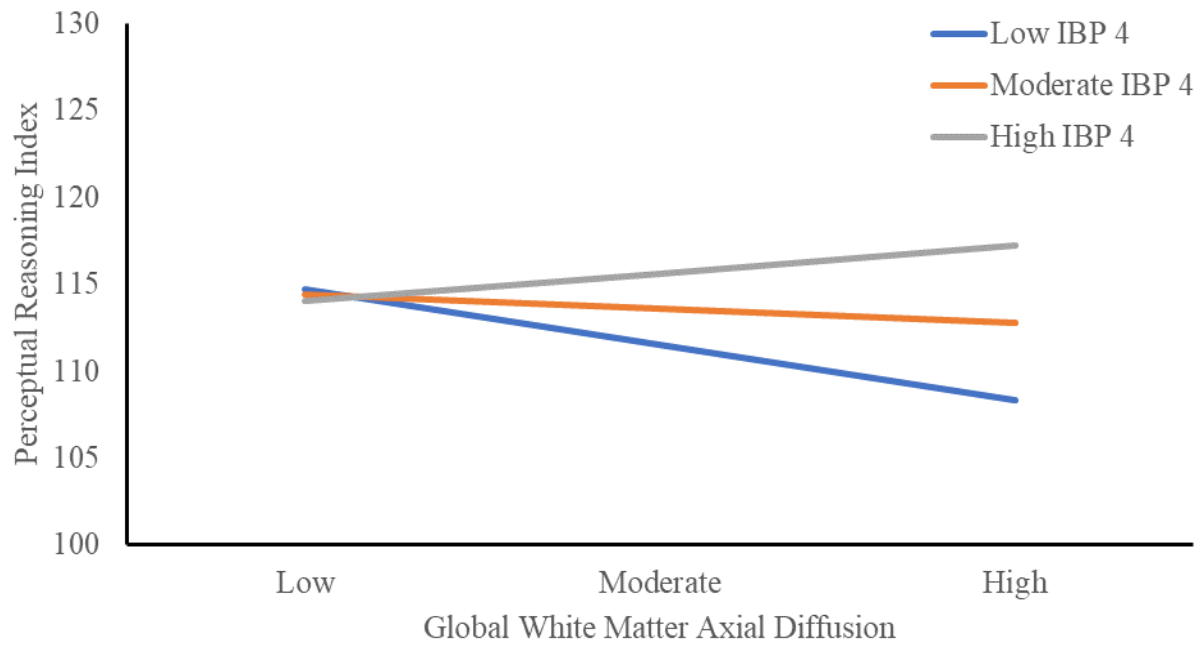


Figure 3.60 | IBP 4 conditionally moderates the relationship between global white matter axial diffusion and fluid intelligence. When AxD is high, IBP 4 significantly influences fluid intelligence. Low status and AxD are defined as one *SD* below the mean; high status and AxD are defined as one *SD* above the mean.

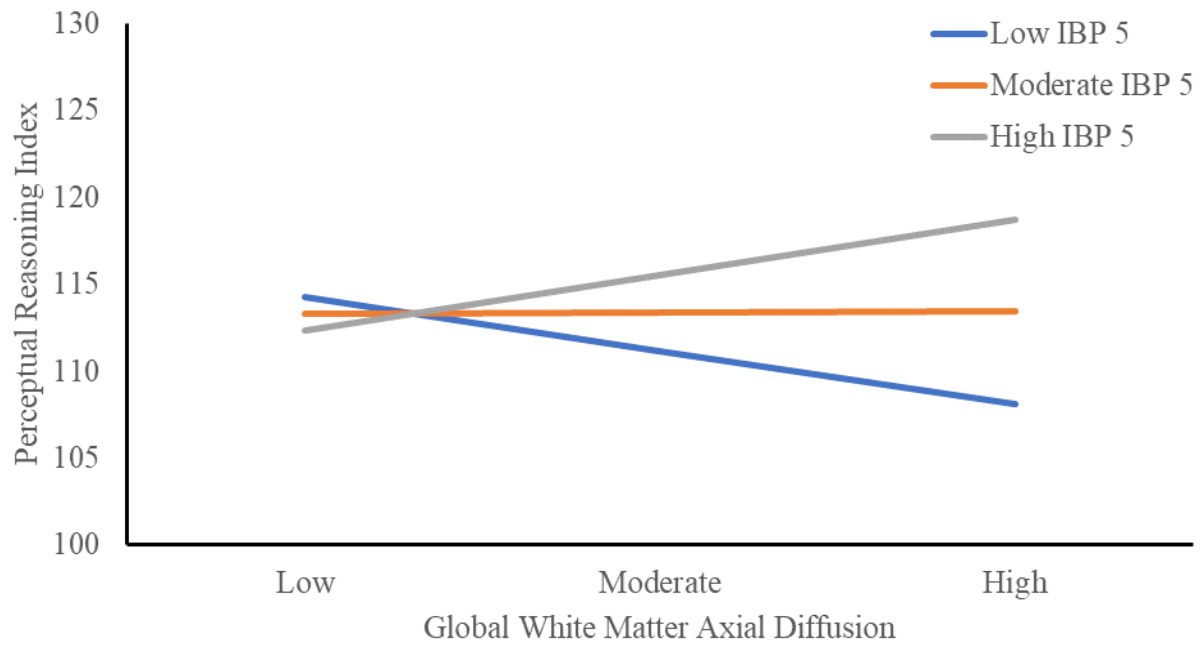


Figure 3.61 | IBP 5 conditionally moderates the relationship between global white matter axial diffusion and fluid intelligence. When AxD is moderate or high, IBP 5 significantly influences fluid intelligence. Low status and AxD are defined as one *SD* below the mean; high status and AxD are defined as one *SD* above the mean.

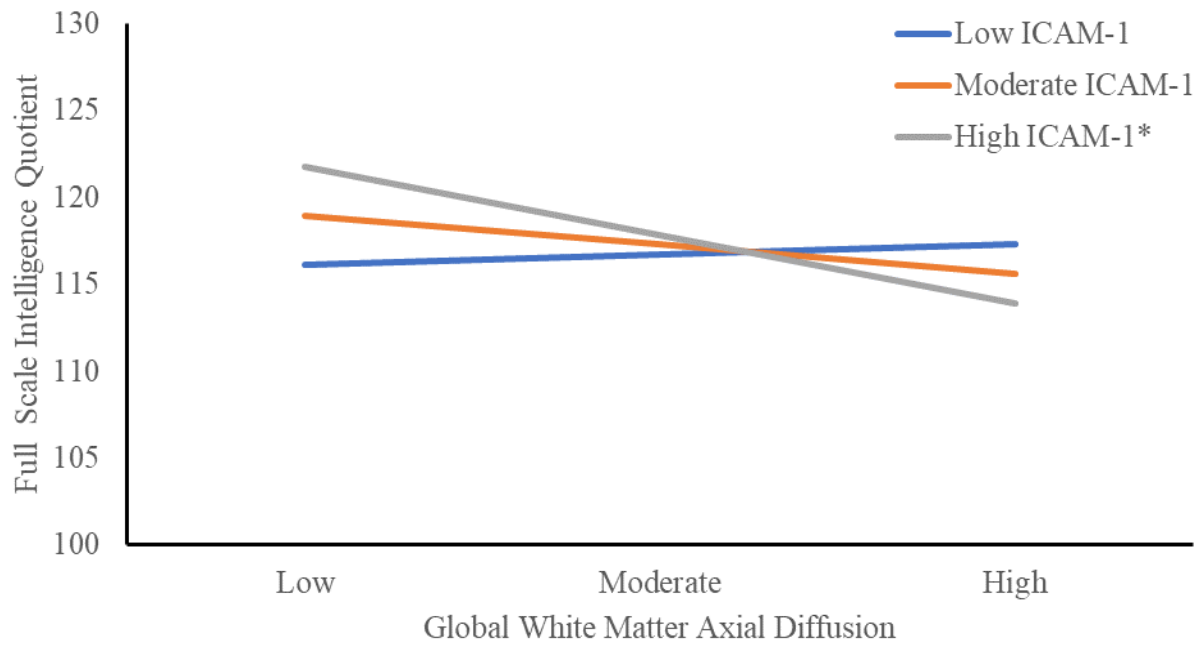


Figure 3.62 | ICAM-1 conditionally moderates the relationship between global white matter axial diffusion and general intelligence. When ICAM-1 status is above the mean, it significantly influences general intelligence. Low status and AxD are defined as one *SD* below the mean; high status and AxD are defined as one *SD* above the mean. $*p < .05$

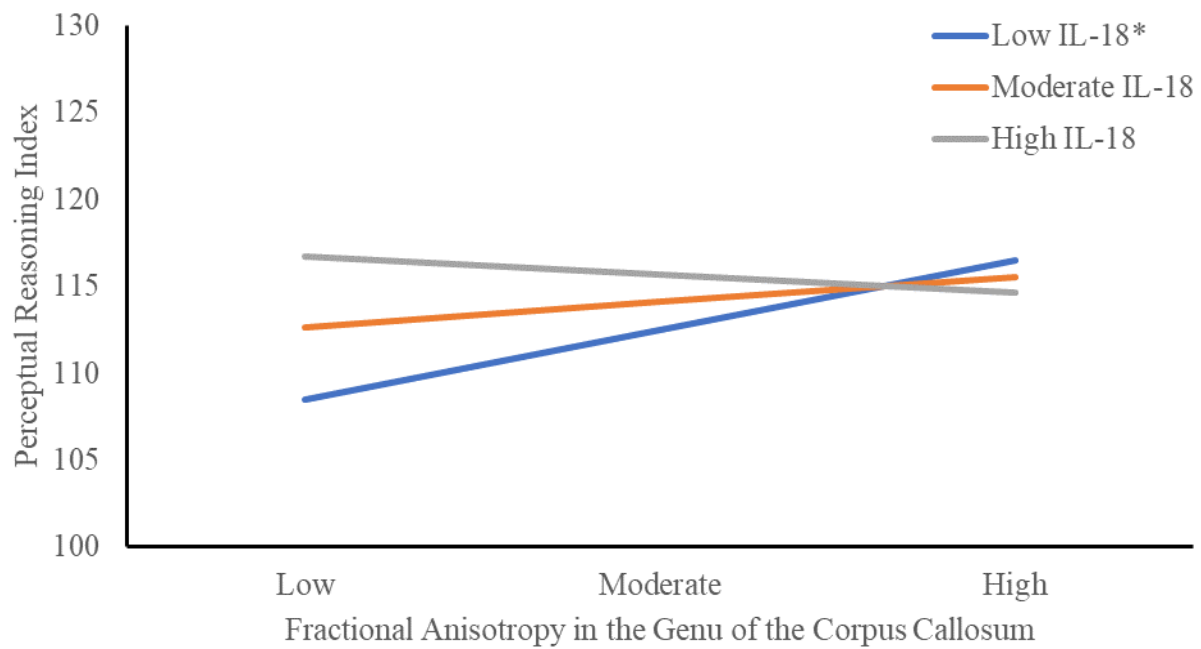


Figure 3.63 | IL-18 conditionally moderates the relationship between fractional anisotropy in the genu of the corpus callosum and fluid intelligence. When IL-18 is below the mean, it significantly influences fluid intelligence. Low status and FA are defined as one *SD* below the mean; high status and FA are defined as one *SD* above the mean. $*p < .05$

Table 3.1 | Cortical ROIs

Banks of superior temporal sulcus	Lateral occipital	Posterior cingulate
Caudal anterior cingulate	Lateral orbito-frontal	Precentral
Caudal middle frontal	Lingual gyrus	Precuneus
Cuneus	Medial orbito-frontal	Rostral anterior cingulate
Entorhinal cortex	Middle temporal	Rostral middle frontal
Frontal Pole	Parahippocampal	Superior frontal
Fusiform gyrus	Paracentral	Superior parietal
Inferior parietal	Pars opercularis	Superior temporal
Inferior temporal	Pars orbitalis	Supramarginal gyrus
Insula	Pars triangularis	Temporal pole
Isthmus cingulate	Pericalcarine	Transverse temporal
	Postcentral	

Table 3.2 | Inflammatory Biomarkers Measured by Myriad RBM

α 1-antitrypsin	IL-1 α ^b	IL-23 ^a
α 2-macroglobulin	IL-1 α RA ^a	Macrophage Inflammatory Protein-1 α ^b
β 2-microglobulin	IL-2 ^b	Macrophage Inflammatory Protein-1 β
Brain-derived neurotrophic factor	IL-3 ^b	Matrix Metalloproteinase-3 (MMP-3)
C-reactive protein (CRP)	IL-4 ^b	Matrix Metalloproteinase-9 (MMP-9)
Complement C3	IL-5 ^b	Monocyte Chemotactic Protein-1 (MCP-1) ^a
Eotaxin-1 (CCL11) ^a	IL-6 ^b	Stem Cell Factor
Factor VII	IL-7 ^b	T-Cell Specific Protein RANTES
Ferritin	IL-8 ^a	Tissue Inhibitor of Metalloproteinases-1
Fibrinogen	IL-10 ^b	Tumor Necrosis Factor- α ^b
Granulocyte-macrophage colony-stimulating factor ^b	IL-12p40 ^a	Tumor Necrosis Factor- β ^b
Haptoglobin	IL-12p70 ^b	Tumor Necrosis Factor Receptor-2
Intercellular Adhesion Molecule-1 (ICAM-1)	IL-15 ^b	Vascular Cell Adhesion Molecule-1 (VCAM-1)
Interferon- γ ^b	IL-17 ^b	Vascular Endothelial Growth Factor
Von Willebrand Factor	IL-18	Vitamin-D Binding Protein

^aBiomarkers omitted from PCA due to missing data^bBiomarkers $N < 50$ subjects with detectable levels were omitted from regression analyses

Table 3.3 | Inflammatory biomarker pattern construction

	IBP 1	IBP 2	IBP 3	IBP 4	IBP 5	IBP 6
Tumor Necrosis Factor Receptor-2	.845*			.290		
β 2-microglobulin	.826*			.318		
Vascular Cell Adhesion Molecule-1 (VCAM-1)	.813*				.283	
C-Reactive Protein (CRP)	.530*			.450	-.398	
Von Willebrand Factor	.530*	.289			.326	.263
Tissue Inhibitor of Metalloproteinases-1 (TIMP-1)	.520*	.446		.360	.304	
Stem Cell Factor	.466		.635*		-.268	
α 1-antitrypsin	.387			.607*		
Matrix Metalloproteinase-3 (MMP-3)	.378	.585*			-.324	
IL-18	.314		.447			
Ferritin	.295			.350		.629*
α 2-macroglobulin	.276				.736*	
Factor VII	-.271		.819*			
Brain-Derived Neurotrophic Factor (BDNF)		.812*				
T-Cell Specific Protein RANTES (RANTES)		.781*		.334	.261	
Vascular Endothelial Growth Factor (VEGF)		.747*			-.304	
Matrix Metalloproteinase-9 (MMP-9)		.477	.255			
Intercellular Adhesion Molecule-1 (ICAM-1)			.642*			
Macrophage Inflammatory Protein-1 β			.283	.339		
Complement C3			.280	.812*		
Fibrinogen				.853*		
Haptoglobin				.784*	-.263	
Vitamin-D Binding Protein				.305		-.693*
% Variance explained by each IBP	17	15	12	9	7	6
% Variance explained with each extraction (cumulative)	17	32	45	54	61	67

IBP = inflammation biomarker pattern

Coefficients < |.25| were excluded from the table for simplification and to emphasize dominant biomarkers for each pattern

*Considered dominant within the pattern

Table 3.4 | Demographic data

Age, $n(\bar{x} \pm SD)$; years	118(68.9 $\pm$ 3.0)
Sex, $n(\%F)$	118(63.6)
Body Mass Index (BMI), $n(\bar{x} \pm SD)$	118(25.9 $\pm$ 3.7)
Income, $n(\%)$	
<15k	1(0.8)
15-25k	5(4.2)
25-50k	22(18.6)
50-75k	25(21.2)
75-100k	28(23.7)
>100k	37(31.4)
Education, $n(\%)$	
Some high school	1(0.8)
High school degree	12(10.2)
Some college	22(18.6)
College degree	83(70.3)
Facets of Intelligence, $n(\bar{x} \pm SD)$	
Auditory Memory	112(113.2 $\pm$ 11.8)
Crystallized Intelligence	111(114.2 $\pm$ 12.6)
Delayed Memory	113(113.0 $\pm$ 12.0)
Fluid Intelligence	111(113.5 $\pm$ 11.4)
General Intelligence	111(116.9 $\pm$ 11.1)
Immediate Memory	113(114.6 $\pm$ 11.3)
Task Switching	112(8.268 $\pm$ 2.00)
Visual Working Memory	112(110.7 $\pm$ 10.3)
Grey Matter Volume, $n(\bar{x} \pm SD)$; mm³	
Banks of Superior Temporal Sulcus	118(4.778 $\times 10^3 \pm 7.233 \times 10^2$)
Caudal Anterior Cingulate	118(4.255 $\times 10^3 \pm 6.578 \times 10^2$)
Entorhinal Cortex	118(3.432 $\times 10^3 \pm 6.574 \times 10^2$)
Fusiform Gyrus	118(1.892 $\times 10^4 \pm 2.600 \times 10^3$)
Frontal Pole	118(1.851 $\times 10^3 \pm 3.620 \times 10^2$)
Inferior Temporal	118(1.914 $\times 10^4 \pm 2.960 \times 10^3$)
Insula	118(1.218 $\times 10^4 \pm 1.355 \times 10^3$)
Lateral Occipital	118(2.145 $\times 10^4 \pm 2.761 \times 10^3$)
Lateral Orbitofrontal	118(1.322 $\times 10^4 \pm 1.505 \times 10^3$)
Lingual Gyrus	118(1.304 $\times 10^4 \pm 1.708 \times 10^3$)
Medial Orbitofrontal	118(9.692 $\times 10^3 \pm 1.202 \times 10^3$)
Paracentral Gyrus	118(5.940 $\times 10^3 \pm 9.457 \times 10^2$)
Pars Opercularis	118(7.533 $\times 10^3 \pm 1.060 \times 10^3$)
Pars Orbitalis	118(4.399 $\times 10^3 \pm 5.269 \times 10^2$)
Posterior Cingulate	118(5.559 $\times 10^3 \pm 7.705 \times 10^2$)
Precuneus	118(1.853 $\times 10^4 \pm 2.056 \times 10^3$)
Rostral Anterior Cingulate	118(4.910 $\times 10^3 \pm 7.199 \times 10^2$)
Superior Frontal	118(4.392 $\times 10^4 \pm 4.103 \times 10^3$)
Superior Parietal	118(2.502 $\times 10^4 \pm 2.674 \times 10^3$)
Superior Temporal	118(2.037 $\times 10^4 \pm 2.771 \times 10^3$)
Supramarginal	118(1.608 $\times 10^4 \pm 2.582 \times 10^3$)
Temporal Pole	118(4.623 $\times 10^3 \pm 6.034 \times 10^2$)

Table 3.4 (cont.) | Demographic data, continued

Inflammation Biomarkers, n($\bar{x} \pm SD$); mg/mL	
α 2-Macroglobulin	118(1.942 ± 0.539)
β 2-Microglobulin	118($2.239 \times 10^{-3} \pm 7.349 \times 10^{-4}$)
Brain-Derived Neurotrophic Factor (BDNF)	118($3.414 \times 10^{-6} \pm 3.198 \times 10^{-6}$)
C-Reactive Protein (CRP)	116($4.321 \times 10^{-3} \pm 8.902 \times 10^{-3}$)
Complement C3	118(1.043 ± 0.264)
Factor VII	118($5.632 \times 10^{-4} \pm 2.124 \times 10^{-4}$)
Ferritin	118($1.627 \times 10^{-4} \pm 1.600 \times 10^{-4}$)
Fibrinogen	118(5.386 ± 1.509)
Haptoglobin	118(1.942 ± 1.174)
Intercellular Adhesion Molecule-1 (ICAM-1)	118($1.309 \times 10^{-4} \pm 4.073 \times 10^{-5}$)
Interleukin-8 (IL-8)	88($1.020 \times 10^{-8} \pm 4.363 \times 10^{-9}$)
Interleukin-18 (IL-18)	118($2.400 \times 10^{-7} \pm 1.365 \times 10^{-7}$)
Macrophage Inflammatory Protein-1 β	118($3.965 \times 10^{-7} \pm 1.620 \times 10^{-7}$)
Matrix Metalloproteinase-3 (MMP-3)	118($8.070 \times 10^{-6} \pm 5.598 \times 10^{-6}$)
Matrix Metalloproteinase-9 (MMP-9)	117($8.114 \times 10^{-5} \pm 4.240 \times 10^{-5}$)
Monocyte Chemotactic Protein-1	79($1.231 \times 10^{-7} \pm 4.042 \times 10^{-8}$)
Stem Cell Factor	117($4.108 \times 10^{-7} \pm 1.145 \times 10^{-7}$)
T-cell Specific Protein (RANTES)	118($1.588 \times 10^{-5} \pm 1.317 \times 10^{-5}$)
Tissue Inhibitor of Metalloproteinase-1	118($8.412 \times 10^{-5} \pm 2.565 \times 10^{-5}$)
Tumor Necrosis Factor Receptor-2	118($8.470 \times 10^{-6} \pm 4.108 \times 10^{-6}$)
Vascular Cell Adhesion Molecule-1 (VCAM-1)	118($8.432 \times 10^{-4} \pm 2.469 \times 10^{-4}$)
Vascular Endothelial Growth Factor (VEGF)	116($1.224 \times 10^{-7} \pm 6.371 \times 10^{-8}$)
Vitamin D-Binding Protein	118($3.134 \times 10^{-1} \pm 1.363 \times 10^{-1}$)
Von Willebrand Factor	118($1.673 \times 10^{-1} \pm 6.894 \times 10^{-2}$)
IBP 1	113($-5.292 \times 10^{-3} \pm 9.911 \times 10^{-1}$)
IBP 2	113($1.609 \times 10^{-2} \pm 1.007$)
IBP 3	113($1.799 \times 10^{-2} \pm 1.006$)
IBP 4	113($-7.051 \times 10^{-3} \pm 1.009$)
IBP 5	113($-3.878 \times 10^{-3} \pm 9.935 \times 10^{-1}$)
IBP 6	113($1.341 \times 10^{-2} \pm 1.009$)

Table 3.5 | Linear Regression models of cortical volumes associated with facets of intelligence

	β	β SE	R^2
<u>Auditory Memory</u>			
Frontal Pole	0.008	0.003	.175*
Inferior Temporal	0.001	0.000	.181*
Posterior Cingulate	0.004	0.001	.162*
<u>Delayed Memory</u>			
Banks of Superior Temporal Sulcus	-0.003	0.002	.138 ^x
Frontal Pole	0.008	0.003	.155*
<u>Fluid Intelligence</u>			
Caudal Anterior Cingulate	0.003	0.002	.202*
Entorhinal Cortex	0.002	0.002	.184*
Fusiform Gyrus	0.000	0.000	.176*
Insula	0.001	0.001	.180*
Lateral Occipital	0.001	0.000	.190*
Lateral Orbitofrontal	0.001	0.001	.187*
Medial Orbitofrontal	0.001	0.001	.179*
Paracentral Gyrus	0.002	0.001	.193*
Pars Opercularis	0.002	0.001	.204**
Pars Orbitalis	0.002	0.002	.177*
Precuneus	0.001	0.001	.178*
Rostral Anterior Cingulate	0.003	0.001	.194*
Superior Frontal	0.000	0.000	.193*
Superior Temporal	0.001	0.000	.193*
Supramarginal	0.001	0.000	.182*
Temporal Pole	0.004	0.002	.209**
<u>General Intelligence</u>			
Caudal Anterior Cingulate	0.003	0.001	.250**
Paracentral Gyrus	0.002	0.001	.241**
Precuneus	0.001	0.000	.244**
Rostral Anterior Cingulate	0.002	0.001	.241**
<u>Immediate Memory</u>			
Frontal Pole	0.006	0.003	.162*
Inferior Temporal	0.001	0.000	.195*
Paracentral Gyrus	0.003	0.001	.175*
Posterior Cingulate	0.004	0.001	.180*
Precuneus	0.001	0.001	.164*
Temporal Pole	0.004	0.002	.176*
<u>Task Switching</u>			
Lingual Gyrus	0.000	0.000	.124 ^x
<u>Visual Working Memory</u>			
Entorhinal Cortex	0.001	0.000	.087
Insula	0.000	0.000	.077
Precuneus	0.000	0.000	.096
Temporal Pole	0.001	0.000	.077
Superior Parietal	0.000	0.000	.091
Supramarginal	0.000	0.000	.087

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

**Table 3.6 | F statistics from moderation analyses, FDR corrected:
caudal anterior cingulate (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.256	.002	.207	0.338	.562	.003
IL-8 (<i>df</i> = 75)	2.411	.022	.205	0.449	.505	.005
IL-18 (<i>df</i> = 102)	3.551	.001	.218	3.090	.082	.024
MCP-1 (<i>df</i> = 64)	1.554	.157	.163	0.000	.982	.000
RANTES (<i>df</i> = 102)	4.457	.000	.259	3.336	.071	.024
ICAM-1 (<i>df</i> = 102)	3.468	.001	.214	0.006	.940	.000
VCAM-1 (<i>df</i> = 102)	3.941	.000	.236	5.403	.002	.040
MMP-3 (<i>df</i> = 102)	3.347	.002	.208	0.170	.681	.001
MMP-9 (<i>df</i> = 101)	3.370	.002	.211	0.494	.484	.004
Complement C3 (<i>df</i> = 102)	3.914	.000	.235	0.057	.812	.000
Ferritin (<i>df</i> = 102)	4.341	.000	.254	2.134	.147	.016
IBP 1 (<i>df</i> = 97)	3.728	.001	.235	3.145	.079	.025
IBP 2 (<i>df</i> = 97)	3.536	.001	.226	4.411	.038	.035
IBP 3 (<i>df</i> = 97)	3.499	.001	.224	2.796	.098	.022
IBP 4 (<i>df</i> = 97)	3.389	.002	.218	0.336	.564	.003
IBP 5 (<i>df</i> = 97)	3.399	.002	.219	0.180	.672	.002
IBP 6 (<i>df</i> = 97)	3.177	.003	.208	0.207	.650	.002
<u>General Intelligence</u>						
CRP (<i>df</i> = 100)	4.424	.000	.261	0.097	.756	.001
IL-8 (<i>df</i> = 75)	3.565	.002	.276	0.105	.747	.001
IL-18 (<i>df</i> = 102)	4.532	.000	.262	1.427	.235	.010
MCP-1 (<i>df</i> = 64)	2.876	.008	.264	0.006	.940	.000
RANTES (<i>df</i> = 102)	5.028	.000	.283	2.098	.151	.015
ICAM-1 (<i>df</i> = 102)	4.234	.000	.249	0.080	.778	.001
VCAM-1 (<i>df</i> = 102)	5.409	.000	.298	5.337	.023	.037
MMP-3 (<i>df</i> = 102)	4.302	.000	.252	0.153	.696	.001
MMP-9 (<i>df</i> = 101)	4.367	.000	.257	0.117	.733	.001
α 2-macroglobulin (<i>df</i> = 102)	4.809	.000	.274	0.996	.320	.007
IBP 1 (<i>df</i> = 97)	4.815	.000	.284	4.542	.036	.034
IBP 2 (<i>df</i> = 97)	4.471	.000	.269	2.193	.142	.016
IBP 3 (<i>df</i> = 97)	4.264	.000	.260	1.416	.237	.011
IBP 4 (<i>df</i> = 97)	4.369	.000	.265	0.094	.760	.001
IBP 5 (<i>df</i> = 97)	5.275	.000	.303	0.878	.351	.006
IBP 6 (<i>df</i> = 97)	4.298	.000	.262	1.573	.213	.012

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 3.7 | F statistics from moderation analyses, FDR corrected: entorhinal cortex (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.132	.003	.200	0.001	.973	.000
IL-8 (<i>df</i> = 75)	2.587	.015	.216	3.230	.076	.034
IL-18 (<i>df</i> = 102)	2.871	.006	.184	0.749	.389	.006
MCP-1 (<i>df</i> = 64)	1.666	.124	.172	2.982	.089	.039
RANTES (<i>df</i> = 102)	3.588	.001	.220	0.000	.995	.000
ICAM-1 (<i>df</i> = 102)	3.238	.002	.202	1.771	.186	.014
VCAM-1 (<i>df</i> = 102)	2.992	.005	.190	1.240	.268	.010
MMP-3 (<i>df</i> = 102)	3.045	.004	.193	0.019	.891	.000
MMP-9 (<i>df</i> = 101)	3.353	.002	.210	0.408	.524	.003
Complement C3 (<i>df</i> = 102)	4.496	.000	.261	5.082	.026	.037
Ferritin (<i>df</i> = 102)	4.061	.000	.242	2.146	.146	.016
IBP 1 (<i>df</i> = 97)	3.378	.002	.218	0.172	.697	.001
IBP 2 (<i>df</i> = 97)	2.881	.006	.192	0.087	.769	.001
IBP 3 (<i>df</i> = 97)	3.042	.004	.201	0.624	.432	.005
IBP 4 (<i>df</i> = 97)	3.534	.001	.226	1.550	.216	.012
IBP 5 (<i>df</i> = 97)	3.789	.001	.238	0.032	.859	.000
IBP 6 (<i>df</i> = 97)	3.265	.002	.212	1.611	.207	.013

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 3.8 | F statistics from moderation analyses, FDR corrected: frontal pole (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Auditory Memory</u>						
CRP (<i>df</i> = 101)	3.365	.002	.210	0.240	.625	.002
IL-8 (<i>df</i> = 75)	2.167	.040	.188	0.348	.557	.004
IL-18 (<i>df</i> = 103)	2.725	.009	.175	0.113	.738	.001
MCP-1 (<i>df</i> = 65)	3.055	.006	.273	3.923	.052	.044
RANTES (<i>df</i> = 103)	3.124	.003	.195	1.313	.255	.010
ICAM-1 (<i>df</i> = 103)	3.128	.003	.196	0.848	.359	.007
VCAM-1 (<i>df</i> = 103)	2.925	.006	.185	0.945	.333	.008
MMP-3 (<i>df</i> = 103)	2.819	.007	.180	0.303	.583	.002
MMP-9 (<i>df</i> = 102)	2.750	.009	.177	0.001	.980	.000
Factor VII (<i>df</i> = 103)	3.292	.002	.204	0.266	.607	.002
IBP 1 (<i>df</i> = 98)	3.037	.004	.199	0.324	.570	.003
IBP 2 (<i>df</i> = 98)	2.878	.006	.190	1.098	.297	.009
IBP 3 (<i>df</i> = 98)	3.134	.003	.204	0.046	.831	.000
IBP 4 (<i>df</i> = 98)	2.860	.007	.189	0.002	.968	.000
IBP 5 (<i>df</i> = 98)	2.760	.009	.184	0.372	.543	.003
IBP 6 (<i>df</i> = 98)	3.587	.001	.226	5.881	.017	.046

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 3.9 | F statistics from moderation analyses, FDR corrected: lingual gyrus (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Task Switching						
CRP (<i>df</i> = 102)	2.623	.012	.171	4.382	.039	.036
IL-8 (<i>df</i> = 76)	1.760	.098	.156	1.180	.281	.013
IL-18 (<i>df</i> = 103)	2.403	.020	.157	0.367	.546	.003
MCP-1 (<i>df</i> = 66)	1.088	.382	.116	0.818	.369	.011
RANTES (<i>df</i> = 103)	2.877	.006	.183	2.643	.107	.021
ICAM-1 (<i>df</i> = 103)	2.793	.008	.178	0.503	.475	.004
VCAM-1 (<i>df</i> = 103)	2.754	.008	.176	4.958	.028	.040
MMP-3 (<i>df</i> = 103)	2.032	.050*	.136	1.020	.315	.009
MMP-9 (<i>df</i> = 102)	1.986	.056	.135	0.273	.602	.002
β 2-microglobulin (<i>df</i> = 103)	2.776	.008	.177	3.591	.061	.029
Complement C3 (<i>df</i> = 103)	2.795	.008	.178	0.000	.982	.000
Fibrinogen (<i>df</i> = 103)	2.696	.010	.173	0.004	.949	.000
TIMP-1 (<i>df</i> = 103)	3.045	.004	.191	1.663	.200	.013
IBP 1 (<i>df</i> = 99)	3.109	.004	.201	7.392	.008	.060
IBP 2 (<i>df</i> = 99)	2.501	.016	.168	1.894	.172	.016
IBP 3 (<i>df</i> = 99)	2.217	.032	.152	0.752	.388	.006
IBP 4 (<i>df</i> = 99)	2.749	.009	.182	0.406	.525	.003
IBP 5 (<i>df</i> = 99)	2.314	.026	.158	0.242	.624	.002
IBP 6 (<i>df</i> = 99)	2.104	.042	.145	0.142	.707	.001

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.10 | F statistics from moderation analyses, FDR corrected:
posterior cingulate (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Immediate Memory</u>						
CRP (<i>df</i> = 102)	3.5698	.0011	.2187	0.1887	.6649	.0014
IL-8 (<i>df</i> = 75)	4.1032	.0004	.3044	1.3788	.2440	.0128
IL-18 (<i>df</i> = 104)	3.5675	.0011	.2153	4.4431	.0374	.0335
MCP-1 (<i>df</i> = 67)	2.8523	.0086	.2540	0.3336	.5655	.0037
RANTES (<i>df</i> = 104)	2.8785	.0062	.1813	0.0083	.9276	.0001
ICAM-1 (<i>df</i> = 104)	3.2208	.0026	.1986	0.6677	.4157	.0051
VCAM-1 (<i>df</i> = 104)	3.6645	.0008	.2199	2.9500	.0889	.0221
MMP-3 (<i>df</i> = 104)	3.1671	.0030	.1959	0.4932	.4841	.0038
MMP-9 (<i>df</i> = 103)	3.4621	.0014	.2119	3.7795	.0546	.0289
IBP 1 (<i>df</i> = 99)	4.0459	.0003	.2464	2.4456	.1210	.0186
IBP 2 (<i>df</i> = 99)	2.8934	.0061	.1895	0.8614	.3556	.0071
IBP 3 (<i>df</i> = 99)	3.5885	.0011	.2248	1.9910	.1614	.0156
IBP 4 (<i>df</i> = 99)	3.0854	.0038	.1996	0.4564	.5009	.0037
IBP 5 (<i>df</i> = 99)	3.0309	.0043	.1967	1.7109	.1939	.0139
IBP 6 (<i>df</i> = 99)	2.8900	.0062	.1893	0.6112	.4362	.0050

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.11 | F statistics from moderation analyses, FDR corrected:
precuneus (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Fluid Intelligence						
CRP (<i>df</i> = 100)	2.8691	.0065	.1867	0.3050	.5820	.0025
IL-8 (<i>df</i> = 75)	2.5414	.0166	.2133	4.0777	.0470	.0428
IL-18 (<i>df</i> = 102)	3.1416	.0032	.1977	3.9168	.0505	.0308
MCP-1 (<i>df</i> = 64)	1.2161	.3041	.1320	0.0347	.8527	.0005
RANTES (<i>df</i> = 102)	3.3747	.0018	.2093	0.4345	.5113	.0034
ICAM-1 (<i>df</i> = 102)	2.9841	.0048	.1897	1.0230	.3142	.0081
VCAM-1 (<i>df</i> = 102)	2.7617	.0084	.1780	0.9219	.3392	.0074
MMP-3 (<i>df</i> = 102)	2.8179	.0073	.1810	0.0048	.9450	.0000
MMP-9 (<i>df</i> = 101)	3.0386	.0042	.1940	0.9835	.3237	.0078
Complement C3 (<i>df</i> = 102)	3.4887	.0013	.2148	1.1564	.2848	.0089
Ferritin (<i>df</i> = 102)	3.5074	.0013	.2157	0.0075	.9313	.0001
IBP 1 (<i>df</i> = 97)	2.8567	.0068	.1907	0.2785	.5989	.0023
IBP 2 (<i>df</i> = 97)	2.7494	.0089	.1848	2.7546	.1002	.0231
IBP 3 (<i>df</i> = 97)	2.5843	.0133	.1757	0.2395	.6257	.0020
IBP 4 (<i>df</i> = 97)	2.6771	.0106	.1809	0.0351	.8517	.0003
IBP 5 (<i>df</i> = 97)	3.0072	.0047	.1987	0.0504	.8228	.0004
IBP 6 (<i>df</i> = 97)	2.7678	.0085	.1858	0.9886	.3226	.0083

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.12 | F statistics from moderation analyses, FDR corrected:
superior temporal (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Fluid Intelligence						
CRP (<i>df</i> = 100)	3.1652	.0031	.2021	0.0814	.7761	.0006
IL-8 (<i>df</i> = 75)	2.8030	.0090	.2302	1.3375	.2511	.0137
IL-18 (<i>df</i> = 102)	3.3194	.0021	.2066	2.5900	.1106	.0201
MCP-1 (<i>df</i> = 64)	1.3199	.2499	.1416	0.0027	.9586	.0000
RANTES (<i>df</i> = 102)	4.0992	.0003	.2433	2.8451	.0947	.0211
ICAM-1 (<i>df</i> = 102)	3.3542	.0019	.2083	0.9552	.3307	.0074
VCAM-1 (<i>df</i> = 102)	3.2879	.0022	.2050	2.3493	.1284	.0183
MMP-3 (<i>df</i> = 102)	3.2369	.0025	.2025	0.4049	.5260	.0032
MMP-9 (<i>df</i> = 101)	3.6525	.0009	.2244	2.5060	.1165	.0192
Complement C3 (<i>df</i> = 102)	3.7832	.0006	.2288	0.8076	.3710	.0061
Ferritin (<i>df</i> = 102)	3.9348	.0004	.2358	0.0129	.9100	.0001
IBP 1 (<i>df</i> = 97)	3.3737	.0019	.2177	1.0411	.3101	.0084
IBP 2 (<i>df</i> = 97)	4.1748	.0003	.2561	8.1724	.0052	.0627
IBP 3 (<i>df</i> = 97)	3.1179	.0035	.2045	0.0052	.9425	.0000
IBP 4 (<i>df</i> = 97)	3.1849	.0030	.2080	0.0438	.8347	.0004
IBP 5 (<i>df</i> = 97)	3.6674	.0009	.2322	0.3111	.5783	.0025
IBP 6 (<i>df</i> = 97)	3.0823	.0039	.2027	0.0655	.7986	.0005

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.13 | F statistics from moderation analyses, FDR corrected:
supramarginal gyrus (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Fluid Intelligence						
CRP (<i>df</i> = 100)	3.0243	.0044	.1948	0.2941	.5888	.0024
IL-8 (<i>df</i> = 75)	3.0508	.0049	.2460	6.1292	.0156	.0616
IL-18 (<i>df</i> = 102)	3.2199	.0026	.2016	3.6953	.0574	.0289
MCP-1 (<i>df</i> = 64)	1.3177	.2510	.1414	0.1412	.7083	.0019
RANTES (<i>df</i> = 102)	4.0600	.0003	.2415	3.0751	.0825	.0229
ICAM-1 (<i>df</i> = 102)	3.8634	.0005	.2325	5.7405	.0184	.0432
VCAM-1 (<i>df</i> = 102)	2.8831	.0062	.1844	1.3091	.2552	.0105
MMP-3 (<i>df</i> = 102)	2.9043	.0059	.1855	0.1817	.6708	.0015
MMP-9 (<i>df</i> = 101)	3.1819	.0029	.2013	0.9517	.3316	.0075
Complement C3 (<i>df</i> = 102)	4.5683	.0001	.2638	6.2158	.0143	.0449
Ferritin (<i>df</i> = 102)	3.6535	.0009	.2227	0.4781	.4909	.0036
IBP 1 (<i>df</i> = 97)	3.0072	.0047	.1987	0.6525	.4212	.0054
IBP 2 (<i>df</i> = 97)	3.1918	.0029	.2084	4.2407	.0421	.0346
IBP 3 (<i>df</i> = 97)	2.9975	.0048	.1982	1.6710	.1992	.0138
IBP 4 (<i>df</i> = 97)	3.1971	.0029	.2087	2.2857	.1338	.0186
IBP 5 (<i>df</i> = 97)	3.3281	.0021	.2154	0.3884	.5346	.0031
IBP 6 (<i>df</i> = 97)	2.9700	.0051	.1968	1.4590	.2300	.0121

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 3.14 | Demographic data

Age, $n(\bar{x} \pm SD)$; years	99(68.8 $\pm$ 3.0)
Sex, $n(\%F)$	99(62.6)
Body Mass Index (BMI), $n(\bar{x} \pm SD)$	99(26.0 $\pm$ 3.8)
Income, $n(\%)$	
<15k	1(1.0)
15-25k	3(3.0)
25-50k	15(15.2)
50-75k	24(24.2)
75-100k	24(24.2)
>100k	32(32.3)
Education, $n(\%)$	
Some high school	1(1.0)
High school degree	11(11.1)
Some college	17(17.2)
College degree	70(70.7)
Facets of Intelligence, $n(\bar{x} \pm SD)$	
Auditory Memory	94(112.7 $\pm$ 11.0)
Fluid Intelligence	92(113.4 $\pm$ 11.4)
General Intelligence	93(116.4 $\pm$ 11.0)
Immediate Memory	95(114.3 $\pm$ 11.0)
Task Switching	93(8.344 $\pm$ 2.00)
Default Mode Network (DMN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(2.466 $\times 10^{-1} \pm 0.030$)
Local Efficiency	99(3.004 $\times 10^{-1} \pm 0.023$)
Small World Propensity	99(6.670 $\times 10^{-1} \pm 0.051$)
Frontoparietal Network (FPN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(2.700 $\times 10^{-1} \pm 0.046$)
Local Efficiency	99(3.295 $\times 10^{-1} \pm 0.039$)
Small World Propensity	99(6.558 $\times 10^{-1} \pm 0.077$)
Limbic Network (LN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(3.006 $\times 10^{-1} \pm 0.044$)
Local Efficiency	99(3.549 $\times 10^{-1} \pm 0.042$)
Small World Propensity	99(5.543 $\times 10^{-1} \pm 0.147$)
Somatomotor Network (SMN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(3.435 $\times 10^{-1} \pm 0.053$)
Local Efficiency	99(3.818 $\times 10^{-1} \pm 0.036$)
Small World Propensity	99(5.149 $\times 10^{-1} \pm 0.122$)
Dorsal Attention Network (DAN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(3.021 $\times 10^{-1} \pm 0.040$)
Local Efficiency	99(3.524 $\times 10^{-1} \pm 0.028$)
Small World Propensity	99(5.840 $\times 10^{-1} \pm 0.104$)
Ventral Attention Network (VAN) Characteristics, $n(\bar{x} \pm SD)$	
Global Efficiency	99(3.328 $\times 10^{-1} \pm 0.049$)
Local Efficiency	99(3.800 $\times 10^{-1} \pm 0.041$)
Small World Propensity	99(5.179 $\times 10^{-1} \pm 0.137$)

Table 3.14 (cont.) | Demographic data, continued

Inflammation Biomarkers, n($\bar{x} \pm SD$); mg/mL	
α 2-Macroglobulin	99(1.850 $\pm$ 0.503)
β 2-Microglobulin	99(2.220 $\times 10^{-3} \pm 7.621 \times 10^{-4}$)
C-Reactive Protein (CRP)	97(4.745 $\times 10^{-3} \pm 9.652 \times 10^{-3}$)
Complement C3	99(1.022 $\pm$ 0.229)
Factor VII	99(5.314 $\times 10^{-4} \pm 1.870 \times 10^{-4}$)
Ferritin	99(1.670 $\times 10^{-4} \pm 1.637 \times 10^{-4}$)
Fibrinogen	99(5.263 $\pm$ 1.389)
Intercellular Adhesion Molecule-1 (ICAM-1)	99(1.272 $\times 10^{-4} \pm 3.625 \times 10^{-5}$)
Interleukin-8 (IL-8)	73(1.001 $\times 10^{-8} \pm 4.502 \times 10^{-9}$)
Interleukin-18 (IL-18)	99(2.348 $\times 10^{-7} \pm 1.294 \times 10^{-7}$)
Matrix Metalloproteinase-3 (MMP-3)	99(8.085 $\times 10^{-6} \pm 5.904 \times 10^{-6}$)
Matrix Metalloproteinase-9 (MMP-9)	98(8.053 $\times 10^{-5} \pm 4.435 \times 10^{-5}$)
Monocyte Chemotactic Protein-1 (MCP-1)	68(1.215 $\times 10^{-7} \pm 4.202 \times 10^{-8}$)
T-cell Specific Protein (RANTES)	99(1.495 $\times 10^{-5} \pm 1.318 \times 10^{-5}$)
Tissue Inhibitor of Metalloproteinase-1 (TIMP-1)	99(8.043 $\times 10^{-5} \pm 2.398 \times 10^{-5}$)
Vascular Cell Adhesion Molecule-1 (VCAM-1)	99(8.519 $\times 10^{-6} \pm 4.337 \times 10^{-6}$)
IBP 1	95(3.072 $\times 10^{-2} \pm 1.054$)
IBP 2	95(-2.333 $\times 10^{-2} \pm 1.055$)
IBP 3	95(-1.154 $\times 10^{-1} \pm 8.226 \times 10^{-1}$)
IBP 4	95(-6.788 $\times 10^{-2} \pm 9.549 \times 10^{-1}$)
IBP 5	95(-1.309 $\times 10^{-1} \pm 9.837 \times 10^{-1}$)
IBP 6	95(6.925 $\times 10^{-2} \pm 1.048$)

Table 3.15 | Linear regression models of network characteristics associated with facets of intelligence: WASI-II

	<u>Fluid Intelligence</u>			<u>General Intelligence</u>		
	β	β SE	R^2	β	β SE	R^2
<u>Default Mode Network</u>						
Local Efficiency	15.57	48.88	.169 ^x	29.179	45.182	.229*
Global Efficiency	1.68	40.20	.168 ^x	2.181	37.225	.225*
Small World Propensity	-22.70	22.78	.178*	-51.502	20.471	.278**
<u>Frontoparietal Network</u>						
Local Efficiency	29.54	29.35	.178*	42.801	26.949	.247**
Global Efficiency	6.41	25.04	.169 ^x	16.687	23.126	.229*
Small World Propensity	4.39	14.84	.169 ^x	3.783	13.747	.225*
<u>Limbic Network</u>						
Local Efficiency	-24.13	26.95	.176*	-11.44	25.04	.227*
Global Efficiency	-6.69	25.91	.169*	-14.97	23.94	.228*
Small World Propensity	9.31	8.03	.181*	-2.94	7.49	.226*
<u>Somatomotor Network</u>						
Local Efficiency	40.24	31.78	.183*	23.56	29.60	.230*
Global Efficiency	20.70	21.99	.177 ^x	20.71	20.35	.234*
Small World Propensity	-1.18	9.72	.168 ^x	-10.28	8.93	.237*
<u>Dorsal Attention Network</u>						
Local Efficiency	-21.08	40.35	.171 ^x	-79.988	36.411	.266**
Global Efficiency	-15.24	28.58	.171 ^x	-49.129	25.971	.256**
Small World Propensity	2.66	11.09	.169 ^x	14.812	10.146	.244**
<u>Ventral Attention Network</u>						
Local Efficiency	-46.91	27.68	.195*	-54.193	25.399	.264**
Global Efficiency	-26.19	24.16	.179*	-45.711	21.975	.262**
Small World Propensity	1.25	8.23	.168 ^x	-0.154	7.619	.225*

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

Table 3.16 | Linear regression models of network characteristics associated with facets of intelligence WMS – IV and DKEFS Trails

Network Characteristics	<u>Auditory Memory</u>			<u>Immediate Memory</u>			<u>Task Switching</u>		
	β	β SE	R^2	β	β SE	R^2	β	β SE	R^2
<u>Default Mode Network</u>									
Local Efficiency	12.56	51.72	.113	45.745	48.490	.136 ^x	-0.325	8.868	.092
Global Efficiency	0.984	42.52	.112	19.542	40.002	.130	-0.117	7.289	.092
Small World Propensity	-25.96	24.07	.124	-11.734	22.79	.130	-7.095	4.082	.123
<u>Frontoparietal Network</u>									
Local Efficiency	21.46	31.15	.117	20.125	29.342	.132 ^x	4.129	5.335	.098
Global Efficiency	9.987	26.48	.114	12.392	24.925	.130	2.103	4.536	.094
Small World Propensity	3.171	15.71	.113	4.569	14.791	.128	0.400	2.692	.092
<u>Limbic Network</u>									
Local Efficiency	26.20	28.50	.121	26.30	26.83	.137 ^x	0.120	4.908	.092
Global Efficiency	24.52	27.29	.120	24.77	25.69	.136 ^x	-1.649	4.696	.093
Small World Propensity	2.074	8.559	.113	3.403	8.057	.129	0.343	1.467	.092
<u>Somatomotor Network</u>									
Local Efficiency	83.89	32.72	.175*	38.77	31.70	.142 ^x	-5.920	5.781	.103
Global Efficiency	42.22	22.94	.145 ^x	18.53	21.94	.134 ^x	-6.052	3.955	.116
Small World Propensity	-19.13	10.07	.147 ^x	-14.72	9.553	.150 ^x	3.109	1.729	.125
<u>Dorsal Attention Network</u>									
Local Efficiency	30.88	42.61	.117	13.170	40.239	.128	-5.708	7.301	.098
Global Efficiency	33.63	30.06	.125	14.924	28.477	.130	-0.858	5.189	.092
Small World Propensity	-12.37	11.66	.123	-1.212	11.051	.127	4.188	1.960	.138 ^x
<u>Ventral Attention Network</u>									
Local Efficiency	-22.18	29.68	.118	-40.058	27.717	.147 ^x	-2.342	5.097	.094
Global Efficiency	-7.457	25.71	.113	-11.356	24.203	.129	-2.853	4.399	.096
Small World Propensity	-0.145	8.703	.112	2.029	8.195	.128	-0.040	1.492	.092

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

**Table 3.17 | F statistics from moderation analyses, FDR corrected:
FPN efficiency (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 81)	2.551	.016	.201	0.014	.905	.000
IL-8 (<i>df</i> = 60)	1.646	.131	.180	0.312	.578	.004
IL-18 (<i>df</i> = 83)	2.224	.176	.034	0.035	.852	.000
MCP-1 (<i>df</i> = 53)	1.667	.128	.201	3.420	.070	.052
RANTES (<i>df</i> = 83)	2.582	.014	.199	0.100	.752	.001
ICAM-1 (<i>df</i> = 83)	2.812	.008	.213	3.857	.053	.037
VCAM-1 (<i>df</i> = 83)	2.667	.012	.204	2.606	.110	.025
MMP-3 (<i>df</i> = 83)	2.551	.016	.197	1.069	.304	.010
MMP-9 (<i>df</i> = 82)	2.689	.011	.208	0.000	.994	.000
α2-macroglobulin (<i>df</i> = 83)	2.929	.006	.220	4.043	.048	.038
β 2-microglobulin (<i>df</i> = 83)	2.267	.030	.179	0.021	.884	.000
Complement C3 (<i>df</i> = 81)	2.551	.016	.201	0.014	.905	.000
Factor VII (<i>df</i> = 83)	2.418	.021	.189	0.152	.698	.002
Ferritin (<i>df</i> = 83)	2.994	.005	.224	1.002	.320	.009
Fibrinogen (<i>df</i> = 83)	2.476	.018	.193	0.142	.707	.001
TIMP-1 (<i>df</i> = 83)	2.274	.030	.180	0.403	.527	.004
IBP 1 (<i>df</i> = 79)	2.313	.028	.190	0.363	.549	.004
IBP 2 (<i>df</i> = 79)	1.871	.076	.159	0.255	.615	.003
IBP 3 (<i>df</i> = 79)	1.981	.060	.167	0.062	.805	.001
IBP 4 (<i>df</i> = 79)	2.078	.048*	.174	0.672	.415	.007
IBP 5 (<i>df</i> = 79)	3.192	.003	.244	5.368	.023	.051
IBP 6 (<i>df</i> = 79)	2.034	.053	.171	0.148	.702	.002

*Indicates overall models that did not survive FDR correction; significant interactions are in bold

**Table 3.18 | F statistics from moderation analyses, FDR corrected:
FPN efficiency (IV), general intelligence (DV)**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Local Efficiency						
CRP (<i>df</i> = 82)	3.513	.002	.255	0.467	.496	.004
IL-8 (<i>df</i> = 61)	2.690	.013	.261	0.092	.763	.001
IL-18 (<i>df</i> = 84)	3.331	.002	.241	0.626	.431	.006
MCP-1 (<i>df</i> = 54)	1.586	.151	.190	0.012	.912	.000
RANTES (<i>df</i> = 84)	3.681	.001	.260	0.113	.738	.001
ICAM-1 (<i>df</i> = 84)	3.077	.004	.227	0.008	.928	.000
VCAM-1 (<i>df</i> = 84)	3.375	.002	.243	0.022	.883	.000
MMP-3 (<i>df</i> = 84)	3.206	.003	.234	0.896	.347	.008
MMP-9 (<i>df</i> = 83)	3.522	.002	.253	1.462	.230	.013
α2-macroglobulin (<i>df</i> = 84)	4.384	.000	.294	2.944	.029	.042
β 2-microglobulin (<i>df</i> = 84)	3.081	.004	.227	0.223	.638	.002
Complement C3 (<i>df</i> = 84)	4.145	.003	.532	1.066	.305	.009
Factor VII (<i>df</i> = 84)	3.070	.004	.226	0.012	.914	.000
Ferritin (<i>df</i> = 84)	3.750	.001	.263	0.537	.470	.005
Fibrinogen (<i>df</i> = 84)	3.520	.002	.251	1.637	.204	.015
TIMP-1 (<i>df</i> = 84)	3.266	.003	.237	0.175	.677	.002
IBP 1 (<i>df</i> = 80)	3.146	.004	.239	1.695	.197	.016
IBP 2 (<i>df</i> = 80)	2.928	.006	.226	0.039	.844	.000
IBP 3 (<i>df</i> = 80)	2.865	.008	.223	0.000	.994	.000
IBP 4 (<i>df</i> = 80)	3.080	.004	.236	0.172	.679	.002
IBP 5 (<i>df</i> = 80)	4.861	.000	.327	2.959	.089	.025
IBP 6 (<i>df</i> = 80)	2.882	.007	.224	0.256	.614	.002
Global Efficiency						
CRP (<i>df</i> = 81)	3.331	.002	.245	0.947	.333	.009
IL-8 (<i>df</i> = 61)	2.180	.042	.222	0.003	.954	.000
IL-18 (<i>df</i> = 84)	3.078	.004	.227	0.787	.378	.007
MCP-1 (<i>df</i> = 54)	1.994	.065	.228	3.028	.088	.043
RANTES (<i>df</i> = 84)	3.179	.003	.232	0.218	.642	.002
ICAM-1 (<i>df</i> = 84)	2.906	.006	.217	0.818	.368	.008
VCAM-1 (<i>df</i> = 84)	3.080	.004	.227	0.052	.820	.000
MMP-3 (<i>df</i> = 84)	2.938	.006	.219	0.929	.338	.009
MMP-9 (<i>df</i> = 83)	3.229	.003	.237	1.288	.260	.012
α2-macroglobulin (<i>df</i> = 84)	4.050	.000	.278	4.980	.028	.043
β 2-microglobulin (<i>df</i> = 84)	2.847	.008	.213	0.589	.445	.006
Complement C3 (<i>df</i> = 84)	3.831	.001	.267	1.259	.265	.011
Factor VII (<i>df</i> = 84)	2.813	.008	.211	0.156	.693	.002
Ferritin (<i>df</i> = 84)	3.325	.002	.240	0.187	.667	.002
Fibrinogen (<i>df</i> = 84)	3.004	.005	.222	0.472	.494	.004
TIMP-1 (<i>df</i> = 84)	2.914	.006	.217	0.000	.990	.000
IBP 1 (<i>df</i> = 80)	2.881	.007	.224	1.415	.238	.014
IBP 2 (<i>df</i> = 80)	2.759	.010	.216	0.656	.420	.006
IBP 3 (<i>df</i> = 80)	2.637	.013	.209	0.008	.928	.000
IBP 4 (<i>df</i> = 80)	2.834	.008	.221	0.024	.878	.000
IBP 5 (<i>df</i> = 80)	4.342	.000	.303	1.627	.206	.014
IBP 6 (<i>df</i> = 80)	2.640	.013	.209	0.075	.785	.001

**Table 3.18 (cont.) | F statistics from moderation analyses, FDR corrected:
FPN efficiency (IV), general intelligence (DV), continued**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 82)	3.216	.003	.239	0.528	.470	.005
IL-8 (<i>df</i> = 61)	2.407	.025	.240	1.627	.207	.020
IL-18 (<i>df</i> = 84)	2.973	.006	.221	0.010	.919	.000
MCP-1 (<i>df</i> = 54)	1.632	.137	.195	0.126	.724	.002
RANTES (<i>df</i> = 84)	3.043	.005	.225	0.214	.645	.002
ICAM-1 (<i>df</i> = 84)	3.185	.003	.233	2.782	.099	.025
VCAM-1 (<i>df</i> = 84)	3.124	.004	.229	0.616	.435	.006
MMP-3 (<i>df</i> = 84)	2.803	.008	.211	0.058	.811	.000
MMP-9 (<i>df</i> = 83)	3.017	.005	.225	0.049	.825	.000
α2-macroglobulin (<i>df</i> = 84)	3.919	.001	.272	4.710	.033	.041
β 2-microglobulin (<i>df</i> = 84)	2.893	.007	.216	0.976	.326	.009
Complement C3 (<i>df</i> = 84)	3.776	.001	.264	1.222	.272	.011
Factor VII (<i>df</i> = 84)	3.071	.004	.226	1.837	.179	.017
Ferritin (<i>df</i> = 84)	3.258	.003	.237	0.039	.844	.000
Fibrinogen (<i>df</i> = 84)	2.920	.006	.218	0.026	.874	.000
TIMP-1 (<i>df</i> = 84)	2.925	.006	.218	0.321	.573	.003
IBP 1 (<i>df</i> = 80)	2.773	.009	.217	0.519	.473	.005
IBP 2 (<i>df</i> = 80)	2.770	.009	.217	0.704	.404	.007
IBP 3 (<i>df</i> = 80)	2.806	.009	.219	0.936	.336	.009
IBP 4 (<i>df</i> = 80)	2.917	.007	.226	0.268	.606	.003
IBP 5 (<i>df</i> = 80)	4.960	.000	.332	6.405	.013	.054
IBP 6 (<i>df</i> = 80)	2.751	.010	.216	0.578	.449	.006

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.19 | F statistics from moderation analyses, FDR corrected:
LN efficiency (IV), fluid intelligence (DV)**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Local Efficiency						
CRP (<i>df</i> = 81)	2.779	.009	.215	0.574	.451	.006
IL-8 (<i>df</i> = 60)	2.251	.036	.231	0.022	.884	.000
IL-18 (<i>df</i> = 83)	2.472	.019	.192	1.117	.294	.011
MCP-1 (<i>df</i> = 53)	1.188	.324	.152	0.028	.868	.000
RANTES (<i>df</i> = 83)	2.697	.011	.206	0.056	.813	.000
ICAM-1 (<i>df</i> = 83)	2.879	.007	.217	3.778	.055	.036
VCAM-1 (<i>df</i> = 83)	2.489	.018	.194	0.742	.392	.007
MMP-3 (<i>df</i> = 83)	2.509	.017	.195	0.372	.544	.004
MMP-9 (<i>df</i> = 82)	2.836	.008	.217	0.233	.631	.002
α 2-macroglobulin (<i>df</i> = 83)	2.616	.013	.201	1.460	.230	.014
β 2-microglobulin (<i>df</i> = 83)	2.375	.024	.186	0.144	.706	.001
Complement C3 (<i>df</i> = 83)	2.943	.006	.221	0.019	.891	.000
Factor VII (<i>df</i> = 83)	2.812	.008	.213	2.244	.138	.021
Ferritin (<i>df</i> = 83)	3.082	.004	.229	1.013	.317	.009
Fibrinogen (<i>df</i> = 83)	2.523	.016	.196	0.056	.813	.000
TIMP-1 (<i>df</i> = 83)	2.306	.028	.182	0.077	.782	.001
IBP 1 (<i>df</i> = 79)	2.728	.010	.216	2.599	.111	.026
IBP 2 (<i>df</i> = 79)	2.005	.056	.169	0.644	.425	.007
IBP 3 (<i>df</i> = 79)	2.860	.008	.225	5.686	.020	.056
IBP 4 (<i>df</i> = 79)	2.062	.050	.173	0.194	.660	.002
IBP 5 (<i>df</i> = 79)	2.471	.019	.200	0.275	.602	.003
IBP 6 (<i>df</i> = 79)	2.639	.013	.211	3.886	.052	.039
Global Efficiency						
CRP (<i>df</i> = 81)	2.620	.013	.206	0.271	.604	.003
IL-8 (<i>df</i> = 60)	1.781	.099	.192	0.248	.620	.003
IL-18 (<i>df</i> = 83)	2.303	.028	.182	0.584	.447	.006
MCP-1 (<i>df</i> = 53)	1.281	.274	.162	0.286	.595	.004
RANTES (<i>df</i> = 83)	2.575	.015	.199	0.014	.905	.000
ICAM-1 (<i>df</i> = 83)	3.202	.003	.236	6.452	.013	.059
VCAM-1 (<i>df</i> = 83)	2.306	.028	.182	0.262	.610	.003
MMP-3 (<i>df</i> = 83)	2.390	.023	.187	0.099	.754	.001
MMP-9 (<i>df</i> = 82)	2.789	.009	.214	0.517	.474	.005
α 2-macroglobulin (<i>df</i> = 83)	2.400	.022	.188	0.578	.449	.006
β 2-microglobulin (<i>df</i> = 83)	2.476	.018	.193	1.426	.236	.014
Complement C3 (<i>df</i> = 83)	2.947	.006	.221	0.628	.430	.006
Factor VII (<i>df</i> = 83)	2.540	.016	.197	1.023	.315	.010
Ferritin (<i>df</i> = 83)	3.014	.005	.225	1.168	.283	.011
Fibrinogen (<i>df</i> = 83)	2.485	.018	.193	0.234	.630	.002
TIMP-1 (<i>df</i> = 83)	2.350	.025	.185	0.941	.335	.009
IBP 1 (<i>df</i> = 79)	2.296	.029	.189	0.299	.586	.003
IBP 2 (<i>df</i> = 79)	1.857	.079	.158	0.200	.656	.002
IBP 3 (<i>df</i> = 79)	2.790	.009	.220	5.561	.021	.055
IBP 4 (<i>df</i> = 79)	1.987	.059	.168	0.124	.726	.001
IBP 5 (<i>df</i> = 79)	2.372	.024	.194	0.078	.780	.001
IBP 6 (<i>df</i> = 79)	2.357	.025	.193	2.344	.130	.024

**Table 3.19 (cont.) | F statistics from moderation analyses, FDR corrected:
LN efficiency (IV), fluid intelligence (DV) continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 81)	2.862	.007	.220	0.182	.671	.002
IL-8 (<i>df</i> = 60)	1.931	.072	.205	0.008	.931	.000
IL-18 (<i>df</i> = 83)	2.425	.021	.190	0.299	.586	.003
MCP-1 (<i>df</i> = 53)	1.616	.142	.196	3.027	.088	.046
RANTES (<i>df</i> = 83)	3.468	.002	.250	4.964	.029	.045
ICAM-1 (<i>df</i> = 83)	2.446	.020	.191	0.321	.572	.003
VCAM-1 (<i>df</i> = 83)	2.575	.015	.199	0.885	.350	.008
MMP-3 (<i>df</i> = 83)	2.731	.010	.208	1.297	.258	.012
MMP-9 (<i>df</i> = 82)	2.939	.006	.223	0.112	.739	.001
α 2-macroglobulin (<i>df</i> = 83)	2.469	.019	.192	0.054	.816	.000
β 2-microglobulin (<i>df</i> = 83)	2.542	.016	.197	0.628	.430	.006
Complement C3 (<i>df</i> = 83)	3.109	.004	.231	0.019	.890	.000
Factor VII (<i>df</i> = 83)	2.751	.010	.210	1.051	.308	.010
Ferritin (<i>df</i> = 83)	3.064	.004	.228	0.106	.745	.001
Fibrinogen (<i>df</i> = 83)	2.727	.010	.208	0.378	.540	.004
TIMP-1 (<i>df</i> = 83)	2.482	.018	.193	0.658	.420	.006
IBP 1 (<i>df</i> = 79)	2.515	.017	.203	0.753	.388	.008
IBP 2 (<i>df</i> = 79)	2.383	.024	.194	3.071	.084	.031
IBP 3 (<i>df</i> = 79)	2.181	.038	.181	0.774	.382	.008
IBP 4 (<i>df</i> = 79)	2.115	.044*	.176	0.077	.782	.001
IBP 5 (<i>df</i> = 79)	2.632	.013	.210	1.095	.299	.011
IBP 6 (<i>df</i> = 79)	2.128	.043*	.177	0.000	.996	.000

*Indicates overall models that did not survive FDR correction; significant interactions are in bold.

**Table 3.20 | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Global Efficiency						
CRP (<i>df</i> = 81)	2.777	.009	.215	0.028	.866	.000
IL-8 (<i>df</i> = 60)	1.673	.124	.182	0.733	.394	.010
IL-18 (<i>df</i> = 83)	3.107	.004	.230	4.923	.029	.046
MCP-1 (<i>df</i> = 53)	1.773	.103	.211	4.224	.045	.063
RANTES (<i>df</i> = 83)	2.744	.010	.209	0.313	.578	.003
ICAM-1 (<i>df</i> = 83)	2.383	.023	.187	0.096	.757	.001
VCAM-1 (<i>df</i> = 83)	2.445	.020	.191	0.021	.884	.000
MMP-3 (<i>df</i> = 83)	2.628	.013	.202	0.331	.566	.003
MMP-9 (<i>df</i> = 82)	3.098	.004	.232	1.450	.232	.014
α 2-macroglobulin (<i>df</i> = 83)	2.530	.016	.196	0.697	.406	.007
β 2-microglobulin (<i>df</i> = 83)	2.533	.016	.196	0.640	.426	.006
Complement C3 (<i>df</i> = 83)	2.976	.006	.223	0.203	.653	.002
Factor VII (<i>df</i> = 83)	2.512	.017	.195	0.087	.769	.001
Ferritin (<i>df</i> = 83)	2.969	.006	.222	0.130	.719	.001
Fibrinogen (<i>df</i> = 83)	2.586	.014	.200	0.232	.631	.002
TIMP-1 (<i>df</i> = 83)	2.396	.022	.188	0.250	.619	.002
IBP 1 (<i>df</i> = 79)	2.754	.010	.218	0.631	.430	.006
IBP 2 (<i>df</i> = 79)	2.147	.041	.179	0.229	.633	.002
IBP 3 (<i>df</i> = 79)	2.984	.006	.232	4.725	.033	.046
IBP 4 (<i>df</i> = 79)	2.365	.024	.193	0.825	.367	.008
IBP 5 (<i>df</i> = 79)	2.692	.011	.214	0.155	.695	.002
IBP 6 (<i>df</i> = 79)	2.566	.015	.206	1.356	.248	.014

All significant overall models remained significant after FDR correction; significant interactions are in bold.

**Table 3.21 | F statistics from moderation analyses, FDR corrected:
DAN efficiency (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Global Efficiency</u>						
CRP (<i>df</i> = 81)	2.767	.009	.215	0.009	.925	.000
IL-8 (<i>df</i> = 60)	1.955	.068	.207	1.629	.207	.022
IL-18 (<i>df</i> = 83)	2.941	.006	.221	4.219	.043	.040
MCP-1 (<i>df</i> = 53)	1.318	.255	.166	0.987	.325	.016
RANTES (<i>df</i> = 83)	2.767	.009	.210	1.060	.306	.010
ICAM-1 (<i>df</i> = 83)	2.662	.012	.204	2.415	.124	.023
VCAM-1 (<i>df</i> = 83)	3.055	.005	.228	4.487	.037	.042
MMP-3 (<i>df</i> = 83)	2.701	.011	.206	1.576	.213	.015
MMP-9 (<i>df</i> = 82)	2.849	.008	.218	0.895	.347	.008
α 2-macroglobulin (<i>df</i> = 83)	2.379	.023	.186	0.045	.833	.000
β 2-microglobulin (<i>df</i> = 83)	2.376	.024	.186	0.042	.837	.000
Complement C3 (<i>df</i> = 83)	3.034	.005	.226	0.981	.325	.009
Factor VII (<i>df</i> = 83)	2.807	.008	.213	2.342	.130	.022
Ferritin (<i>df</i> = 83)	2.902	.007	.219	0.015	.902	.000
Fibrinogen (<i>df</i> = 83)	2.551	.016	.197	0.240	.626	.002
TIMP-1 (<i>df</i> = 83)	2.610	.013	.201	2.068	.154	.020
IBP 1 (<i>df</i> = 79)	2.383	.024	.194	0.025	.876	.000
IBP 2 (<i>df</i> = 79)	1.935	.066	.164	0.199	.646	.002
IBP 3 (<i>df</i> = 79)	2.044	.052	.172	0.024	.878	.000
IBP 4 (<i>df</i> = 79)	2.107	.045*	.176	0.330	.567	.003
IBP 5 (<i>df</i> = 79)	2.483	.019	.201	0.574	.451	.006
IBP 6 (<i>df</i> = 79)	2.100	.045*	.175	0.000	.999	.000
<u>Small World Propensity</u>						
CRP (<i>df</i> = 81)	2.566	.015	.202	0.101	.751	.001
IL-8 (<i>df</i> = 60)	1.656	.128	.181	0.326	.570	.004
IL-18 (<i>df</i> = 83)	2.858	.007	.216	4.249	.042	.040
MCP-1 (<i>df</i> = 53)	1.444	.200	.179	0.510	.478	.008
RANTES (<i>df</i> = 83)	2.640	.012	.203	0.497	.483	.005
ICAM-1 (<i>df</i> = 83)	2.225	.033	.177	0.014	.907	.000
VCAM-1 (<i>df</i> = 83)	2.464	.019	.192	1.348	.249	.013
MMP-3 (<i>df</i> = 83)	2.392	.023	.187	0.115	.736	.001
MMP-9 (<i>df</i> = 82)	2.918	.006	.222	1.316	.255	.012
α 2-macroglobulin (<i>df</i> = 83)	2.317	.027	.185	0.013	.910	.000
β 2-microglobulin (<i>df</i> = 83)	2.263	.031	.179	0.056	.814	.000
Complement C3 (<i>df</i> = 83)	2.956	.006	.222	0.732	.395	.007
Factor VII (<i>df</i> = 83)	2.408	.022	.188	0.164	.686	.002
Ferritin (<i>df</i> = 83)	4.009	.000	.279	7.433	.008	.065
Fibrinogen (<i>df</i> = 83)	2.539	.016	.197	0.558	.457	.005
TIMP-1 (<i>df</i> = 83)	2.576	.015	.199	2.439	.122	.024
IBP 1 (<i>df</i> = 79)	2.250	.032	.186	0.179	.673	.002
IBP 2 (<i>df</i> = 79)	1.859	.078	.158	0.133	.716	.001
IBP 3 (<i>df</i> = 79)	1.962	.062	.166	0.017	.896	.000
IBP 4 (<i>df</i> = 79)	2.029	.053	.170	0.413	.522	.004
IBP 5 (<i>df</i> = 79)	2.396	.023	.195	0.007	.932	.000
IBP 6 (<i>df</i> = 79)	2.092	.046*	.175	0.567	.454	.006

*Indicates overall models that did not survive FDR correction; significant interactions are in bold

**Table 3.22 | F statistics from moderation analyses, FDR corrected:
DAN efficiency (IV), general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Global Efficiency</u>						
CRP (<i>df</i> = 82)	3.812	.001	.271	0.067	.797	.001
IL-8 (<i>df</i> = 61)	2.639	.015	.257	1.980	.164	.024
IL-18 (<i>df</i> = 84)	4.260	.000	.289	5.412	.022	.046
MCP-1 (<i>df</i> = 56)	1.934	.074	.223	0.005	.944	.000
RANTES (<i>df</i> = 84)	3.389	.002	.244	0.380	.540	.003
ICAM-1 (<i>df</i> = 84)	3.472	.002	.248	2.056	.155	.018
VCAM-1 (<i>df</i> = 84)	4.409	.000	.296	6.164	.015	.052
MMP-3 (<i>df</i> = 84)	3.189	.003	.233	0.012	.912	.000
MMP-9 (<i>df</i> = 83)	3.275	.003	.240	0.016	.901	.000
α 2-macroglobulin (<i>df</i> = 84)	3.608	.001	.256	0.555	.458	.005
β 2-microglobulin (<i>df</i> = 84)	3.259	.003	.237	0.663	.418	.006
Complement C3 (<i>df</i> = 84)	3.913	.001	.272	0.002	.963	.000
Factor VII (<i>df</i> = 84)	4.394	.000	.295	7.574	.007	.064
Ferritin (<i>df</i> = 84)	3.860	.001	.269	1.215	.273	.011
Fibrinogen (<i>df</i> = 84)	3.302	.002	.239	0.118	.732	.001
TIMP-1 (<i>df</i> = 84)	3.480	.002	.249	1.509	.223	.014
IBP 1 (<i>df</i> = 80)	3.292	.003	.248	1.484	.227	.014
IBP 2 (<i>df</i> = 80)	2.997	.005	.231	0.012	.912	.000
IBP 3 (<i>df</i> = 80)	3.037	.005	.233	0.191	.663	.002
IBP 4 (<i>df</i> = 80)	3.221	.003	.244	0.009	.926	.000
IBP 5 (<i>df</i> = 80)	4.154	.000	.294	0.218	.642	.002
IBP 6 (<i>df</i> = 80)	3.215	.003	.243	1.311	.256	.012
<u>Small World Propensity</u>						
CRP (<i>df</i> = 82)	3.422	.002	.250	0.070	.792	.001
IL-8 (<i>df</i> = 61)	2.049	.055	.212	0.126	.724	.002
IL-18 (<i>df</i> = 84)	4.250	.000	.288	6.374	.014	.054
MCP-1 (<i>df</i> = 56)	1.571	.155	.189	0.042	.839	.001
RANTES (<i>df</i> = 84)	3.327	.002	.241	0.209	.648	.002
ICAM-1 (<i>df</i> = 84)	3.102	.004	.228	0.440	.509	.004
VCAM-1 (<i>df</i> = 84)	3.512	.002	.251	1.460	.230	.013
MMP-3 (<i>df</i> = 84)	3.141	.004	.230	0.343	.560	.003
MMP-9 (<i>df</i> = 83)	3.191	.003	.235	0.057	.813	.000
α 2-macroglobulin (<i>df</i> = 84)	3.388	.002	.244	0.011	.917	.000
β 2-microglobulin (<i>df</i> = 84)	3.214	.003	.234	1.236	.269	.011
Complement C3 (<i>df</i> = 84)	4.059	.000	.279	0.050	.823	.000
Factor VII (<i>df</i> = 84)	3.194	.003	.233	0.772	.381	.007
Ferritin (<i>df</i> = 84)	4.661	.000	.307	6.191	.015	.051
Fibrinogen (<i>df</i> = 84)	3.353	.002	.242	0.350	.556	.003
TIMP-1 (<i>df</i> = 84)	3.567	.001	.254	2.500	.118	.022
IBP 1 (<i>df</i> = 80)	3.081	.004	.236	1.311	.256	.012
IBP 2 (<i>df</i> = 80)	2.925	.006	.226	0.638	.427	.006
IBP 3 (<i>df</i> = 80)	2.827	.008	.220	0.082	.775	.001
IBP 4 (<i>df</i> = 80)	3.201	.003	.242	0.249	.619	.002
IBP 5 (<i>df</i> = 80)	4.022	.000	.287	0.053	.818	.000
IBP 6 (<i>df</i> = 80)	3.126	.004	.238	1.952	.166	.019

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.23 | F statistics from moderation analyses, FDR corrected:
VAN efficiency (IV), fluid intelligence (DV)**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Local Efficiency						
CRP (<i>df</i> = 81)	2.944	.006	.225	0.137	.713	.001
IL-8 (<i>df</i> = 60)	1.710	.115	.186	0.065	.800	.001
IL-18 (<i>df</i> = 83)	3.206	.003	.236	3.379	.070	.031
MCP-1 (<i>df</i> = 53)	1.291	.268	.163	0.594	.444	.009
RANTES (<i>df</i> = 83)	2.912	.006	.219	0.000	.990	.000
ICAM-1 (<i>df</i> = 83)	3.835	.001	.270	7.270	.008	.064
VCAM-1 (<i>df</i> = 83)	3.345	.002	.244	4.086	.046	.037
MMP-3 (<i>df</i> = 83)	3.361	.002	.245	3.051	.084	.028
MMP-9 (<i>df</i> = 82)	3.246	.003	.240	0.873	.353	.008
α2-macroglobulin (<i>df</i> = 83)	4.419	.000	.299	10.633	.002	.090
β 2-microglobulin (<i>df</i> = 83)	2.878	.007	.217	1.038	.311	.010
Complement C3 (<i>df</i> = 83)	3.778	.001	.267	3.698	.058	.033
Factor VII (<i>df</i> = 83)	3.002	.005	.224	0.916	.341	.009
Ferritin (<i>df</i> = 83)	3.813	.001	.269	3.448	.067	.030
Fibrinogen (<i>df</i> = 83)	2.858	.007	.216	0.006	.936	.000
TIMP-1 (<i>df</i> = 83)	3.271	.003	.240	3.804	.054	.035
IBP 1 (<i>df</i> = 79)	3.039	.005	.235	2.198	.142	.021
IBP 2 (<i>df</i> = 79)	2.483	.019	.201	1.213	.274	.012
IBP 3 (<i>df</i> = 79)	2.473	.019	.200	0.058	.810	.001
IBP 4 (<i>df</i> = 79)	2.644	.013	.211	1.064	.306	.011
IBP 5 (<i>df</i> = 79)	4.272	.000	.302	9.356	.003	.083
IBP 6 (<i>df</i> = 79)	2.785	.009	.220	2.019	.159	.020
Global Efficiency						
CRP (<i>df</i> = 81)	2.778	.009	.215	0.495	.484	.005
IL-8 (<i>df</i> = 60)	1.642	.132	.180	0.099	.754	.001
IL-18 (<i>df</i> = 83)	2.519	.017	.195	0.348	.557	.003
MCP-1 (<i>df</i> = 53)	1.154	.344	.148	0.049	.825	.001
RANTES (<i>df</i> = 83)	2.943	.006	.221	1.185	.280	.011
ICAM-1 (<i>df</i> = 83)	2.730	.010	.208	1.650	.202	.016
VCAM-1 (<i>df</i> = 83)	2.672	.012	.205	1.071	.304	.010
MMP-3 (<i>df</i> = 83)	2.972	.006	.223	2.142	.147	.020
MMP-9 (<i>df</i> = 82)	3.023	.005	.228	0.451	.504	.004
α2-macroglobulin (<i>df</i> = 83)	3.770	.001	.266	7.876	.006	.070
β 2-microglobulin (<i>df</i> = 83)	2.498	.018	.194	0.001	.980	.000
Complement C3 (<i>df</i> = 83)	3.727	.001	.264	4.188	.044	.037
Factor VII (<i>df</i> = 83)	2.640	.012	.203	0.099	.754	.001
Ferritin (<i>df</i> = 83)	3.646	.001	.260	3.599	.061	.032
Fibrinogen (<i>df</i> = 83)	2.770	.009	.211	0.328	.568	.003
TIMP-1 (<i>df</i> = 83)	2.506	.017	.195	0.280	.598	.003
IBP 1 (<i>df</i> = 79)	2.547	.016	.205	0.299	.586	.003
IBP 2 (<i>df</i> = 79)	3.039	.005	.235	6.128	.015	.059
IBP 3 (<i>df</i> = 79)	2.250	.032	.186	0.059	.809	.001
IBP 4 (<i>df</i> = 79)	2.565	.015	.206	1.483	.227	.015
IBP 5 (<i>df</i> = 79)	3.081	.004	.238	3.279	.074	.032
IBP 6 (<i>df</i> = 79)	2.326	.027	.191	0.424	.517	.004

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.24 | F statistics from moderation analyses, FDR corrected:
VAN efficiency (IV), general intelligence (DV)**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Local Efficiency						
CRP (<i>df</i> = 82)	3.649	.001	.262	0.010	.920	.000
IL-8 (<i>df</i> = 61)	2.172	.042	.222	0.010	.921	.000
IL-18 (<i>df</i> = 84)	3.856	.001	.269	1.707	.195	.015
MCP-1 (<i>df</i> = 54)	1.910	.077	.221	0.939	.337	.014
RANTES (<i>df</i> = 84)	3.621	.001	.256	0.610	.437	.005
ICAM-1 (<i>df</i> = 84)	4.034	.000	.278	3.960	.050	.034
VCAM-1 (<i>df</i> = 84)	4.171	.000	.284	2.412	.124	.020
MMP-3 (<i>df</i> = 84)	4.222	.000	.287	4.776	.032	.041
MMP-9 (<i>df</i> = 83)	3.912	.001	.274	1.899	.172	.017
α2-macroglobulin (<i>df</i> = 84)	4.909	.000	.319	6.751	.011	.055
β 2-microglobulin (<i>df</i> = 84)	3.408	.002	.245	0.315	.576	.003
Complement C3 (<i>df</i> = 84)	4.276	.000	.289	1.134	.290	.010
Factor VII (<i>df</i> = 84)	3.762	.001	.264	2.171	.144	.019
Ferritin (<i>df</i> = 84)	4.174	.000	.284	2.019	.159	.017
Fibrinogen (<i>df</i> = 84)	3.484	.002	.249	0.000	.988	.000
TIMP-1 (<i>df</i> = 84)	3.608	.001	.256	0.881	.351	.008
IBP 1 (<i>df</i> = 80)	3.663	.001	.268	2.314	.132	.021
IBP 2 (<i>df</i> = 80)	3.538	.002	.261	1.633	.205	.015
IBP 3 (<i>df</i> = 80)	3.281	.003	.247	0.000	.992	.000
IBP 4 (<i>df</i> = 80)	3.594	.001	.264	0.523	.472	.005
IBP 5 (<i>df</i> = 80)	5.172	.000	.341	4.199	.044	.035
IBP 6 (<i>df</i> = 80)	3.866	.001	.279	3.409	.068	.031
Global Efficiency						
CRP (<i>df</i> = 82)	3.676	.001	.264	0.312	.578	.003
IL-8 (<i>df</i> = 61)	2.214	.038	.225	0.041	.841	.000
IL-18 (<i>df</i> = 84)	3.728	.001	.262	0.581	.448	.005
MCP-1 (<i>df</i> = 54)	2.332	.031	.257	3.423	.070	.047
RANTES (<i>df</i> = 84)	3.992	.000	.275	2.591	.111	.022
ICAM-1 (<i>df</i> = 84)	3.483	.002	.249	0.667	.416	.006
VCAM-1 (<i>df</i> = 84)	3.806	.001	.266	0.363	.548	.003
MMP-3 (<i>df</i> = 84)	4.113	.000	.282	4.189	.044	.036
MMP-9 (<i>df</i> = 83)	3.820	.001	.269	0.844	.361	.007
α2-macroglobulin (<i>df</i> = 84)	4.730	.000	.311	5.659	.020	.046
β 2-microglobulin (<i>df</i> = 84)	3.418	.002	.246	0.313	.577	.003
Complement C3 (<i>df</i> = 84)	4.242	.000	.288	0.262	.610	.002
Factor VII (<i>df</i> = 84)	3.438	.002	.247	0.273	.602	.003
Ferritin (<i>df</i> = 84)	4.038	.000	.278	1.047	.309	.009
Fibrinogen (<i>df</i> = 84)	3.762	.001	.264	1.165	.284	.010
TIMP-1 (<i>df</i> = 84)	3.543	.001	.252	0.285	.595	.002
IBP 1 (<i>df</i> = 80)	3.362	.002	.252	0.098	.756	.001
IBP 2 (<i>df</i> = 80)	4.225	.000	.297	5.355	.023	.047
IBP 3 (<i>df</i> = 80)	3.372	.002	.252	0.054	.818	.000
IBP 4 (<i>df</i> = 80)	3.679	.001	.269	0.010	.921	.000
IBP 5 (<i>df</i> = 80)	4.790	.000	.324	2.176	.144	.018
IBP 6 (<i>df</i> = 80)	3.562	.001	.263	1.057	.307	.010

All significant overall models remained significant after FDR correction; significant interactions are in bold

Table 3.25 | Demographic data

Age, $n(\bar{x} \pm SD)$; years	115(68.9 $\pm$ 2.98)
Sex, $n(\%F)$	115(62.6)
Body Mass Index (BMI), $n(\bar{x} \pm SD)$	115(25.9 $\pm$ 3.8)
Income, n (%)	
<15k	5(4.3)
15-25k	21(3.0)
25-50k	15(18.3)
50-75k	25(21.7)
75-100k	28(24.3)
>100k	36(31.3)
Education, n (%)	
High school degree	11(9.6)
Some college	22(19.1)
College degree	82(71.3)
Facets of Intelligence, $n(\bar{x} \pm SD)$	
Fluid Intelligence	108(113.9 $\pm$ 11.3)
General Intelligence	109(117.1 $\pm$ 11.1)
White Matter Integrity, $n(\bar{x} \pm SD)$	
Global White Matter Ax/D	115(1.266 $\times 10^{-3} \pm 4.325 \times 10^{-5}$)
Global White Matter RD	115(7.017 $\times 10^{-4} \pm 5.109 \times 10^{-5}$)
Global White Matter FA	115(6.074 $\times 10^{-1} \pm 2.451 \times 10^{-2}$)
Corpus Callosum (Genu) Ax/D	115(1.501 $\times 10^{-3} \pm 6.190 \times 10^{-5}$)
Corpus Callosum (Genu) RD	115(5.691 $\times 10^{-4} \pm 8.457 \times 10^{-5}$)
Corpus Callosum (Genu) FA	115(7.281 $\times 10^{-1} \pm 4.708 \times 10^{-2}$)
Inflammation Biomarkers, $n(\bar{x} \pm SD)$; mg/mL	
$\alpha 2$ -Macroglobulin	115(1.933 $\pm$ 0.542)
C-Reactive Protein (CRP)	113(3.954 $\times 10^{-3} \pm 8.151 \times 10^{-3}$)
Complement C3	115(1.038 $\pm$ 0.265)
Factor VII	115(5.576 $\times 10^{-4} \pm 2.089 \times 10^{-4}$)
Ferritin	115(1.628 $\times 10^{-4} \pm 1.618 \times 10^{-4}$)
Intercellular Adhesion Molecule-1 (ICAM-1)	115(1.304 $\times 10^{-4} \pm 4.100 \times 10^{-5}$)
Interleukin-8 (IL-8)	86(9.983 $\times 10^{-9} \pm 3.848 \times 10^{-9}$)
Interleukin-18 (IL-18)	115(2.397 $\times 10^{-7} \pm 1.381 \times 10^{-7}$)
Matrix Metalloproteinase-3 (MMP-3)	115(8.118 $\times 10^{-6} \pm 5.656 \times 10^{-6}$)
T-cell Specific Protein (RANTES)	115(1.612 $\times 10^{-5} \pm 1.324 \times 10^{-5}$)
Vascular Cell Adhesion Molecule-1 (VCAM-1)	115(8.431 $\times 10^{-7} \pm 2.480 \times 10^{-7}$)
IBP 1	110(-1.778 $\times 10^{-2} \pm 9.971 \times 10^{-1}$)
IBP 2	110(3.770 $\times 10^{-2} \pm 1.007$)
IBP 3	110(-8.152 $\times 10^{-3} \pm 9.883 \times 10^{-1}$)
IBP 4	110(-2.321 $\times 10^{-2} \pm 1.008$)
IBP 5	110(1.428 $\times 10^{-4} \pm 9.909 \times 10^{-1}$)
IBP 6	110(1.774 $\times 10^{-2} \pm 1.021$)

Table 3.26 | Linear Regression models of white matter tract characteristics associated with facets of intelligence

	<u>Fluid Intelligence</u>			<u>General Intelligence</u>		
	β	βSE	R^2	β	βSE	R^2
<u>Global White Matter</u>						
Axial Diffusion	-3.539 x10 ³	2.513 x10 ⁴	.168*	-2.977x10 ⁴	2.310 x10 ⁴	.237**
Radial Diffusion	-4.016 x10 ⁴	2.014 x10 ⁴	.200*	-3.685 x10 ⁴	1.868 x10 ⁴	.253**
Fractional Anisotropy	8.468 x10 ¹	4.167 x10 ¹	.201*	6.652 x10 ¹	3.885 x10 ¹	.246**
<u>Genu of the Corpus Callosum</u>						
Axial Diffusion	1.387 x10 ³	1.730 x10 ⁴	.168*	-1.916 x10 ⁴	1.592 x10 ⁴	.236**
Radial Diffusion	-1.629 x10 ⁴	1.223 x10 ⁴	.182*	-1.386 x10 ⁴	1.135 x10 ⁴	.236**
Fractional Anisotropy	2.618 x10 ¹	2.200 x10 ¹	.180*	1.573 x10 ¹	2.048 x10 ¹	.229**

^x $p < 0.05$, * $p < 0.01$, ** $p < 0.001$

**Table 3.27 | F statistics from moderation analyses, FDR corrected:
global white matter (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Axial Diffusion</u>						
CRP (<i>df</i> = 97)	2.317	.026	.160	1.072	.303	.009
IL-8 (<i>df</i> = 73)	1.334	.241	.128	0.029	.865	.000
IL-18 (<i>df</i> = 99)	1.940	.062	.136	0.062	.804	.000
RANTES (<i>df</i> = 99)	2.543	.015	.170	0.355	.553	.003
ICAM-1 (<i>df</i> = 99)	2.402	.021	.162	1.186	.279	.010
VCAM-1 (<i>df</i> = 99)	2.356	.023	.160	2.461	.120	.021
MMP-3 (<i>df</i> = 99)	2.351	.023	.160	1.027	.313	.009
α2-macroglobulin (<i>df</i> = 99)	3.020	.004	.196	5.289	.024	.043
Complement C3 (<i>df</i> = 99)	2.700	.010	.179	0.003	.955	.000
Factor VII (<i>df</i> = 99)	3.335	.002	.212	7.436	.008	.059
Ferritin (<i>df</i> = 99)	4.033	.000	.246	7.598	.007	.058
IBP 1 (<i>df</i> = 94)	2.224	.032	.159	0.034	.854	.000
IBP 2 (<i>df</i> = 94)	2.057	.048*	.149	2.026	.158	.018
IBP 3 (<i>df</i> = 94)	3.058	.004	.206	6.590	.012	.056
IBP 4 (<i>df</i> = 94)	2.845	.007	.195	4.075	.046	.035
IBP 5 (<i>df</i> = 94)	3.115	.004	.210	4.447	.038	.037
IBP 6 (<i>df</i> = 94)	2.176	.036	.156	0.578	.449	.005
<u>Fractional Anisotropy</u>						
CRP (<i>df</i> = 97)	2.713	.010	.183	0.464	.497	.004
IL-8 (<i>df</i> = 73)	1.664	.122	.154	0.100	.753	.001
IL-18 (<i>df</i> = 99)	3.024	.004	.196	3.984	.049	.032
RANTES (<i>df</i> = 99)	2.999	.005	.195	1.240	.268	.010
ICAM-1 (<i>df</i> = 99)	2.933	.006	.192	0.021	.886	.000
VCAM-1 (<i>df</i> = 99)	2.648	.011	.176	0.770	.382	.006
MMP-3 (<i>df</i> = 99)	2.909	.006	.190	0.378	.540	.003
α 2-macroglobulin (<i>df</i> = 99)	2.686	.010	.178	0.021	.886	.000
Complement C3 (<i>df</i> = 99)	3.431	.002	.217	1.823	.180	.014
Factor VII (<i>df</i> = 99)	3.032	.004	.197	1.321	.253	.011
Ferritin (<i>df</i> = 99)	3.644	.001	.228	0.131	.718	.001
IBP 1 (<i>df</i> = 94)	2.973	.005	.202	1.501	.224	.013
IBP 2 (<i>df</i> = 94)	2.194	.035	.157	0.422	.518	.004
IBP 3 (<i>df</i> = 94)	2.644	.012	.184	0.192	.663	.002
IBP 4 (<i>df</i> = 94)	2.998	.005	.203	2.184	.143	.018
IBP 5 (<i>df</i> = 94)	2.920	.006	.199	0.497	.482	.004
IBP 6 (<i>df</i> = 94)	2.787	.008	.192	0.886	.349	.008

*Indicates overall models that did not survive FDR correction; significant interactions are in bold

**Table 3.28 | F statistics from moderation analyses, FDR corrected:
global white matter (IV), general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Axial Diffusion</u>						
CRP (<i>df</i> = 98)	4.601	.000	.273	2.682	.105	.020
IL-8 (<i>df</i> = 74)	3.182	.004	.256	0.249	.619	.002
IL-18 (<i>df</i> = 100)	4.310	.000	.256	0.409	.524	.003
RANTES (<i>df</i> = 100)	4.408	.000	.261	0.872	.352	.006
ICAM-1 (<i>df</i> = 100)	4.638	.000	.271	3.953	.050	.029
VCAM-1 (<i>df</i> = 100)	4.846	.000	.279	3.430	.067	.025
MMP-3 (<i>df</i> = 100)	4.485	.000	.264	2.382	.126	.018
α 2-macroglobulin (<i>df</i> = 100)	4.797	.000	.277	1.576	.212	.011
Complement C3 (<i>df</i> = 100)	4.654	.000	.271	0.335	.564	.002
Factor VII (<i>df</i> = 100)	4.798	.000	.277	4.522	.036	.033
Ferritin (<i>df</i> = 100)	4.562	.000	.267	2.329	.130	.017
IBP 1 (<i>df</i> = 95)	4.064	.000	.255	0.928	0.338	.007
IBP 2 (<i>df</i> = 95)	3.937	.000	.249	0.359	.550	.003
IBP 3 (<i>df</i> = 95)	4.844	.000	.290	5.968	.016	.045
IBP 4 (<i>df</i> = 95)	4.177	.000	.260	0.030	.864	.000
IBP 5 (<i>df</i> = 95)	5.173	.000	.304	1.331	.252	.010
IBP 6 (<i>df</i> = 95)	3.953	.000	.250	0.476	.492	.004

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table 3.29 | F statistics from moderation analyses, FDR corrected:
genu of the corpus callosum (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fractional Anisotropy</u>						
CRP (<i>df</i> = 97)	2.357	0.023	.163	0.349	.556	.003
IL-8 (<i>df</i> = 73)	1.463	.186	.138	0.002	.965	.000
IL-18 (<i>df</i> = 99)	2.676	.010	.178	4.080	.046	.034
RANTES (<i>df</i> = 99)	2.807	.008	.185	1.378	.243	.011
ICAM-1 (<i>df</i> = 99)	2.459	.018	.166	0.000	.983	.000
VCAM-1 (<i>df</i> = 99)	2.482	.017	.167	2.145	.146	.018
MMP-3 (<i>df</i> = 99)	2.575	.014	.172	1.317	.254	.011
α 2-macroglobulin (<i>df</i> = 99)	2.422	.020	.164	0.386	.536	.003
Complement C3 (<i>df</i> = 99)	3.007	.005	.196	1.351	.248	.011
Factor VII (<i>df</i> = 99)	2.636	.012	.176	1.321	.253	.011
Ferritin (<i>df</i> = 99)	3.188	.003	.205	0.133	.716	.001
IBP 1 (<i>df</i> = 94)	2.641	.012	.184	1.864	.175	.016
IBP 2 (<i>df</i> = 94)	1.906	.068	.140	0.401	.528	.004
IBP 3 (<i>df</i> = 94)	2.262	.029	.161	0.263	.609	.002
IBP 4 (<i>df</i> = 94)	2.383	.022	.169	0.405	.526	.004
IBP 5 (<i>df</i> = 94)	2.756	.009	.190	1.648	.202	.014
IBP 6 (<i>df</i> = 94)	2.386	.022	.169	1.328	.252	.012

All significant overall models remained significant after FDR correction

CHAPTER 4: DISCUSSION AND FUTURE DIRECTIONS

4.1 *The Moderation Analysis*

This dissertation systematically employed a series of moderation analyses to elucidate the nature of influence peripheral biomarkers have on healthy brain aging by understanding how they interact with measures of brain structure and function acquired by multi-modal imaging to predict facets of intelligence. Moderation analyses address the nature of an effect between three factors and inform the circumstances of an interaction (Hayes & Rockwood, 2017). Moderators are particularly helpful in identifying potential targets for intervention studies and in precision medicine because they can define subpopulations that may experience more pronounced effects from these approaches. Further, moderators can inform randomized trial design of possible mediators, both within the general population and in moderator-elucidated subgroups (Kraemer, 2016).

Importantly, moderation analyses performed on observational data are distinct from those performed on data collected from a randomized trial in that the discrimination between moderator and input variable is purely conceptual. In other words, lack of experimental manipulation renders these variables statistically interchangeable (Baron & Kelly, 1986). As a result, interpreting an exploratory moderation analysis relies heavily on existing literature to inform which variable should comprise the pseudo-causal pathway with the outcome variable and which would modify that pathway.

In the case of xanthophylls, facets of intelligence, and aging considerable evidence exists from both cross-sectional and intervention studies. This is also the case in the aging literature relating facets of intelligence to imaging measures. Well documented relationships between

facets of intelligence and brain structure and connectivity combined with intervention studies informing relationships between xanthophylls and facets of intelligence provide a contextual framework within which moderation analyses can be interpreted. Here, that contextual framework lent to two interpretations regarding the nature of xanthophyll influence: an ameliorating effect and a fostering effect.

An ameliorating effect mitigates a behavior by a compensatory mechanism. For example, if a genetic factor results in a negative behavior then a peripheral biomarker would have an ameliorating effect if it reduces the negative behavior by compensating for the fixed genetic factor. A fostering effect attenuates a behavior by an auxiliary mechanism. For example, if a factor indicates a system's susceptibility to a negative behavior then a peripheral biomarker would have a fostering effect if it reduces the behavior by supplementing that system.

These effects differ mostly in the reasoning behind and mechanism of their action. In both cases, the peripheral biomarker is exerting a positive effect on the behavioral outcome. This is important to note because it is reliant on the body of evidence linking xanthophyll carotenoids to positive cognitive performance. These same inferences cannot be drawn about all peripheral biomarkers because it is not well established whether they have positive or negative influences on cognitive performance. Notably, these interpretations are still limited by the nature of the moderation framework. Additional research is necessary to identify a true predictor variable and to elucidate the directional nature of underlying mechanisms.

Interpretations are limited even more when a contextual framework is underdeveloped because less support is available to justify which variable is assigned the predictor. One of the goals for this dissertation was to understand how peripheral biomarkers, which are presumed to be modifiable lifestyle factors, interact with various components of brain aging. From that

perspective the component hypotheses approached the peripheral biomarkers as moderators. However, it is still not entirely understood how some factors, such as AxD or inflammation biomarkers, relate to facets of intelligence during aging on their own. Therefore, it is not appropriate to interpret some moderations in the context of an “ameliorating” or “fostering” effect as there is not replicated evidence in the literature to support such interpretations of the moderation analysis. However, studies of this nature were still important because they identified several peripheral biomarkers that influence different levels of brain health and may be targets for intervention studies or precision medicine approaches. Additionally, these novel observations contribute to the young fields of nutritional cognitive neuroscience and psychoneuroimmunology and make a compelling case for using a multi-modal imaging approach to understand relationships between peripheral biomarkers and brain health in aging.

4.2 *Peripheral Biomarkers Moderate Brain Health*

The studies comprising this dissertation investigated two classes of peripheral biomarkers and their relationship to brain health and found that both influenced facets of intelligence at the structural, functional, and microstructural level. Each class of biomarker influenced general intelligence, but nutrition biomarkers preferentially influenced relationships predicting crystallized intelligence while inflammation biomarkers influenced relationships predicting fluid intelligence. Studies of cognitive aging indicate that crystallized and fluid intelligence are differently susceptible to decline (Nyberg & Tulving, 1996; Nyberg et. al., 2003; Salthouse, 2009) and are differently represented in network topology (Barbey, 2018; Gu et. al., 2015).

This dichotomous influence suggest that peripheral biomarkers may have divergent roles within the aging brain. Though claims cannot be made about directionality of influence, finding that different types of peripheral biomarkers tend to influence different types of intelligence is

rather interesting. Since crystallized intelligence is largely stable with aging, perhaps xanthophyll carotenoids act in maintaining structure and connectivity important for this function. Another explanation is that xanthophylls support restructuring as a compensatory mechanism during aging, an idea previously proposed after observing increased connectivity between networks following mixed xanthophyll supplementation (Lindbergh et. al., 2019). Conversely, inflammation biomarkers could be contributing to decline in fluid intelligence by inhibiting network connectivity or damaging brain structure. Another possible explanation, though, is that inflammation biomarkers influence fluid intelligence because they are acting to repair brain structure or network connectivity in areas most susceptible to aging. Future studies accounting for causation will be able to further differentiate these interpretations and help understand whether inflammation biomarkers exert a positive or negative influence on cognitive function during aging.

Until then, this collection of studies importantly observed that peripheral biomarkers tend to influence different facets of intelligence. Further, these biomarkers influence cognitive function by nature of brain structure, network connectivity, and white matter integrity. Importantly these observations identify xanthophylls and inflammation biomarkers as potential targets for intervention studies and precision medicine approaches. Additionally, these findings suggest that addressing one modifiable lifestyle factor, such as nutrition, may be limited in attenuating age-related cognitive changes and that multiple lifestyle factors should be addressed concurrently to facilitate optimum brain health during aging.

4.3 *Other Limitations and Future Directions*

Aside from the limitations mentioned briefly within chapter discussions and limitations of the moderation analysis addressed above, there are some limitations that apply to both chapters in this dissertation. First, xanthophyll carotenoids and many inflammation biomarkers exhibit a non-normal distribution when extracted from blood samples. Due to this non-normal distribution, the interpretation of influence is limited. This limitation is mostly relevant to coefficient size, however, and due to the cross-sectional nature of this study coefficient sizes were not used to interpret the results. Additionally, the sample size is sufficiently large that that regression-based analyses are still useful (Lumley et. al., 2002).

Second, genetic data was not available for participants in this dataset. A number of genetic polymorphisms relevant to this study are known and controlling for such genetic predispositions would allow for a better understanding of biomarker influence on brain health. For example, six genetic loci are associated with lobular brain volume, four of which affect the occipital lobe (van der Lee et. al., 2019). Other polymorphisms, such as those present on the ApoE gene are frequently associated with cognitive decline, and a polymorphism on the VEGF gene is positively correlated with larger brain volumes (Takeuchi et. al., 2017). Understanding how genetic factors such as these interact with peripheral biomarkers and their relationship to brain aging is important for understanding age-related cognitive decline.

Third, data regarding prescription or supplement use and physical health were not available. Statin use in particular is a concern when working with serum xanthophyll measures because high-density lipoprotein level is related to these nutrients (Renzi et. al., 2012). Though statin use is not indicated in volumetric brain changes (Samaras et. al., 2019), other medications may be, so

it is important to consider when planning future studies. Physical fitness could also affect brain health and is known to account for different levels of variance in grey matter volume across sex (Pentikainen et. al., 2017). Incorporating these measures as controls for future studies will limit variance and allow for more clarity in understanding how peripheral biomarkers relate to brain health in aging.

Finally, though it represented females and males nearly equally, the population studied in this dissertation was well educated, lived in a relatively low-pollution environment, and was entirely Caucasian. These factors greatly limit the generalizability of findings from these studies to populations that are more diverse or living in metropolitan areas. It is important that future studies investigate the influence of peripheral biomarkers with these limitations in mind to provide a more complete characterization of healthy brain aging.

Despite the breadth of associations investigated in this dissertation, questions remain regarding the nature of association between peripheral biomarkers and brain health. Even in the present dataset alone, there are many continuations from the present dissertation that would further impact the fields of nutritional cognitive neuroscience and psychoneuroimmunology. Here, I will briefly mention a few possible continuations.

The enclosed studies evaluated only relationships between inflammation biomarkers, white matter integrity, and intelligence globally and within the genu of the corpus callosum. Expanding exploration to include other fibers known to be susceptible to aging would provide a better understanding of how inflammation biomarkers interact with white matter integrity to influence cognitive performance in aging.

Carotene carotenoids should also be evaluated. They are known to accumulate in the brain and it is important to understand whether findings reported in these studies are specific to xanthophylls or if other carotenoids influence these relationships as well. Preliminary investigations into precuneus and cuneus grey matter volume indicated that significant findings were not replicated with carotenes, but it is possible that these nutrients influence relationships in other brain regions or at different levels of brain structure or connectivity. Additionally, carotenoids are better absorbed when accompanied by fatty acids, so it would be interesting to investigate omega-3 polyunsaturated fatty acids in conjunction with xanthophyll carotenoids. One possible route would be to produce a composite score for xanthophylls and fatty acids, but another would be to investigate these nutrients on their own.

Finally, future investigation could apply more complex statistical methods (e.g. mediated-moderation or structural equation modeling) to produce a more complete picture of peripheral biomarkers interacting with brain health. These methods could investigate related findings to understand how the influence may compound. For example, previously in the Decision Neuroscience Laboratory Mícheál Key published a finding that a particular nutrient biomarker pattern moderated the relationship between frontal pole volume and auditory memory (Key et. al., 2019). This dissertation observed that a particular inflammation biomarker pattern (IBP 6) moderated the relationship between frontal pole volume and auditory memory within the same population. Employing more advanced statistical methods could elucidate interactions between these peripheral biomarker patterns, providing a more detailed characterization of auditory memory in the aging brain.

In conclusion, the observations within this series of studies combined with the current literature in nutritional cognitive neuroscience and psychoneuroimmunology affirm the importance of understanding peripheral biomarkers in the context of healthy brain aging. More specifically, the multi-modal imaging approach used here provides converging evidence that peripheral biomarkers are related to brain health at multiple levels including brain structure, network connectivity, and white matter microstructure. The work performed in this dissertation reasons that nutritional and inflammatory biomarkers independently influence cognitive function in elders and are potential targets for intervention studies and precision medicine approaches. These observations are promising for future endeavors into the fields of nutritional cognitive neuroscience and psychoneuroimmunology that wish to incorporate cutting-edge imaging methods from cognitive neuroscience. Importantly, these observations are also promising for improving quality of life years through slowing cognitive decline and consequently easing the impact aging has on loved ones and the health care system.

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APPENDIX A: CHAPTER 2 NON-SIGNIFICANT RESULTS

This appendix includes tables with non-significant results from **Chapter 2: Xanthophyll carotenoids and brain behavior, structure, and function in healthy, aging adults** and is divided into three sections: (A.1) Xanthophylls and Grey Matter Volume, (A.2) Xanthophylls and Functional Connectivity, and (A.3) Xanthophylls and White Matter Structure.

A.1 Xanthophylls and Grey Matter Volume

Table A.1a | F statistics from moderation analyses, FDR corrected: auditory memory (DV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Cuneus						
Cryptoxanthin (<i>df</i> = 99)	2.279	.028	.155	3.307	.072	.028
Lutein (<i>df</i> = 100)	1.967	.058	.136	1.448	.232	.012
Zeaxanthin (<i>df</i> = 100)	2.954	.005	.191	3.618	.060	.029
Inferior Parietal						
Cryptoxanthin (<i>df</i> = 99)	1.939	.062	.136	0.757	.386	.007
Lutein (<i>df</i> = 100)	1.879	.072	.131	0.159	.691	.001
Zeaxanthin (<i>df</i> = 100)	2.754	.009	.181	2.257	.136	.018
Lateral Occipital						
Cryptoxanthin (<i>df</i> = 99)	2.080	.045*	.144	0.506	.479	.004
Lutein (<i>df</i> = 100)	2.160	.037*	.147	0.964	.328	.008
Zeaxanthin (<i>df</i> = 100)	2.812	.008	.184	0.702	.404	.006
Precuneus						
Cryptoxanthin (<i>df</i> = 99)	2.427	0.019	0.164	0.652	0.421	0.006
Lutein (<i>df</i> = 100)	2.699	0.010	0.178	0.049	0.826	0.000
Zeaxanthin (<i>df</i> = 100)	3.089	0.004	0.198	1.336	0.251	0.011
Superior Parietal						
Cryptoxanthin (<i>df</i> = 99)	2.298	.026	.157	3.356	.070	.029
Lutein (<i>df</i> = 100)	1.983	.056	.137	1.302	.257	.011
Zeaxanthin (<i>df</i> = 100)	2.565	.014	.170	0.904	.344	.008

*Overall models not significant after FDR correction

**Table A.1b | F statistics from moderation analyses, FDR corrected:
crystallized intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Cuneus						
Cryptoxanthin (<i>df</i> = 97)	6.153	.000	0.337	0.663	0.418	0.004
Lutein (<i>df</i> = 96)	5.768	.000	0.325	0.059	0.808	0.000
Zeaxanthin (<i>df</i> = 98)	7.036	.000	0.365	1.084	0.300	0.007
Inferior Parietal						
Cryptoxanthin (<i>df</i> = 97)	6.061	.000	0.333	0.863	0.355	0.006
Lutein (<i>df</i> = 96)	5.697	.000	0.322	0.256	0.614	0.002
Zeaxanthin (<i>df</i> = 98)	6.931	.000	0.361	0.684	0.410	0.004
Lateral Occipital						
Cryptoxanthin (<i>df</i> = 97)	5.986	.000	0.330	0.032	0.858	0.000
Lutein (<i>df</i> = 96)	5.619	.000	0.319	0.067	0.797	0.000
Zeaxanthin (<i>df</i> = 98)	6.625	.000	0.351	0.129	0.720	0.001
Precuneus						
Cryptoxanthin (<i>df</i> = 97)	5.925	.000	0.328	0.134	0.716	0.001
Lutein (<i>df</i> = 96)	5.698	.000	0.322	0.511	0.476	0.004
Zeaxanthin (<i>df</i> = 98)	6.649	.000	0.352	0.175	0.676	0.001
Superior Parietal						
Cryptoxanthin (<i>df</i> = 97)	6.041	.000	0.333	0.695	0.407	0.005
Lutein (<i>df</i> = 96)	5.606	.000	0.318	0.010	0.922	0.000
Zeaxanthin (<i>df</i> = 98)	6.603	.000	0.350	0.015	0.902	0.000

All significant overall models remained significant after FDR correction

Table A.1c | F statistics from moderation analyses, FDR corrected: delayed memory (DV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Inferior Parietal						
Cryptoxanthin (<i>df</i> = 100)	2.054	.048	.141	0.648	.423	.006
Lutein (<i>df</i> = 100)	2.035	.050	.140	2.782	.098	.024
Zeaxanthin (<i>df</i> = 101)	2.566	.014	.169	1.872	.174	.015
Lateral Occipital						
Cryptoxanthin (<i>df</i> = 100)	2.283	.028	.154	0.524	.471	.004
Lutein (<i>df</i> = 100)	2.311	.026	.156	2.384	.126	.020
Zeaxanthin (<i>df</i> = 101)	2.814	.007	.182	0.727	.396	.006
Precuneus						
Cryptoxanthin (<i>df</i> = 100)	2.231	0.031	0.151	0.006	0.939	0.000
Lutein (<i>df</i> = 100)	2.282	0.028	0.154	1.795	0.183	0.015
Zeaxanthin (<i>df</i> = 101)	2.859	0.007	0.185	1.698	0.196	0.014

All significant overall models remained significant after FDR correction

**Table A.1d | F statistics from moderation analyses, FDR corrected:
inferior parietal lobule (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
General Intelligence						
Cryptoxanthin (<i>df</i> = 97)	3.081	0.004	0.203	0.098	0.755	0.001
Lutein (<i>df</i> = 96)	3.599	0.001	0.231	0.410	0.523	0.003
Zeaxanthin (<i>df</i> = 98)	5.225	0.000	0.299	0.271	0.604	0.002
Immediate Memory						
Cryptoxanthin (<i>df</i> = 99)	3.471	0.001	0.219	0.889	0.348	0.007
Lutein (<i>df</i> = 99)	2.122	0.040	0.146	0.427	0.515	0.004
Zeaxanthin (<i>df</i> = 100)	2.617	0.012	0.173	0.566	0.454	0.005

All significant overall models remained significant after FDR correction

**Table A.1e | F statistics from moderation analyses, FDR corrected:
lateral occipital cortex (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
General Intelligence						
Cryptoxanthin (<i>df</i> = 97)	3.258	0.002	0.212	0.279	0.599	0.002
Lutein (<i>df</i> = 96)	3.571	0.001	0.229	0.086	0.770	0.001
Zeaxanthin (<i>df</i> = 98)	5.133	0.000	0.295	0.374	0.542	0.003
Immediate Memory						
Cryptoxanthin (<i>df</i> = 99)	3.284	0.002	0.210	0.032	0.858	0.000
Lutein (<i>df</i> = 99)	2.341	0.024	0.159	2.336	0.130	0.020
Zeaxanthin (<i>df</i> = 100)	2.902	0.006	0.188	2.304	0.132	0.019

All significant overall models remained significant after FDR correction

**Table A.1f | F statistics from moderation analyses, FDR corrected:
superior parietal lobule (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
General Intelligence						
Cryptoxanthin (<i>df</i> = 97)	3.375	0.002	0.218	0.007	0.933	0.000
Lutein (<i>df</i> = 96)	3.927	0.000	0.247	0.641	0.452	0.005
Zeaxanthin (<i>df</i> = 98)	5.336	0.000	0.303	0.436	0.511	0.003
Immediate Memory						
Cryptoxanthin (<i>df</i> = 99)	3.609	0.001	0.226	0.114	0.705	0.001
Lutein (<i>df</i> = 99)	2.287	0.027	0.156	1.002	0.319	0.009
Zeaxanthin (<i>df</i> = 100)	2.764	0.008	0.186	0.679	0.412	0.006

All significant overall models remained significant after FDR correction

A.2 *Xanthophylls and Functional Connectivity*

Table A.2a| F statistics from moderation analyses, FDR corrected: VisN efficiency (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>General Intelligence</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.277	.030	.187	0.488	.487	.005
Lutein (<i>df</i> = 78)	3.042	.005	.238	1.088	.300	.011
Zeaxanthin (<i>df</i> = 80)	3.904	.001	.281	0.036	.850	.000
Global Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.451	.020	.199	0.672	.415	.007
Lutein (<i>df</i> = 78)	3.302	.003	.253	2.197	.142	.021
Zeaxanthin (<i>df</i> = 80)	3.996	.001	.286	0.150	.699	.001
Small World Propensity						
Cryptoxanthin (<i>df</i> = 79)	2.381	.024	.194	0.959	.330	.010
Lutein (<i>df</i> = 78)	3.228	.003	.249	1.579	.213	.015
Zeaxanthin (<i>df</i> = 80)	3.944	.001	.283	0.188	.666	.002
<u>Crystallized Intelligence</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	5.388	.000	.347	0.077	.783	.001
Lutein (<i>df</i> = 80)	6.019	.000	.376	1.327	.253	.010
Zeaxanthin (<i>df</i> = 82)	6.550	.000	.390	0.462	.499	.003
Global Efficiency						
Cryptoxanthin (<i>df</i> = 81)	5.785	.000	.364	0.419	.520	.003
Lutein (<i>df</i> = 80)	6.447	.000	.392	2.279	.135	.017
Zeaxanthin (<i>df</i> = 82)	7.034	.000	.407	1.243	.268	.009
Small World Propensity						
Cryptoxanthin (<i>df</i> = 81)	5.753	.000	.362	1.056	.307	.008
Lutein (<i>df</i> = 80)	6.156	.000	.381	1.000	.320	.008
Zeaxanthin (<i>df</i> = 82)	6.890	.000	.402	0.894	.347	.006
<u>Immediate Memory</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 81)	2.632	.013	.206	.456	.502	.004
Lutein (<i>df</i> = 81)	1.745	.100	.147	1.433	.235	.015
Zeaxanthin (<i>df</i> = 82)	2.288	.029	.182	2.925	.091	.029
Global Efficiency						
Cryptoxanthin (<i>df</i> = 81)	2.501	.018	.198	0.000	.987	.000
Lutein (<i>df</i> = 81)	1.756	.098	.148	1.892	.173	.020
Zeaxanthin (<i>df</i> = 82)	2.168	.038	.175	2.587	.112	.026

All significant overall models remained significant after FDR correction

**Table A.2b | F statistics from moderation analyses, FDR corrected:
general intelligence (DV)**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Default Mode Network</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.645	.013	.211	2.427	.123	.024
Lutein (<i>df</i> = 78)	2.888	.007	.228	0.157	.693	.002
Zeaxanthin (<i>df</i> = 80)	3.883	.001	.280	0.004	.952	.000
Global Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.608	.014	.209	2.828	.097	.028
Lutein (<i>df</i> = 78)	2.875	.007	.228	0.130	.719	.001
Zeaxanthin (<i>df</i> = 80)	3.886	.001	.280	0.040	.842	.000
Small World Propensity						
Cryptoxanthin (<i>df</i> = 79)	3.110	.004	.240	0.010	.920	.000
Lutein (<i>df</i> = 78)	4.430	.000	.312	0.975	.326	.009
Zeaxanthin (<i>df</i> = 80)	5.342	.000	.348	0.115	.736	.001
<u>Frontoparietal Network</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 79)	3.176	.004	.243	3.540	.064	.034
Lutein (<i>df</i> = 78)	3.513	.002	.265	0.021	.885	.000
Zeaxanthin (<i>df</i> = 80)	4.756	.000	.322	0.010	.919	.000
Global Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.748	.010	.218	3.138	.080	.031
Lutein (<i>df</i> = 78)	3.093	.004	.241	0.574	.451	.006
Zeaxanthin (<i>df</i> = 80)	4.138	.000	.293	0.116	.734	.001
Small World Propensity						
Cryptoxanthin (<i>df</i> = 79)	2.196	.036	.1819	0.025	.875	.000
Lutein (<i>df</i> = 78)	3.354	.002	.2559	3.085	.083	.029
Zeaxanthin (<i>df</i> = 80)	4.114	.000	.2915	0.077	.783	.001
<u>Dorsal Attention Network</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.633	.013	.2105	0.100	.753	.001
Lutein (<i>df</i> = 78)	3.425	.002	.2600	0.583	.448	.006
Zeaxanthin (<i>df</i> = 80)	4.637	.000	.3168	0.006	.941	.000
Global Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.631	.013	.210	0.386	.536	.004
Lutein (<i>df</i> = 78)	3.640	.001	.272	2.124	.149	.020
Zeaxanthin (<i>df</i> = 80)	4.373	.000	.304	0.083	.774	.001
Small World Propensity						
Cryptoxanthin (<i>df</i> = 79)	2.803	.009	.221	1.761	.188	.017
Lutein (<i>df</i> = 78)	3.449	.002	.261	3.328	.072	.032
Zeaxanthin (<i>df</i> = 80)	4.189	.000	.295	0.588	.446	.005
<u>Ventral Attention Network</u>						
Local Efficiency						
Cryptoxanthin (<i>df</i> = 79)	3.059	.005	.236	0.829	.365	.008
Lutein (<i>df</i> = 78)	3.496	.002	.264	0.755	.388	.007
Zeaxanthin (<i>df</i> = 80)	4.934	.000	.330	1.604	.209	.013
Global Efficiency						
Cryptoxanthin (<i>df</i> = 79)	2.939	.006	.229	0.679	.412	.007
Lutein (<i>df</i> = 78)	3.262	.003	.251	0.038	.846	.000
Zeaxanthin (<i>df</i> = 80)	4.808	.000	.325	1.136	.290	.010
Small World Propensity						
Cryptoxanthin (<i>df</i> = 79)	2.188	.037	.181	0.016	.899	.000
Lutein (<i>df</i> = 78)	2.879	.007	.228	0.157	.693	.002
Zeaxanthin (<i>df</i> = 80)	3.390	.001	.281	0.134	.716	.001

All significant overall models remained significant after FDR correction; significant interactions are in bold

A.3 *Xanthophylls and White Matter Structure*

Table A.3a | F statistics from moderation analyses, FDR corrected: fornix (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.470	.000	.353	0.020	.889	.000
Lutein (<i>df</i> = 94)	6.309	.000	.349	0.197	.658	.001
Zeaxanthin (<i>df</i> = 97)	6.913	.000	.363	0.005	.946	.000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.627	.000	.358	0.311	.578	.002
Lutein (<i>df</i> = 94)	6.318	.000	.350	0.102	.750	.001
Zeaxanthin (<i>df</i> = 97)	6.973	.000	.365	0.000	.991	.000
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.511	.000	.354	0.255	.615	.002
Lutein (<i>df</i> = 94)	6.291	.000	.349	0.113	.738	.001
Zeaxanthin (<i>df</i> = 97)	6.919	.000	.363	0.030	.863	.000
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.762	.001	.241	0.038	.846	.000
Lutein (<i>df</i> = 94)	4.207	.000	.264	0.022	.883	.000
Zeaxanthin (<i>df</i> = 97)	5.533	.000	.313	0.020	.888	.000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.453	.002	.225	0.019	.892	.000
Lutein (<i>df</i> = 94)	3.947	.000	.252	0.324	.571	.003
Zeaxanthin (<i>df</i> = 97)	5.325	.000	.305	0.173	.679	.001
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.576	.001	.231	0.000	.988	.000
Lutein (<i>df</i> = 94)	4.101	.000	.259	0.350	.556	.003
Zeaxanthin (<i>df</i> = 97)	5.422	.000	.309	0.185	.668	.185
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	5.617	.000	.317	1.401	.239	.010
Lutein (<i>df</i> = 97)	4.114	.000	.253	0.336	.564	.003
Zeaxanthin (<i>df</i> = 99)	4.704	.000	.275	1.269	.263	.009
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	5.756	.000	.322	2.687	.104	.019
Lutein (<i>df</i> = 97)	4.213	.002	.258	0.543	.463	.004
Zeaxanthin (<i>df</i> = 99)	4.707	.000	.276	0.598	.441	.004
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	5.790	.000	.323	1.383	.242	.010
Lutein (<i>df</i> = 97)	4.477	.000	.270	0.790	.376	.006
Zeaxanthin (<i>df</i> = 99)	5.015	.000	.288	1.412	.238	.010

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table A.3b | F statistics from moderation analyses, FDR corrected:
cingulum – cingulate gyrus (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.472	.000	.353	0.006	.939	.000
Lutein (<i>df</i> = 94)	6.500	.000	.356	0.347	.557	.002
Zeaxanthin (<i>df</i> = 97)	7.158	.000	.371	0.103	.749	.001
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.466	.000	.352	0.113	.738	.001
Lutein (<i>df</i> = 94)	6.990	.000	.373	2.837	.095	.019
Zeaxanthin (<i>df</i> = 97)	7.851	.000	.393	3.169	.078	.020
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.493	.000	.354	0.144	.706	.001
Lutein (<i>df</i> = 94)	6.646	.000	.361	1.617	.207	.011
Zeaxanthin (<i>df</i> = 97)	7.025	.000	.367	0.144	.705	.001
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.489	.001	.227	0.480	.490	.004
Lutein (<i>df</i> = 94)	4.103	.000	.259	1.232	.270	.010
Zeaxanthin (<i>df</i> = 97)	5.177	.000	.299	0.759	.386	.006
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.136	.003	.209	0.095	.759	.001
Lutein (<i>df</i> = 94)	4.093	.000	.258	3.078	.083	.024
Zeaxanthin (<i>df</i> = 97)	5.555	.000	.314	3.239	.075	.023
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.562	.001	.231	0.708	.402	.006
Lutein (<i>df</i> = 94)	4.652	.000	.284	3.460	.066	.026
Zeaxanthin (<i>df</i> = 97)	5.463	.000	.311	1.704	.195	.012
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.752	.001	.236	0.035	.851	.000
Lutein (<i>df</i> = 97)	2.418	.020	.166	0.213	.646	.002
Zeaxanthin (<i>df</i> = 99)	2.827	.007	.186	0.053	.819	.000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.812	.001	.239	0.159	.691	.001
Lutein (<i>df</i> = 97)	2.747	.009	.185	2.630	.108	.022
Zeaxanthin (<i>df</i> = 99)	2.814	.008	.185	0.000	.996	.000
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.756	.001	.236	0.046	.832	.000
Lutein (<i>df</i> = 97)	2.561	.014	.174	1.226	.271	.010
Zeaxanthin (<i>df</i> = 99)	2.804	.008	.185	0.153	.697	.001

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table A.3c | F statistics from moderation analyses, FDR corrected:
inferior cerebellar peduncle (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Crystallized Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.462	.000	.352	0.000	.992	.000
Lutein (<i>df</i> = 94)	6.536	.000	.357	0.605	.439	.004
Zeaxanthin (<i>df</i> = 97)	7.204	.000	.373	0.412	.522	.003
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.565	.000	.356	0.525	.470	.004
Lutein (<i>df</i> = 94)	6.402	.000	.353	0.077	.782	.000
Zeaxanthin (<i>df</i> = 97)	7.221	.000	.373	1.065	.305	.007
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.480	.000	.353	0.108	.743	.001
Lutein (<i>df</i> = 94)	6.526	.000	.357	0.742	.391	.005
Zeaxanthin (<i>df</i> = 97)	7.187	.000	.372	0.508	.478	.003
<u>General Intelligence</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.879	.000	.246	1.483	.226	.012
Lutein (<i>df</i> = 94)	3.999	.000	.254	0.157	.693	.001
Zeaxanthin (<i>df</i> = 97)	5.231	.000	.301	0.143	.706	.001
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.542	.001	.230	1.641	.203	.013
Lutein (<i>df</i> = 94)	3.731	.001	.241	0.192	.662	.002
Zeaxanthin (<i>df</i> = 97)	5.158	.000	.298	0.299	.586	.002
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.567	.001	.231	1.152	.286	.009
Lutein (<i>df</i> = 94)	3.827	.001	.246	0.324	.571	.003
Zeaxanthin (<i>df</i> = 97)	5.046	.000	.294	0.086	.770	.001
<u>Immediate Memory</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.757	.001	.237	0.289	.592	.002
Lutein (<i>df</i> = 97)	2.377	.022	.164	0.120	.729	.001
Zeaxanthin (<i>df</i> = 99)	2.922	.006	.191	0.983	.324	.008
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	6.903	.000	.363	0.828	.365	.005
Lutein (<i>df</i> = 97)	4.667	.000	.278	1.398	.240	.010
Zeaxanthin (<i>df</i> = 99)	5.149	.000	.294	0.206	.651	.002
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.753	.001	.236	0.557	.457	.004
Lutein (<i>df</i> = 97)	2.364	.023	.163	0.106	.746	.001
Zeaxanthin (<i>df</i> = 99)	2.766	.008	.183	0.086	.770	.001

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table A.3d | F statistics from moderation analyses, FDR corrected:
crystallized intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Genu of the Corpus Callosum</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.7346	.0000	.3619	0.3384	.5621	.0023
Lutein (<i>df</i> = 94)	6.8498	.0000	.3683	1.9776	.1629	.0133
Zeaxanthin (<i>df</i> = 97)	7.4520	.0000	.3807	1.8445	.1776	.0118
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.1996	.0000	.3774	1.7575	.1881	.0115
Lutein (<i>df</i> = 94)	6.9339	.0000	.3711	1.2233	.2715	.0082
Zeaxanthin (<i>df</i> = 97)	7.4914	.0000	.3819	0.6123	.4358	.0039
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.6782	.0000	.3599	0.8285	.3650	.0056
Lutein (<i>df</i> = 94)	6.7162	.0000	.3637	1.9390	.1671	.0131
Zeaxanthin (<i>df</i> = 97)	7.3145	.0000	.3763	1.8016	.1827	.0116
<u>Body of the Corpus Callosum</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.4882	.0000	.3533	0.0924	.7618	.0006
Lutein (<i>df</i> = 94)	6.6280	.0000	.3606	1.1711	.2819	.0080
Zeaxanthin (<i>df</i> = 97)	7.0195	.0000	.3667	0.1043	.7474	.0007
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	7.2055	.0000	.3776	1.7387	.1905	.0114
Lutein (<i>df</i> = 94)	7.1783	.0000	.3792	1.7092	.1943	.0113
Zeaxanthin (<i>df</i> = 97)	7.3621	.0000	.3778	0.1573	.6925	.0010
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.4772	.0000	.3529	0.1976	.6577	.0013
Lutein (<i>df</i> = 94)	6.5011	.0000	.3562	0.9375	.3354	.0064
Zeaxanthin (<i>df</i> = 97)	6.9561	.0000	.3646	0.0758	.7837	.0005
<u>Corona Radiata – Posterior</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.5986	.0000	.3572	0.0123	.9120	.0001
Lutein (<i>df</i> = 94)	6.7353	.0000	.3644	1.5675	.2137	.0106
Zeaxanthin (<i>df</i> = 97)	7.0641	.0000	.3681	0.0022	.9626	.0000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.6593	.0000	.3593	0.1291	.7202	.0009
Lutein (<i>df</i> = 94)	7.1715	.0000	.3790	3.1771	.0779	.0210
Zeaxanthin (<i>df</i> = 97)	7.6050	.0000	.3855	2.3415	.1292	.0148
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.5909	.0000	.3569	0.1650	.6855	.0011
Lutein (<i>df</i> = 94)	6.9902	.0000	.3730	2.3949	.1251	.0160
Zeaxanthin (<i>df</i> = 97)	7.1477	.0000	.3709	0.2868	.5935	.0019

**Table A.3d | F statistics from moderation analyses, FDR corrected:
crystallized intelligence (DV) continued**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>External Capsule</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.4614	.0000	.3524	0.0736	.7867	.0005
Lutein (<i>df</i> = 94)	6.6069	.0000	.3599	1.7507	.1890	.0119
Zeaxanthin (<i>df</i> = 97)	7.0617	.0000	.3681	0.7133	.4004	.0046
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.6408	.0000	.3587	0.5185	.4732	.0035
Lutein (<i>df</i> = 94)	7.0237	.0000	.3741	2.1603	.1450	.0144
Zeaxanthin (<i>df</i> = 97)	7.8518	.0000	.3930	2.9273	.0903	.0183
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.4854	.0000	.3532	0.1862	.6671	.0013
Lutein (<i>df</i> = 94)	6.6525	.0000	.3615	1.9396	.1670	.0132
Zeaxanthin (<i>df</i> = 97)	7.0816	.0000	.3687	0.8327	.3637	.0054
<u>Posterior Thalamic Radiation</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.5912	.0000	.3569	0.7458	.3900	.0050
Lutein (<i>df</i> = 94)	6.5047	.0000	.3563	1.0851	.3002	.0074
Zeaxanthin (<i>df</i> = 97)	6.9602	.0000	.3647	0.1039	.7479	.0007
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.8842	.0000	.3670	1.2463	.2671	.0083
Lutein (<i>df</i> = 94)	7.0832	.0000	.3761	1.8670	.1751	.0124
Zeaxanthin (<i>df</i> = 97)	7.5687	.0000	.3843	0.8808	.3503	.0056
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.6427	.0000	.3587	1.0569	.3065	.0071
Lutein (<i>df</i> = 94)	6.6547	.0000	.3616	2.0049	.1601	.0136
Zeaxanthin (<i>df</i> = 97)	6.9123	.0000	.3631	0.0001	.9926	.0000
<u>Uncinate Fasciculus</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	6.6427	.0000	.3587	0.0526	.8191	.0004
Lutein (<i>df</i> = 94)	6.3566	.0000	.3511	0.1248	.7247	.0009
Zeaxanthin (<i>df</i> = 97)	7.1659	.0000	.3715	0.9884	.3226	.0064
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.9150	.0000	.3680	1.7176	.1932	.0114
Lutein (<i>df</i> = 94)	6.4371	.0000	.3539	0.8195	.3676	.0056
Zeaxanthin (<i>df</i> = 97)	7.0046	.0000	.3662	0.0236	.8783	.0002
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	6.6459	.0000	.3588	1.0736	.3028	.0072
Lutein (<i>df</i> = 94)	6.3435	.0000	.3506	0.3706	.5442	.0026
Zeaxanthin (<i>df</i> = 97)	6.9729	.0000	.3651	0.2684	.6056	.0018

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table A.3e | F statistics from moderation analyses, FDR corrected:
general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Body of the Corpus Callosum</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.3204	.0022	.2185	0.7623	.3848	.0063
Lutein (<i>df</i> = 94)	3.8782	.0005	.2482	1.5569	.2152	.0125
Zeaxanthin (<i>df</i> = 97)	5.0007	.0000	.2920	0.1215	.7282	.0009
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.6683	.0009	.2360	2.9472	.0893	.0237
Lutein (<i>df</i> = 94)	4.2144	.0002	.2640	2.6749	.1053	.0209
Zeaxanthin (<i>df</i> = 97)	5.2332	.0000	.3015	1.1159	.2934	.0080
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.4246	.0017	.2238	1.0078	.3180	.0082
Lutein (<i>df</i> = 94)	3.9466	.0005	.2514	1.6286	.2050	.0130
Zeaxanthin (<i>df</i> = 97)	5.0730	.0000	.2950	0.3363	.5633	.0024
<u>Cingulum – Hippocampus</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.2429	.0026	.2145	0.0577	.8108	.0005
Lutein (<i>df</i> = 94)	3.6560	.0010	.2373	0.0006	.9812	.0000
Zeaxanthin (<i>df</i> = 97)	4.9854	.0000	.2914	0.0006	.9805	.0000
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.4451	.0016	.2249	0.0365	.8488	.0003
Lutein (<i>df</i> = 94)	4.7087	.0001	.2861	3.6716	.0584	.0279
Zeaxanthin (<i>df</i> = 97)	5.9085	.0000	.3276	2.2049	.1408	.0153
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.4311	.0016	.2242	0.1016	.7506	.0008
Lutein (<i>df</i> = 94)	3.9385	.0005	.2510	0.3436	.5592	.0027
Zeaxanthin (<i>df</i> = 97)	5.1744	.0000	.2991	0.0168	.8972	.0001
<u>Corona Radiata – Superior</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 95)	3.8905	.0005	.2468	2.1769	.1434	.0173
Lutein (<i>df</i> = 94)	4.2201	.0002	.2643	1.3000	.2571	.0102
Zeaxanthin (<i>df</i> = 97)	5.4314	.0000	.3094	1.5930	.2099	.0113
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.2678	.0025	.2158	0.2236	.6374	.0018
Lutein (<i>df</i> = 94)	4.3351	.0002	.2695	2.6150	.1092	.0203
Zeaxanthin (<i>df</i> = 97)	5.8122	.0000	.3240	2.9139	.0910	.0203
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 95)	3.8267	.0006	.2437	1.9658	.1642	.0156
Lutein (<i>df</i> = 94)	4.5037	.0001	.2771	2.0856	.1520	.0160
Zeaxanthin (<i>df</i> = 97)	5.5448	.0000	.3138	1.4931	.2247	.0106

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table A.3f | F statistics from moderation analyses, FDR corrected:
immediate memory (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Cerebellar Peduncle – Middle</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.6896	.0008	.2333	0.1547	.6950	.0012
Lutein (<i>df</i> = 97)	2.6228	.0121	.1778	2.1244	.1482	.0180
Zeaxanthin (<i>df</i> = 99)	2.9099	.0059	.1904	1.1892	.2781	.0097
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.7485	.0007	.2362	0.3693	.5448	.0029
Lutein (<i>df</i> = 97)	2.5181	.0156	.1720	1.5005	.2236	.0128
Zeaxanthin (<i>df</i> = 99)	2.9461	.0054	.1923	1.5937	.2098	.0130
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.6505	.0009	.2314	0.0000	.9982	.0000
Lutein (<i>df</i> = 97)	2.6346	.0118	.1785	2.2879	.1336	.0194
Zeaxanthin (<i>df</i> = 99)	2.9581	.0052	.1920	1.6541	.2014	.0135
<u>Cerebellar Peduncle – Superior</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.7621	.0007	.2368	0.2014	.6546	.0016
Lutein (<i>df</i> = 97)	2.3133	.0258	.1602	0.0453	.8318	.0004
Zeaxanthin (<i>df</i> = 99)	2.7093	.0097	.1796	0.0515	.8209	.0004
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.7251	.0008	.2350	0.2631	.6091	.0021
Lutein (<i>df</i> = 97)	2.3788	.0220	.1640	0.3464	.5576	.0030
Zeaxanthin (<i>df</i> = 99)	2.8258	.0072	.1859	0.4748	.4924	.0039
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.6861	.0009	.2331	0.0003	.9872	.0000
Lutein (<i>df</i> = 97)	2.3044	.0263	.1597	0.0685	.7941	.0006
Zeaxanthin (<i>df</i> = 99)	2.8529	.0068	.4328	0.7930	.3753	.0065
<u>Corona Radiata – Anterior</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.9081	.0005	.2438	0.0001	.9903	.0000
Lutein (<i>df</i> = 97)	2.6675	.0108	.1803	1.4402	.2330	.0122
Zeaxanthin (<i>df</i> = 99)	2.9117	.0059	.1905	0.0152	.9020	.0001
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	4.0361	.0004	.2497	2.5268	.1152	.0195
Lutein (<i>df</i> = 97)	2.5174	.0157	.1719	1.3151	.2543	.0112
Zeaxanthin (<i>df</i> = 99)	2.7773	.0082	.1833	0.1913	.6628	.0016
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.8982	.0005	.2433	0.0857	.7703	.0007
Lutein (<i>df</i> = 97)	2.5975	.0129	.1764	1.1672	.2827	.0099
Zeaxanthin (<i>df</i> = 99)	2.8287	.0072	.1861	0.0342	.8536	.0003

**Table A.3f | F statistics from moderation analyses, FDR corrected:
immediate memory (DV) continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	<i>R</i> ²
<u>Corona Radiata – Posterior</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.8476	.0006	.2409	1.3622	.2460	.0107
Lutein (<i>df</i> = 97)	2.5684	.0138	.1748	1.8083	.1818	.0154
Zeaxanthin (<i>df</i> = 99)	2.7047	.0098	.1794	0.0215	.8837	.0002
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	4.0617	.0003	.2509	0.0439	.8344	.0003
Lutein (<i>df</i> = 97)	2.4939	.0166	.1706	0.2715	.6035	.0023
Zeaxanthin (<i>df</i> = 99)	3.1179	.0035	.2012	2.1348	.1472	.0172
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.9118	.0005	.2439	1.1599	.2842	.0090
Lutein (<i>df</i> = 97)	2.5107	.0159	.1715	1.3983	.2399	.0119
Zeaxanthin (<i>df</i> = 99)	2.7255	.0093	.1805	0.1410	.7081	.0012
<u>Corona Radiata – Superior</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.6417	.0010	.2310	0.0690	.7934	.0005
Lutein (<i>df</i> = 97)	2.3120	.0258	.1601	0.0628	.8026	.0005
Zeaxanthin (<i>df</i> = 99)	2.7080	.0097	.1795	0.0345	.8530	.0003
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.7313	.0008	.2353	0.0134	.9079	.0001
Lutein (<i>df</i> = 97)	2.5447	.0147	.1735	0.0383	.8452	.0003
Zeaxanthin (<i>df</i> = 99)	2.8834	.0063	.1890	0.2210	.6393	.0018
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.7195	.0008	.2348	0.0031	.9557	.0000
Lutein (<i>df</i> = 97)	2.3469	.0237	.1622	0.0030	.9563	.0000
Zeaxanthin (<i>df</i> = 99)	2.7892	.0079	.1839	0.3226	.5713	.0027
<u>External Capsule</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.9079	.0005	.2437	1.3331	.2511	.0104
Lutein (<i>df</i> = 97)	2.4807	.0171	.1698	1.2547	.2654	.0107
Zeaxanthin (<i>df</i> = 99)	2.8706	.0065	.1883	1.1126	.2941	.0091
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.8011	.0006	.2387	1.0350	.3115	.0081
Lutein (<i>df</i> = 97)	2.4693	.0176	.1692	0.5736	.4507	.0049
Zeaxanthin (<i>df</i> = 99)	2.7625	.0085	.1825	0.0159	.8998	.0001
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.8445	.0006	.2407	0.0065	.9360	.0001
Lutein (<i>df</i> = 97)	2.4621	.0179	.1688	0.3091	.5795	.0026
Zeaxanthin (<i>df</i> = 99)	2.8322	.0071	.1862	0.0601	.8068	.0005

**Table A.3f | F statistics from moderation analyses, FDR corrected:
immediate memory (DV) continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	<i>R</i> ²
<u>Internal Capsule – Anterior Limb</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.8717	.0005	.2420	0.9685	.3275	.0076
Lutein (<i>df</i> = 97)	2.3940	.0212	.1649	0.0712	.7902	.0006
Zeaxanthin (<i>df</i> = 99)	2.8671	.0065	.1881	0.6068	.4379	.0050
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.8171	.0006	.2394	1.1860	.2788	.0093
Lutein (<i>df</i> = 97)	2.4811	.0171	.1699	1.2582	.2648	.0108
Zeaxanthin (<i>df</i> = 99)	2.7452	.0089	.1816	0.0855	.7707	.0007
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.6668	.0009	.2322	0.1307	.7185	.0010
Lutein (<i>df</i> = 97)	2.3535	.0234	.1626	0.2594	.6117	.0022
Zeaxanthin (<i>df</i> = 99)	2.7191	.0094	.1801	0.0773	.7816	.0006
<u>Internal Capsule – Posterior Limb</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	4.2513	.0002	.2596	3.5648	.0620	.0272
Lutein (<i>df</i> = 97)	2.3913	.0213	.1647	0.0796	.7784	.0007
Zeaxanthin (<i>df</i> = 99)	2.9286	.0056	.1917	1.0250	.3138	.0084
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.7813	.0007	.2377	0.4927	.4844	.0039
Lutein (<i>df</i> = 97)	2.7704	.0084	.1860	3.0565	.0836	.0256
Zeaxanthin (<i>df</i> = 99)	3.1693	.0031	.2039	2.7837	.0984	.0224
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	4.1137	.0003	.2533	2.8931	.0922	.0223
Lutein (<i>df</i> = 97)	2.3722	.0223	.1636	0.2975	.5867	.0026
Zeaxanthin (<i>df</i> = 99)	2.9461	.0054	.1923	1.3985	.2398	.0114
<u>Posterior Thalamic Radiation</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.7454	.0007	.2360	0.3116	.5780	.0025
Lutein (<i>df</i> = 97)	2.3165	.0256	.1604	0.1275	.7218	.0011
Zeaxanthin (<i>df</i> = 99)	2.7881	.0080	.1839	0.5289	.4688	.0044
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.7338	.0008	.2354	0.6810	.4113	.0054
Lutein (<i>df</i> = 97)	2.5684	.0138	.1748	1.8202	.1804	.0155
Zeaxanthin (<i>df</i> = 99)	2.7486	.0088	.1817	0.0008	.9773	.0000
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.8075	.0006	.2390	0.1709	.6802	.0013
Lutein (<i>df</i> = 97)	2.3695	.0225	.1635	0.3392	.5616	.0029
Zeaxanthin (<i>df</i> = 99)	2.8014	.0077	.1846	0.4994	.4814	.0041

**Table A.3f | F statistics from moderation analyses, FDR corrected:
immediate memory (DV) continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	<i>R</i> ²
<u>Superior Longitudinal Fasciculus</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.8276	.0006	.2399	0.0009	.9763	.0000
Lutein (<i>df</i> = 97)	2.4836	.0170	.1700	0.6781	.4123	.0058
Zeaxanthin (<i>df</i> = 99)	2.8982	.0061	.1898	0.5369	.4655	.0044
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.6824	.0009	.2330	0.3188	.5737	.0025
Lutein (<i>df</i> = 97)	2.4566	.0182	.1685	0.7474	.3894	.0064
Zeaxanthin (<i>df</i> = 99)	2.7611	.0085	.1824	0.0002	.9894	.0000
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.8529	.0006	.2411	0.0043	.9477	.0000
Lutein (<i>df</i> = 97)	2.5056	.0161	.1713	0.8381	.3622	.0072
Zeaxanthin (<i>df</i> = 99)	2.8251	.0073	.1859	0.1575	.6923	.0013
<u>Uncinate Fasciculus</u>						
Fractional Anisotropy						
Cryptoxanthin (<i>df</i> = 97)	3.9642	.0004	.2464	1.9503	.1657	.0152
Lutein (<i>df</i> = 97)	2.3503	.0235	.1624	0.1029	.7491	.0009
Zeaxanthin (<i>df</i> = 99)	3.3184	.0021	.2115	3.8169	.0536	.0304
Axial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.9550	.0004	.2460	1.4223	.2359	.0111
Lutein (<i>df</i> = 97)	2.4798	.0172	.1698	0.1055	.7461	.0009
Zeaxanthin (<i>df</i> = 99)	2.8360	.0071	.1864	0.1815	.6710	.0015
Radial Diffusion						
Cryptoxanthin (<i>df</i> = 97)	3.9420	.0005	.2453	0.7900	.3763	.0061
Lutein (<i>df</i> = 97)	2.3648	.0227	.1632	0.1592	.6908	.0014
Zeaxanthin (<i>df</i> = 99)	3.2478	.0025	.2079	3.3012	.0723	.0264

All significant overall models remained significant after FDR correction; significant interactions are in bold

APPENDIX B: CHAPTER 3 NON-SIGNIFICANT RESULTS

This appendix includes tables with non-significant results from **Chapter 3: Peripheral biomarkers and brain behavior, structure, and function in healthy, aging adults** and is divided into three sections: (B.1) Peripheral Biomarkers and Grey Matter Volume, (B.2) Peripheral Biomarkers and Functional Connectivity, and (B.3) Peripheral Biomarkers and White Matter Structure.

B. 1 Peripheral Biomarkers and Structural Volume

Table B.1a | F statistics from moderation analyses, FDR corrected: delayed memory (DV)

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Banks of Superior Temporal Sulcus</u>						
CRP (<i>df</i> = 102)	2.6566	.0109	.1724	0.1297	.7195	.0011
IL-8 (<i>df</i> = 75)	1.7885	.0926	.1602	0.5719	.4519	.0064
IL-18 (<i>df</i> = 104)	2.4263	.0191	.1573	1.6759	.1983	.0136
MCP-1 (<i>df</i> = 66)	2.0216	.0572	.1968	0.0029	.9574	.0000
RANTES (<i>df</i> = 104)	2.4196	.0194	.1569	1.4516	.2310	.0118
ICAM-1 (<i>df</i> = 104)	2.2838	.0271	.1494	0.7097	.4015	.0058
VCAM-1 (<i>df</i> = 104)	2.8473	.0067	.1797	0.0926	.7615	.0007
MMP-3 (<i>df</i> = 104)	2.2001	.0332	.1447	0.0011	.9740	.0000
MMP-9 (<i>df</i> = 103)	2.2041	.0329	.1462	0.0144	.9047	.0001
IBP 1 (<i>df</i> = 99)	3.0746	.0039	.1990	0.2924	.5899	.0024
IBP 2 (<i>df</i> = 99)	2.1072	.0420	.1455	0.0062	.9376	.0001
IBP 3 (<i>df</i> = 99)	2.3900	.0212	.1619	0.2040	.6525	.0017
IBP 4 (<i>df</i> = 99)	2.1346	.0393	.1471	0.0418	.8384	.0004
IBP 5 (<i>df</i> = 99)	2.1762	.0356	.1496	0.3446	.5585	.0030
IBP 6 (<i>df</i> = 99)	2.4918	.0166	.1676	2.6261	.1083	.0221
<u>Frontal Pole</u>						
CRP (<i>df</i> = 102)	2.8090	.0074	.1805	1.2205	.2719	.0098
IL-8 (<i>df</i> = 75)	1.8086	.0886	.1617	0.2636	.6092	.0029
IL-18 (<i>df</i> = 104)	2.4927	.0162	.1609	0.1923	.6619	.0016
MCP-1 (<i>df</i> = 66)	2.5350	.0180	.2350	0.8753	.3529	.0101
RANTES (<i>df</i> = 104)	2.6326	.0115	.1684	0.7562	.3865	.0060
ICAM-1 (<i>df</i> = 104)	2.7226	.0091	.1732	1.4466	.2318	.0115
VCAM-1 (<i>df</i> = 104)	2.8180	.0072	.1782	0.6883	.4086	.0054
MMP-3 (<i>df</i> = 104)	2.4725	.0170	.1598	0.0019	.9653	.0000
MMP-9 (<i>df</i> = 103)	2.6442	.0112	.1704	0.5756	.4498	.0046
IBP 1 (<i>df</i> = 99)	2.7473	.0088	.1817	0.2739	.6019	.0023
IBP 2 (<i>df</i> = 99)	2.2793	.0278	.1555	0.4265	.5152	.0036
IBP 3 (<i>df</i> = 99)	2.5517	.0143	.1710	0.0242	.8768	.0002
IBP 4 (<i>df</i> = 99)	2.3077	.0259	.1572	0.3262	.5692	.0028
IBP 5 (<i>df</i> = 99)	2.2460	.0301	.1536	0.0218	.8829	.0002
IBP 6 (<i>df</i> = 99)	2.8002	.0077	.1845	3.8934	.0513	.0321

All significant overall models remained significant after FDR correction

**Table B.1b | F statistics from moderation analyses, FDR corrected:
fusiform gyrus (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	2.8734	.0064	.1869	0.0182	.8929	.0001
IL-8 (<i>df</i> = 75)	2.0329	.0537	.1782	0.2307	.6324	.0025
IL-18 (<i>df</i> = 102)	2.7469	.0087	.1773	1.3388	.2499	.0108
MCP-1 (<i>df</i> = 64)	1.3425	.2392	.1437	1.0089	.3189	.0135
RANTES (<i>df</i> = 102)	3.3003	.0022	.2056	0.4171	.5198	.0032
ICAM-1 (<i>df</i> = 102)	2.9166	.0057	.1862	0.0482	.8267	.0004
VCAM-1 (<i>df</i> = 102)	2.7154	.0094	.1756	0.7178	.3988	.0058
MMP-3 (<i>df</i> = 102)	2.8435	.0068	.1824	0.0028	.9578	.0000
MMP-9 (<i>df</i> = 101)	3.2678	.0024	.2056	2.6047	.1097	.0205
Complement C3 (<i>df</i> = 102)	3.4281	.0016	.2119	0.8410	.3613	.0065
Ferritin (<i>df</i> = 102)	3.5104	.0013	.2159	0.0338	.8545	.0003
IBP 1 (<i>df</i> = 97)	3.0229	.0045	.1996	0.9069	.3433	.0075
IBP 2 (<i>df</i> = 97)	2.4670	.0177	.1691	0.4691	.4950	.0040
IBP 3 (<i>df</i> = 97)	2.7497	.0088	.1849	0.0105	.9184	.0001
IBP 4 (<i>df</i> = 97)	2.7605	.0086	.1854	0.1762	.6756	.0015
IBP 5 (<i>df</i> = 97)	3.1074	.0036	.2040	0.0215	.8837	.0002
IBP 6 (<i>df</i> = 97)	2.7633	.0086	.1856	0.8212	.3671	.0069

All significant overall models remained significant after FDR correction

**Table B.1c | F statistics from moderation analyses, FDR corrected:
inferior temporal (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Auditory Memory</u>						
CRP (<i>df</i> = 101)	2.7047	.0097	.1764	0.3774	.5404	.0031
IL-8 (<i>df</i> = 75)	2.0653	.0499*	.1805	0.2251	.6366	.0025
IL-18 (<i>df</i> = 103)	2.7009	.0097	.1734	2.2254	.1388	.0179
MCP-1 (<i>df</i> = 65)	2.3265	.0291	.2226	0.7724	.3827	.0092
RANTES (<i>df</i> = 103)	2.5123	.0155	.1633	0.1188	.7310	.0010
ICAM-1 (<i>df</i> = 103)	3.0574	.0040	.1919	2.2403	.1375	.0176
VCAM-1 (<i>df</i> = 103)	2.5104	.0156	.1632	0.0266	.8706	.0002
MMP-3 (<i>df</i> = 103)	2.4854	.0166	.1618	0.0888	.7663	.0007
MMP-9 (<i>df</i> = 102)	2.4524	.0180	.1613	0.4198	.5185	.0035
Factor VII (<i>df</i> = 103)	2.9727	.0049	.1876	0.1789	.6732	.0014
IBP 1 (<i>df</i> = 98)	2.7905	.0080	.1855	0.0003	.9859	.0000
IBP 2 (<i>df</i> = 98)	2.2973	.0267	.1573	0.0093	.9235	.0001
IBP 3 (<i>df</i> = 98)	2.8646	.0066	.1895	1.1975	.2765	.0099
IBP 4 (<i>df</i> = 98)	2.4165	.0200	.1648	0.9237	.3389	.0079
IBP 5 (<i>df</i> = 98)	2.2911	.0271	.1576	0.0863	.7695	.0007
IBP 6 (<i>df</i> = 99)	3.2356	.0026	.2073	0.0832	.7736	.0007
<u>Immediate Memory</u>						
CRP (<i>df</i> = 102)	4.3735	.0001	.2554	3.0263	.0849	.0221
IL-8 (<i>df</i> = 75)	3.6379	.0013	.2796	0.0522	.8200	.0005
IL-18 (<i>df</i> = 104)	3.8264	.0006	.2274	2.9089	.0911	.0216
MCP-1 (<i>df</i> = 67)	3.4706	.0021	.2930	0.0254	.8737	.0003
RANTES (<i>df</i> = 104)	3.3387	.0019	.2043	0.1802	.6721	.0014
ICAM-1 (<i>df</i> = 104)	3.5985	.0010	.2168	0.1664	.6841	.0013
VCAM-1 (<i>df</i> = 104)	3.9159	.0004	.2315	2.2238	.1389	.0164
MMP-3 (<i>df</i> = 104)	3.6009	.0010	.2169	0.0359	.8500	.0003
MMP-9 (<i>df</i> = 103)	3.6210	.0010	.2195	1.5813	.2114	.0120
IBP 1 (<i>df</i> = 99)	4.5592	.0001	.2692	2.9131	.0910	.0215
IBP 2 (<i>df</i> = 99)	3.2231	.0027	.2066	0.1376	.7115	.0011
IBP 3 (<i>df</i> = 99)	3.7567	.0007	.2329	0.9422	.3341	.0073
IBP 4 (<i>df</i> = 99)	3.4500	.0015	.2180	0.6044	.4388	.0048
IBP 5 (<i>df</i> = 99)	3.4491	.0015	.2180	1.5446	.2169	.01223
IBP 6 (<i>df</i> = 99)	3.2356	.0026	.2073	0.0832	.7736	.0007

*Indicates overall models that did not survive FDR correction

**Table B.1d | F statistics from moderation analyses, FDR corrected:
insula (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	2.9618	.0051	.1916	0.0955	.7579	.0008
IL-8 (<i>df</i> = 75)	2.0907	.0471*	.1823	0.0004	.9842	.0000
IL-18 (<i>df</i> = 102)	3.2068	.0027	.2010	3.6035	.0605	.0282
MCP-1 (<i>df</i> = 64)	1.5264	.1658	.1602	1.1538	.2868	.0151
RANTES (<i>df</i> = 102)	3.5973	.0010	.2201	1.0658	.3043	.0081
ICAM-1 (<i>df</i> = 102)	2.8851	.0061	.1845	0.0352	.8516	.0003
VCAM-1 (<i>df</i> = 102)	2.7374	.0089	.1767	0.1692	.6817	.0014
MMP-3 (<i>df</i> = 102)	2.9383	.0054	.1873	0.0424	.8372	.0003
MMP-9 (<i>df</i> = 101)	3.1336	.0033	.1989	1.6010	.2087	.0127
Complement C3 (<i>df</i> = 102)	3.7341	.0007	.2265	1.8344	.1786	.0139
Ferritin (<i>df</i> = 102)	4.0399	.0003	.2406	2.8491	.0945	.0212
IBP 1 (<i>df</i> = 97)	2.9669	.0052	.1966	0.0165	.8981	.0001
IBP 2 (<i>df</i> = 97)	2.6178	.0123	.1776	0.5479	.4610	.0046
IBP 3 (<i>df</i> = 97)	2.8674	.0066	.1913	0.8630	.3552	.0072
IBP 4 (<i>df</i> = 97)	2.8936	.0062	.1927	0.0078	.9297	.0001
IBP 5 (<i>df</i> = 97)	3.3291	.0021	.2154	0.0041	.9489	.0000
IBP 6 (<i>df</i> = 97)	2.7146	.0096	.1829	0.0078	.9299	.0001

*Indicates overall models that did not survive FDR correction

**Table B.1e | F statistics from moderation analyses, FDR corrected:
lateral occipital (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.0590	.0040	.1966	0.2150	.6439	.0017
IL-8 (<i>df</i> = 75)	2.5445	.0165	.2135	0.5447	.4628	.0057
IL-18 (<i>df</i> = 102)	2.7925	.0078	.1719	0.1128	.7376	.0009
MCP-1 (<i>df</i> = 64)	1.7572	.1024	.1801	0.8551	.3586	.0110
RANTES (<i>df</i> = 102)	3.6664	.0009	.2233	0.0442	.8339	.0003
ICAM-1 (<i>df</i> = 102)	3.2537	.0024	.2033	1.4474	.2317	.0113
VCAM-1 (<i>df</i> = 102)	2.9896	.0047	.1899	1.0310	.3123	.0082
MMP-3 (<i>df</i> = 102)	3.0883	.0037	.1950	0.3900	.5337	.0031
MMP-9 (<i>df</i> = 101)	3.0917	.0037	.1967	0.2445	.6220	.0019
Complement C3 (<i>df</i> = 102)	3.5665	.0011	.2186	0.2149	.6439	.0016
Ferritin (<i>df</i> = 102)	3.7983	.0006	.22295	0.1172	.7328	.0009
IBP 1 (<i>df</i> = 97)	3.3862	.0018	.2183	2.8752	.0932	.0232
IBP 2 (<i>df</i> = 97)	2.6381	.0117	.1787	0.7424	.3910	.0063
IBP 3 (<i>df</i> = 97)	2.8024	.0078	.1877	0.9030	.3443	.0076
IBP 4 (<i>df</i> = 97)	2.8352	.0072	.1895	0.0069	.9341	.0001
IBP 5 (<i>df</i> = 97)	3.2017	.0029	.2089	0.1890	.6647	.0015
IBP 6 (<i>df</i> = 97)	2.7030	.0099	.1823	0.0865	.7692	.0007

All significant overall models remained significant after FDR correction

**Table B.1f | F statistics from moderation analyses, FDR corrected:
lateral orbitofrontal (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.0672	.0039	.1970	0.1194	.7304	.0010
IL-8 (<i>df</i> = 75)	2.1361	.0425	.1856	0.1217	.7282	.0013
IL-18 (<i>df</i> = 102)	3.0964	.0036	.1954	2.2181	.1395	.0175
MCP-1 (<i>df</i> = 64)	1.4670	.1870	.1550	1.4427	.2341	.0190
RANTES (<i>df</i> = 102)	3.6435	.0009	.2223	0.8700	.3531	.0066
ICAM-1 (<i>df</i> = 102)	3.1001	.0036	.1956	0.2262	.6354	.0018
VCAM-1 (<i>df</i> = 102)	2.8977	.0060	.1852	0.6409	.4252	.0051
MMP-3 (<i>df</i> = 102)	3.0409	.0042	.1926	0.0024	.9611	.0000
MMP-9 (<i>df</i> = 101)	3.2594	.0024	.2052	1.8071	.1819	.0142
Complement C3 (<i>df</i> = 102)	3.5039	.0013	.2156	0.1206	.7291	.0009
Ferritin (<i>df</i> = 102)	4.2845	.0002	.2515	3.3680	.0694	.0247
IBP 1 (<i>df</i> = 97)	3.0509	.0042	.2010	0.3434	.5592	.0028
IBP 2 (<i>df</i> = 97)	2.8905	.0062	.1925	2.0908	.1514	.0174
IBP 3 (<i>df</i> = 97)	2.8510	.0069	.1904	0.5588	.4566	.0047
IBP 4 (<i>df</i> = 97)	2.9689	.0051	.1967	0.5568	.4574	.0046
IBP 5 (<i>df</i> = 97)	3.7026	.0008	.2339	2.0889	.1516	.0165
IBP 6 (<i>df</i> = 97)	2.9026	.0061	.1932	0.2610	.6106	.0022

All significant overall models remained significant after FDR correction

**Table B.1g | F statistics from moderation analyses, FDR corrected:
medial orbitofrontal (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	2.9868	.0048	.1929	0.1778	.6742	.0014
IL-8 (<i>df</i> = 75)	2.0725	.0491*	.1810	0.6310	.4295	.0069
IL-18 (<i>df</i> = 102)	2.7824	.0080	.1791	1.0363	.3111	.0083
MCP-1 (<i>df</i> = 64)	1.2818	.2688	.1381	0.0076	.4544	.0076
RANTES (<i>df</i> = 102)	3.3706	.0018	.2091	0.6721	.4142	.0052
ICAM-1 (<i>df</i> = 102)	2.9439	.0053	.1876	0.3024	.5836	.0024
VCAM-1 (<i>df</i> = 102)	2.7349	.0090	.1766	0.4508	.5035	.0036
MMP-3 (<i>df</i> = 102)	2.9236	.0056	.1865	0.0459	.8309	.0004
MMP-9 (<i>df</i> = 101)	3.3563	.0019	.2100	2.3854	.1256	.0187
Complement C3 (<i>df</i> = 102)	3.4187	.0016	.2114	0.0299	.8630	.0002
Ferritin (<i>df</i> = 102)	3.8700	.0005	.2329	2.3398	.1292	.0176
IBP 1 (<i>df</i> = 97)	2.8844	.0063	.1922	0.0131	.9091	.0001
IBP 2 (<i>df</i> = 97)	2.4707	.0176	.1693	0.1865	.6668	.0016
IBP 3 (<i>df</i> = 97)	2.8367	.0071	.1896	0.3599	.5500	.0030
IBP 4 (<i>df</i> = 97)	2.8635	.0067	.1910	0.5725	.4511	.0048
IBP 5 (<i>df</i> = 97)	3.1744	.0031	.2075	0.0025	.9604	.0000
IBP 6 (<i>df</i> = 97)	2.7019	.0100	.1822	0.1151	.7352	.0010

*Indicates overall models that did not survive FDR correction

Table B.1h | F statistics from moderation analyses, FDR corrected: paracentral gyrus (IV)

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>General Intelligence</u>						
CRP (<i>df</i> = 100)	4.4424	.0001	.2622	0.0373	.8472	.0003
IL-8 (<i>df</i> = 75)	4.3633	.0002	.3176	0.0036	.9526	.0000
IL-18 (<i>df</i> = 102)	4.2388	.0002	.2495	0.0385	.8449	.0003
MCP-1 (<i>df</i> = 64)	2.6683	.0136	.2501	0.8529	.3592	.0100
RANTES (<i>df</i> = 102)	5.1686	.0000	.2885	3.2281	.0753	.0225
ICAM-1 (<i>df</i> = 102)	4.1212	.0003	.2443	0.0053	.9423	.0000
VCAM-1 (<i>df</i> = 102)	4.4431	.0001	.2584	0.0165	.8982	.0001
MMP-3 (<i>df</i> = 102)	4.2386	.0002	.2495	0.1754	.6762	.0013
MMP-9 (<i>df</i> = 101)	4.2677	.0002	.2526	0.2341	.6295	.0017
α 2-macroglobulin (<i>df</i> = 102)	4.8381	.0000	.2751	0.9883	.3225	.0070
IBP 1 (<i>df</i> = 97)	4.0732	.0003	.2515	1.1797	.2801	.0091
IBP 2 (<i>df</i> = 97)	4.3345	.0002	.2633	2.5573	.1130	.0194
IBP 3 (<i>df</i> = 97)	3.8497	.0006	.2410	0.0807	.7769	.0006
IBP 4 (<i>df</i> = 97)	4.1012	.0003	.2528	0.2111	.6469	.0016
IBP 5 (<i>df</i> = 97)	5.1693	.0000	.2989	0.4658	.4966	.0034
IBP 6 (<i>df</i> = 97)	4.0018	.0004	.2481	0.9001	.3451	.0070
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.0480	.0041	.1960	0.1367	.7124	.0011
IL-8 (<i>df</i> = 75)	2.8560	.0079	.2335	1.1451	.2880	.0117
IL-18 (<i>df</i> = 102)	2.8308	.0070	.1817	0.0628	.8026	.0005
MCP-1 (<i>df</i> = 64)	1.8210	.0893	.1854	2.9830	.0890	.0380
RANTES (<i>df</i> = 102)	3.9128	.0005	.2348	1.6400	.2032	.0123
ICAM-1 (<i>df</i> = 102)	3.1193	.0034	.1966	0.2459	.6210	.0019
VCAM-1 (<i>df</i> = 102)	2.8666	.0064	.1836	0.0782	.7803	.0006
MMP-3 (<i>df</i> = 102)	3.1211	.0034	.1967	0.2510	.6175	.0020
MMP-9 (<i>df</i> = 101)	3.0898	.0037	.1966	0.3602	.5497	.0029
Complement C3 (<i>df</i> = 102)	3.6143	.0010	.2209	0.0015	.9696	.0000
Ferritin (<i>df</i> = 102)	3.9378	.0004	.2360	0.7160	.3994	.0054
IBP 1 (<i>df</i> = 97)	3.0179	.0045	.1993	0.3734	.5426	.0031
IBP 2 (<i>df</i> = 97)	3.0727	.0040	.2022	3.4932	.0646	.0287
IBP 3 (<i>df</i> = 97)	2.7594	.0086	.1854	0.1142	.7362	.0010
IBP 4 (<i>df</i> = 97)	2.9479	.0054	.1956	0.2990	.5858	.0025
IBP 5 (<i>df</i> = 97)	3.3534	.0020	.2167	0.9651	.3284	.0078
IBP 6 (<i>df</i> = 97)	2.8493	.0069	.1903	0.4125	.5222	.0034

**Table B.1h | F statistics from moderation analyses, FDR corrected:
paracentral gyrus (IV), continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	<i>R</i> ²
<u>Immediate Memory</u>						
CRP (<i>df</i> = 102)	3.5381	.0012	.2172	1.0472	.2086	.0080
IL-8 (<i>df</i> = 75)	3.6420	.0012	.2798	0.0426	.8371	.0004
IL-18 (<i>df</i> = 104)	3.2960	.0022	.2023	2.8915	.0920	.0222
MCP-1 (<i>df</i> = 67)	3.1105	.0048	.2708	0.0159	.9001	.0002
RANTES (<i>df</i> = 104)	3.1322	.0033	.1942	1.9717	.1632	.0153
ICAM-1 (<i>df</i> = 104)	3.1266	.0033	.1939	0.4906	.4852	.0038
VCAM-1 (<i>df</i> = 104)	3.2315	.0025	.1991	1.0385	.3105	.0080
MMP-3 (<i>df</i> = 104)	3.0780	.0037	.1914	0.2414	.6243	.0019
MMP-9 (<i>df</i> = 103)	2.9443	.0053	.1861	0.8644	.3547	.0068
IBP 1 (<i>df</i> = 99)	3.8039	.0006	.2351	2.3024	.1324	.0178
IBP 2 (<i>df</i> = 99)	2.9006	.0060	.1899	1.6616	.2004	.0136
IBP 3 (<i>df</i> = 99)	3.0614	.0040	.1983	0.0410	.8399	.0003
IBP 4 (<i>df</i> = 99)	3.1134	.0035	.2010	1.7965	.1832	.0145
IBP 5 (<i>df</i> = 99)	2.8287	.0072	.1861	1.1548	.2852	.0095
IBP 6 (<i>df</i> = 99)	2.8834	.0063	.1890	1.4119	.2376	.0116

All significant overall models remained significant after FDR correction

**Table B.1i | F statistics from moderation analyses, FDR corrected:
pars opercularis (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.3784	.0018	.2128	0.0420	.8379	.0003
IL-8 (<i>df</i> = 75)	2.6202	.0138	.2184	2.7227	.1031	.0284
IL-18 (<i>df</i> = 102)	3.1468	.0032	.1979	0.0038	.9509	.0000
MCP-1 (<i>df</i> = 64)	1.4079	.2104	.1496	0.0286	.8664	.0004
RANTES (<i>df</i> = 102)	4.3368	.0002	.2538	1.0334	.3118	.0076
ICAM-1 (<i>df</i> = 102)	3.4909	.0013	.2149	0.0702	.7915	.0005
VCAM-1 (<i>df</i> = 102)	3.2188	.0027	.2016	0.1908	.6632	.0015
MMP-3 (<i>df</i> = 102)	3.4400	.0015	.2125	0.0000	.9954	.0000
MMP-9 (<i>df</i> = 101)	3.5338	.0012	.2187	0.0508	.8221	.0004
Complement C3 (<i>df</i> = 102)	4.1549	.0002	.2458	0.0561	.8132	.0004
Ferritin (<i>df</i> = 102)	4.0735	.0003	.2421	0.0959	.7574	.0007
IBP 1 (<i>df</i> = 97)	3.6237	.0010	.2301	0.9300	.3372	.0074
IBP 2 (<i>df</i> = 97)	3.5296	.0013	.2255	2.7523	.1003	.0220
IBP 3 (<i>df</i> = 97)	3.3732	.0019	.2177	0.3563	.5519	.0029
IBP 4 (<i>df</i> = 97)	3.5804	.0011	.2280	0.3882	.5347	.0031
IBP 5 (<i>df</i> = 97)	4.1480	.0003	.2549	1.3453	.2490	.0103
IBP 6 (<i>df</i> = 97)	3.4325	.0016	.2205	0.1362	.7129	.0011

All significant overall models remained significant after FDR correction

**Table B.1j | F statistics from moderation analyses, FDR corrected:
pars orbitalis (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	2.9919	.0048	.1931	0.1162	.7339	.0009
IL-8 (<i>df</i> = 75)	1.9454	.0654	.1718	0.0038	.9509	.0000
IL-18 (<i>df</i> = 102)	2.7054	.0096	.1750	0.9237	.3388	.0075
MCP-1 (<i>df</i> = 64)	1.2619	.2792	.1362	0.2376	.6276	.0032
RANTES (<i>df</i> = 102)	3.2924	.0022	.2053	0.1427	.7064	.0011
ICAM-1 (<i>df</i> = 102)	3.4345	.0015	.2122	3.8883	.0513	.0300
VCAM-1 (<i>df</i> = 102)	2.7817	.0080	.1791	0.96`2	.3292	.0077
MMP-3 (<i>df</i> = 102)	2.9594	.0051	.1884	0.6844	.4100	.0054
MMP-9 (<i>df</i> = 101)	2.9143	.0057	.1875	0.5403	.4640	.0043
Complement C3 (<i>df</i> = 102)	3.5414	.0012	.2174	1.5873	.2106	.0122
Ferritin (<i>df</i> = 102)	3.9787	.0004	.2378	3.0132	.0856	.0225
IBP 1 (<i>df</i> = 97)	3.1589	.0032	.2067	2.1965	.1416	.0180
IBP 2 (<i>df</i> = 97)	2.6421	.0115	.1789	2.0714	.1533	.0175
IBP 3 (<i>df</i> = 97)	2.7559	.0087	.1852	1.5196	.2207	.0128
IBP 4 (<i>df</i> = 97)	2.8832	.0064	.1921	1.2963	.2577	.0108
IBP 5 (<i>df</i> = 97)	3.0836	.0039	.2028	0.0014	.9703	.0000
IBP 6 (<i>df</i> = 97)	2.6420	.0115	.1789	0.4008	.5281	.0034

All significant overall models remained significant after FDR correction

**Table B.1k | F statistics from moderation analyses, FDR corrected:
rostral anterior cingulate (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.1919	.0029	.2034	0.1109	.7398	.0009
IL-8 (<i>df</i> = 75)	2.3109	.0284	.1978	0.5127	.4762	.0055
IL-18 (<i>df</i> = 102)	3.5282	.0012	.2167	3.9234	.0503	.0301
MCP-1 (<i>df</i> = 64)	1.3021	.2586	.1400	0.0477	.8279	.0006
RANTES (<i>df</i> = 102)	3.9211	.0005	.2352	1.0993	.2969	.0082
ICAM-1 (<i>df</i> = 102)	3.2120	.0027	.2012	0.0114	.9151	.0001
VCAM-1 (<i>df</i> = 102)	3.2436	.0025	.2028	1.7489	.1890	.0137
MMP-3 (<i>df</i> = 102)	3.2307	.0026	.2022	0.0028	.9579	.0000
MMP-9 (<i>df</i> = 101)	3.1831	.0029	.2014	0.3564	.5519	.0028
Complement C3 (<i>df</i> = 102)	3.9083	.0005	.2346	1.0609	.3054	.0080
Ferritin (<i>df</i> = 102)	3.7102	.0008	.2254	0.0458	.8310	.0003
IBP 1 (<i>df</i> = 97)	3.3420	.0020	.2161	1.1450	.2873	.0093
IBP 2 (<i>df</i> = 97)	3.0632	.0041	.2017	2.0497	.1554	.0169
IBP 3 (<i>df</i> = 97)	3.1577	.0032	.2066	1.5383	.2179	.0126
IBP 4 (<i>df</i> = 97)	3.3082	.0022	.2144	0.8279	.3651	.0067
IBP 5 (<i>df</i> = 97)	3.4653	.0015	.2223	0.0030	.9563	.0000
IBP 6 (<i>df</i> = 97)	2.9465	.0054	.1955	0.0573	.8113	.0005
<u>General Intelligence</u>						
CRP (<i>df</i> = 100)	4.4129	.0001	.2609	0.4181	.5193	.0031
IL-8 (<i>df</i> = 75)	3.4579	.0019	.2695	0.6166	.4348	.0060
IL-18 (<i>df</i> = 102)	4.3008	.0002	.2522	0.6931	.4071	.0051
MCP-1 (<i>df</i> = 64)	2.4660	.0214	.2356	0.2576	.6135	.0031
RANTES (<i>df</i> = 102)	4.7608	.0001	.2719	1.6218	.2057	.0116
ICAM-1 (<i>df</i> = 102)	4.0862	.0003	.2427	0.2722	.6030	.0020
VCAM-1 (<i>df</i> = 102)	4.4123	.0001	.2571	1.2264	.2707	.0089
MMP-3 (<i>df</i> = 102)	4.1634	.0002	.2462	0.0941	.7596	.0007
MMP-9 (<i>df</i> = 101)	4.2415	.0002	.2515	0.4832	.4886	.0036
α 2-macroglobulin (<i>df</i> = 102)	4.8259	.0000	.2746	1.2431	.2675	.0088
IBP 1 (<i>df</i> = 97)	4.4082	.0001	.2666	3.1084	.0810	.0235
IBP 2 (<i>df</i> = 97)	4.2030	.0002	.2574	1.7395	.1903	.0133
IBP 3 (<i>df</i> = 97)	3.9051	.0005	.2436	0.3466	.5574	.0027
IBP 4 (<i>df</i> = 97)	4.1343	.0003	.2453	0.0009	.9756	.0000
IBP 5 (<i>df</i> = 97)	5.4026	.0000	.3082	1.2968	.2576	.0092
IBP 6 (<i>df</i> = 97)	3.8798	.0005	.2424	0.0002	.9902	.0000

All significant overall models remained significant after FDR correction

**Table B.1m | F statistics from moderation analyses, FDR corrected:
superior frontal (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	3.1045	.0036	.1989	0.0190	.8908	.0002
IL-8 (<i>df</i> = 75)	2.4581	.0202	.2077	0.7658	.3843	.0081
IL-18 (<i>df</i> = 102)	3.2908	.0022	.2052	2.6550	.1063	.0207
MCP-1 (<i>df</i> = 64)	1.4945	.1769	.1574	1.1248	.2929	.0148
RANTES (<i>df</i> = 102)	3.6654	.0009	.2233	0.0988	.7539	.0008
ICAM-1 (<i>df</i> = 102)	3.2531	.0024	.2033	0.0051	.9432	.0000
VCAM-1 (<i>df</i> = 102)	2.8928	.0060	.1849	0.0371	.8476	.0003
MMP-3 (<i>df</i> = 102)	3.1239	.0034	.1968	0.0085	.9268	.0001
MMP-9 (<i>df</i> = 101)	3.4886	.0014	.2165	2.4314	.1221	.0189
Complement C3 (<i>df</i> = 102)	3.8956	.0005	.2340	0.3263	.5691	.0025
Ferritin (<i>df</i> = 102)	4.1710	.0002	.2465	1.2348	.2691	.0091
IBP 1 (<i>df</i> = 97)	3.0650	.0040	.2018	0.0016	.9687	.0000
IBP 2 (<i>df</i> = 97)	3.1401	.0034	.2057	2.6691	.1056	.0219
IBP 3 (<i>df</i> = 97)	3.0329	.0044	.2001	0.0097	.9217	.0001
IBP 4 (<i>df</i> = 97)	3.1619	.0032	.2068	0.2723	.6030	.0022
IBP 5 (<i>df</i> = 97)	3.7137	.0008	.2345	1.1740	.2813	.0093
IBP 6 (<i>df</i> = 97)	3.0558	.0041	.2013	0.3459	.5578	.0028

All significant overall models remained significant after FDR correction

**Table B.1n | F statistics from moderation analyses, FDR corrected:
temporal pole (IV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Fluid Intelligence</u>						
CRP (<i>df</i> = 100)	4.0098	.0004	.2429	0.3969	.5301	.0030
IL-8 (<i>df</i> = 75)	2.7539	.0101	.2271	1.3136	.2554	.0135
IL-18 (<i>df</i> = 102)	3.3469	.0019	.2079	0.6241	.4314	.0048
MCP-1 (<i>df</i> = 64)	1.4371	.1985	.1523	0.0015	.9688	.0000
RANTES (<i>df</i> = 102)	3.9819	.0004	.2380	0.2253	.6360	.0017
ICAM-1 (<i>df</i> = 102)	3.4202	.0016	.2115	0.1623	.6879	.0013
VCAM-1 (<i>df</i> = 102)	3.4760	.0014	.2142	1.2981	.2572	.0100
MMP-3 (<i>df</i> = 102)	3.6574	.0009	.2229	0.6239	.4315	.0048
MMP-9 (<i>df</i> = 101)	3.6630	.0009	.2249	0.9154	.3410	.0070
Complement C3 (<i>df</i> = 102)	4.3887	.0001	.2561	2.0901	.1513	.0152
Ferritin (<i>df</i> = 102)	4.6000	.0001	.2651	2.1441	.1462	.0154
IBP 1 (<i>df</i> = 97)	3.7799	.0007	.2377	1.0816	.2009	.0085
IBP 2 (<i>df</i> = 97)	3.1723	.0031	.2074	0.3205	.5726	.0026
IBP 3 (<i>df</i> = 97)	3.3766	.0019	.2178	0.2273	.6346	.0018
IBP 4 (<i>df</i> = 97)	3.6960	.0008	.2336	1.4771	.2272	.0117
IBP 5 (<i>df</i> = 97)	4.3168	.0002	.2626	0.3711	.5439	.0028
IBP 6 (<i>df</i> = 97)	3.1705	.0031	.2073	0.0096	.9221	.0001
<u>Immediate Memory</u>						
CRP (<i>df</i> = 102)	3.9485	.0004	.2365	0.0223	.8816	.0002
IL-8 (<i>df</i> = 75)	3.3475	.0025	.2631	1.9787	.1637	.0194
IL-18 (<i>df</i> = 104)	3.0698	.0038	.1910	0.4794	.4902	.0037
MCP-1 (<i>df</i> = 67)	2.7947	.0099	.2502	1.3157	.2554	.0147
RANTES (<i>df</i> = 104)	2.9714	.0049	.1860	0.0299	.8630	.0002
ICAM-1 (<i>df</i> = 104)	3.1416	.0032	.1946	0.7035	.4035	.0054
VCAM-1 (<i>df</i> = 104)	3.0835	.0037	.1917	0.0448	.8328	.0003
MMP-3 (<i>df</i> = 104)	3.1888	.0028	.1970	0.0553	.8146	.0004
MMP-9 (<i>df</i> = 103)	3.1523	.0031	.1967	1.1840	.2791	.0092
IBP 1 (<i>df</i> = 99)	3.5622	.0011	.2235	0.2433	.6229	.0019
IBP 2 (<i>df</i> = 99)	2.9332	.0055	.1916	1.1066	.2954	.0090
IBP 3 (<i>df</i> = 99)	3.1416	.0033	.2025	0.1146	.7357	.0009
IBP 4 (<i>df</i> = 99)	3.2314	.0026	.2071	0.7775	.3800	.0062
IBP 5 (<i>df</i> = 99)	2.9035	.0060	.1900	0.8702	.3532	.0071
IBP 6 (<i>df</i> = 99)	3.1732	.0030	.2041	0.9528	.3314	.0077

All significant overall models remained significant after FDR correction

**Table B.1p | F statistics from moderation analyses, FDR corrected:
frontal pole (IV) and immediate memory (DV)**

Moderating Variable	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
CRP (<i>df</i> = 102)	3.8128	.0006	.2302	0.3462	.5575	.0026
IL-8 (<i>df</i> = 75)	3.1202	.0043	.2497	0.0032	.9549	.0000
IL-18 (<i>df</i> = 104)	2.7683	.0082	.1756	0.6679	.4156	.0053
MCP-1 (<i>df</i> = 67)	3.3719	.0026	.2870	0.2301	.6330	.0024
RANTES (<i>df</i> = 104)	2.6300	.0115	.1683	0.0018	.9661	.0000
ICAM-1 (<i>df</i> = 104)	2.8144	.0073	.1780	0.2498	.6183	.0020
VCAM-1 (<i>df</i> = 104)	3.0266	.0043	.1888	1.4881	.2253	.0116
MMP-3 (<i>df</i> = 104)	2.7814	.0079	.1762	0.0513	.8213	.0004
MMP-9 (<i>df</i> = 103)	2.9059	.0058	.1841	1.1734	.2812	.0093
IBP 1 (<i>df</i> = 99)	3.6439	.0009	.2275	1.3772	.2434	.0107
IBP 2 (<i>df</i> = 99)	2.8276	.0072	.1860	0.0701	.7917	.0006
IBP 3 (<i>df</i> = 99)	3.3048	.0022	.2108	0.7504	.3884	.0060
IBP 4 (<i>df</i> = 99)	3.3360	.0020	.2133	0.4325	.5123	.0034
IBP 5 (<i>df</i> = 99)	2.8244	.0073	.1858	0.0075	.9311	.0001
IBP 6 (<i>df</i> = 99)	3.3835	.0018	.2147	3.3114	.0718	.0263

All significant overall models remained significant after FDR correction

**Table B.1q | F statistics from moderation analyses, FDR corrected:
posterior cingulate (IV) and auditory memory (DV)**

Moderating Variable	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
CRP (<i>df</i> = 101)	2.8666	.0065	.1850	1.4988	.2237	.0121
IL-8 (<i>df</i> = 75)	2.3872	.0238	.2030	1.1049	.2966	.0117
IL-18 (<i>df</i> = 103)	2.6187	.0119	.1690	1.9574	.1648	.0158
MCP-1 (<i>df</i> = 65)	1.8807	.0782	.1880	0.4370	.5109	.0055
RANTES (<i>df</i> = 103)	2.5113	.0155	.1632	0.3366	.5631	.0027
ICAM-1 (<i>df</i> = 103)	2.7416	.0088	.1756	0.3225	.5714	.0026
VCAM-1 (<i>df</i> = 103)	2.5337	.0147	.1644	0.0000	.9970	.0000
MMP-3 (<i>df</i> = 103)	2.4173	.0196	.1581	0.0034	.9535	.0000
MMP-9 (<i>df</i> = 102)	2.6632	.0107	.1728	2.1603	.1447	.0175
Factor VII (<i>df</i> = 103)	3.0621	.0039	.1921	1.1625	.2835	.0091
IBP 1 (<i>df</i> = 98)	2.7428	.0090	.1829	0.0736	.7868	.0006
IBP 2 (<i>df</i> = 98)	2.1788	.0355	.1510	0.0089	.9250	.0001
IBP 3 (<i>df</i> = 98)	3.1007	.0037	.2020	2.9371	.0897	.0239
IBP 4 (<i>df</i> = 98)	2.3321	.0245	.1599	0.9137	.3415	.0078
IBP 5 (<i>df</i> = 98)	2.3797	.0218	.1627	1.4992	.2237	.0128
IBP 6 (<i>df</i> = 98)	2.1948	.0341	.1519	0.1259	.7235	.0011

All significant overall models remained significant after FDR correction

**Table B.1r | F statistics from moderation analyses, FDR corrected:
precuneus (IV)**

General Intelligence	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
CRP (<i>df</i> = 100)	4.2778	.0002	.2550	0.0011	.9732	.0000
IL-8 (<i>df</i> = 75)	3.3845	.0023	.2653	0.3047	.5826	.0030
IL-18 (<i>df</i> = 102)	4.3485	.0002	.2543	1.4680	.2285	.0107
MCP-1 (<i>df</i> = 64)	2.3835	.0258	.2295	0.0781	.7808	.0009
RANTES (<i>df</i> = 102)	4.7258	.0001	.2704	1.7498	.1889	.0125
ICAM-1 (<i>df</i> = 102)	4.3288	.0002	.2535	2.0627	.1540	.0151
VCAM-1 (<i>df</i> = 102)	4.4123	.0001	.2571	1.2264	.2707	.0089
MMP-3 (<i>df</i> = 102)	4.1450	.0003	.2458	0.4361	.5105	.0032
MMP-9 (<i>df</i> = 101)	4.3259	.0002	.2552	0.6257	.4308	.0046
α 2-macroglobulin (<i>df</i> = 102)	4.5826	.0001	.2644	0.0148	.9036	.0001
IBP 1 (<i>df</i> = 97)	3.9943	.0004	.2478	0.8283	.3650	.0064
IBP 2 (<i>df</i> = 97)	4.3538	.0002	.2642	2.9062	.0914	.0220
IBP 3 (<i>df</i> = 97)	3.9934	.0004	.2478	1.1843	.2792	.0092
IBP 4 (<i>df</i> = 97)	4.0243	.0004	.2492	0.0496	.8242	.0004
IBP 5 (<i>df</i> = 97)	5.0389	.0000	.2936	0.1115	.7391	.0008
IBP 6 (<i>df</i> = 97)	4.1301	.0003	.2541	1.9818	.1624	.0152
<u>Immediate Memory</u>						
CRP (<i>df</i> = 102)	3.7370	.0007	.2267	2.7634	.0995	.0210
IL-8 (<i>df</i> = 75)	2.8678	.0077	.2342	0.9106	.3430	.0093
IL-18 (<i>df</i> = 104)	3.0552	.0040	.1903	2.2645	.1354	.0176
MCP-1 (<i>df</i> = 67)	3.2134	.0038	.2773	3.1812	.0790	.0343
RANTES (<i>df</i> = 104)	2.6969	.0098	.1718	0.0049	.9443	.0000
ICAM-1 (<i>df</i> = 104)	2.8985	.0059	.1823	0.1227	.7268	.0010
VCAM-1 (<i>df</i> = 104)	3.2025	.0027	.1978	0.6034	.4390	.0047
MMP-3 (<i>df</i> = 104)	2.8702	.0063	.1809	0.0134	.9081	.0001
MMP-9 (<i>df</i> = 103)	2.7660	.0082	.1768	0.2154	.6436	.0017
IBP 1 (<i>df</i> = 99)	3.9343	.0004	.2412	2.4140	.1234	.0185
IBP 2 (<i>df</i> = 99)	2.6322	.0117	.1754	0.1920	.6622	.0016
IBP 3 (<i>df</i> = 99)	3.5405	.0012	.2225	3.4484	.0663	.0271
IBP 4 (<i>df</i> = 99)	2.8788	.0064	.1887	0.3221	.5716	.0026
IBP 5 (<i>df</i> = 99)	3.0392	.0043	.1972	2.8830	.0927	.0234
IBP 6 (<i>df</i> = 99)	2.9607	.0052	.1931	2.1907	.1420	.0179

All significant overall models remained significant after FDR correction

B. 2 Peripheral Biomarkers and Functional Connectivity

Table B.2a | F statistics from moderation analyses, FDR corrected: DMN efficiency, fluid intelligence

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 81)	2.5673	.0151	.2023	0.0463	.8302	.0005
IL-8 (<i>df</i> = 60)	1.5782	.1506	.1738	0.1027	.7498	.0014
IL-18 (<i>df</i> = 83)	2.4746	.0186	.1926	1.7100	.1946	.0166
MCP-1 (<i>df</i> = 53)	1.1840	.3262	.1516	0.0306	.8617	.0005
RANTES (<i>df</i> = 83)	2.6437	.0124	.2031	0.4495	.5044	.0043
ICAM-1 (<i>df</i> = 83)	2.2785	.0295	.1801	0.3640	.5479	.0036
VCAM-1 (<i>df</i> = 83)	2.3227	.0266	.1829	0.4077	.5249	.0040
MMP-3 (<i>df</i> = 83)	2.3805	.0232	.1866	0.0127	.9107	.0001
MMP-9 (<i>df</i> = 82)	2.7919	.0087	.2141	0.709	.4151	.0064
α 2-macroglobulin (<i>df</i> = 83)	2.3314	.0261	.1835	0.1160	.7343	.0011
β 2-microglobulin (<i>df</i> = 83)	2.2880	.0289	.1807	0.2031	.6534	.0020
Complement C3 (<i>df</i> = 83)	3.4209	.0019	.2480	3.6664	.0590	.0332
Factor VII (<i>df</i> = 83)	2.4076	.0218	.1884	0.1542	.6955	.0015
Ferritin (<i>df</i> = 83)	2.9548	.0059	.2217	0.8020	.3731	.0075
Fibrinogen (<i>df</i> = 83)	2.8235	.0081	.2139	2.4207	.1235	.0229
TIMP-1 (<i>df</i> = 83)	2.2913	.0286	.1809	0.5551	.4583	.0055
IBP 1 (<i>df</i> = 79)	2.2745	.0303	.1872	0.3503	.5556	.0036
IBP 2 (<i>df</i> = 79)	2.0904	.0464*	.1747	1.7844	.1854	.0186
IBP 3 (<i>df</i> = 79)	1.9632	.0620	.1658	0.0050	.9438	.0001
IBP 4 (<i>df</i> = 79)	2.4243	.0214	.1971	2.9808	.0882	.0303
IBP 5 (<i>df</i> = 79)	2.3658	.0245	.1933	0.0262	.8718	.0003
IBP 6 (<i>df</i> = 79)	2.0111	.0556	.1692	0.0138	.9067	.0001
<u>Global Efficiency</u>						
CRP (<i>df</i> = 81)	2.6017	.0139	.2044	0.3404	.5612	.0033
IL-8 (<i>df</i> = 60)	1.5876	.1477	.1747	0.0631	.8026	.0009
IL-18 (<i>df</i> = 83)	2.6843	.0112	.2055	3.0598	.0839	.0293
MCP-1 (<i>df</i> = 53)	1.3650	.2333	.1708	1.4795	.2292	.0231
RANTES (<i>df</i> = 83)	2.5630	.0150	.1981	0.0001	.9931	.0000
ICAM-1 (<i>df</i> = 83)	2.5858	.0142	.1995	2.3505	.1290	.0227
VCAM-1 (<i>df</i> = 83)	2.6255	.0129	.2020	2.3464	.1294	.0226
MMP-3 (<i>df</i> = 83)	2.3868	.0229	.1870	0.0578	.8106	.0006
MMP-9 (<i>df</i> = 82)	2.7444	.0098	.2112	0.3368	.5633	.0032
α 2-macroglobulin (<i>df</i> = 83)	2.3515	.0248	.1848	0.2301	.6327	.0023
β 2-microglobulin (<i>df</i> = 83)	2.3190	.0268	.1827	0.3961	.5308	.0039
Complement C3 (<i>df</i> = 83)	3.0569	.0046	.2276	1.2308	.2705	.0115
Factor VII (<i>df</i> = 83)	2.3993	.0222	.1878	0.0385	.8449	.0004
Ferritin (<i>df</i> = 83)	2.8469	.0076	.2153	0.0670	.7964	.0006
Fibrinogen (<i>df</i> = 83)	2.5096	.0171	.1948	0.2683	.6059	.0026
TIMP-1 (<i>df</i> = 83)	2.3235	.0265	.1830	0.7094	.4021	.0070
IBP 1 (<i>df</i> = 79)	2.3950	.0229	.1952	1.0959	.2984	.0112
IBP 2 (<i>df</i> = 79)	1.8379	.0822	.1569	0.0162	.8990	.0002
IBP 3 (<i>df</i> = 79)	2.0374	.0524	.1710	0.3965	.5307	.0042
IBP 4 (<i>df</i> = 79)	2.2899	.0292	.1882	1.8296	.1800	.0188

Table B.2a (cont.) | F statistics from moderation analyses, FDR corrected: DMN efficiency, fluid intelligence; continued

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Global Efficiency, cont.</u>						
IBP 5 (<i>df</i> = 79)	2.4067	.0223	.1960	0.2782	.5994	.0028
IBP 6 (<i>df</i> = 79)	2.0154	.0551	.1695	0.0002	.9877	.0000
<u>Small World Propensity</u>						
CRP (<i>df</i> = 81)	3.0092	.0052	.2291	0.0264	.8714	.0003
IL-8 (<i>df</i> = 60)	1.8889	.0784	.2012	1.7155	.1953	.0228
IL-18 (<i>df</i> = 83)	2.6796	.0114	.2053	1.6925	.1969	.0162
MCP-1 (<i>df</i> = 53)	1.4984	.1801	.1845	0.6645	.4186	.0102
RANTES (<i>df</i> = 83)	2.9872	.0054	.2236	0.8493	.3594	.0079
ICAM-1 (<i>df</i> = 83)	2.4571	.0193	.1915	0.2365	.6280	.0023
VCAM-1 (<i>df</i> = 83)	2.6081	.0135	.2009	0.9754	.3262	.0094
MMP-3 (<i>df</i> = 83)	2.6117	.0134	.2011	0.0709	.7907	.0007
MMP-9 (<i>df</i> = 82)	3.0127	.0051	.2272	0.6922	.4078	.0065
α 2-macroglobulin (<i>df</i> = 83)	2.5303	.0163	.1961	0.0097	.9217	.0001
β 2-microglobulin (<i>df</i> = 83)	2.5601	.0151	.1979	0.2962	.5877	.0029
Complement C3 (<i>df</i> = 83)	3.0491	.0047	.2271	0.2655	.6078	.0025
Factor VII (<i>df</i> = 83)	3.1011	.0041	.2301	3.5096	.0645	.0326
Ferritin (<i>df</i> = 83)	3.3682	.0022	.2451	1.6762	.1990	.0152
Fibrinogen (<i>df</i> = 83)	2.6859	.0112	.2056	0.1811	.6716	.0017
TIMP-1 (<i>df</i> = 83)	2.6640	.0118	.2043	1.6562	.2017	.0159
IBP 1 (<i>df</i> = 79)	2.5348	.0165	.2043	0.0357	.8506	.0004
IBP 2 (<i>df</i> = 79)	2.0296	.0533	.1705	0.0010	.9751	.0000
IBP 3 (<i>df</i> = 79)	2.1637	.0392	.1797	0.2684	.6058	.0028
IBP 4 (<i>df</i> = 79)	2.2101	.0352	.1829	0.5849	.4467	.0061
IBP 5 (<i>df</i> = 79)	2.7348	.0102	.2169	0.0012	.9730	.0000
IBP 6 (<i>df</i> = 79)	2.3135	.0277	.1898	0.1053	.7465	.0011

*Indicates overall models that did not survive FDR correction

Table B.2b | F statistics from moderation analyses, FDR corrected: DMN efficiency, general intelligence

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 82)	3.2487	.0029	.2407	0.6466	.4237	.0060
IL-8 (<i>df</i> = 61)	2.0002	.0614	.2078	0.0020	.9642	.0000
IL-18 (<i>df</i> = 84)	2.9255	.0062	.2179	0.0001	.9914	.0000
MCP-1 (<i>df</i> = 54)	1.6243	.1396	.1940	0.0059	.9388	.0001
RANTES (<i>df</i> = 84)	3.0157	.0050	.2231	0.0096	.9222	.0001
ICAM-1 (<i>df</i> = 84)	2.7296	.0100	.2063	0.0171	.8961	.0002
VCAM-1 (<i>df</i> = 84)	3.1804	.0034	.2325	0.9993	.3202	.0091
MMP-3 (<i>df</i> = 84)	2.7787	.0089	.2093	0.0602	.8068	.0006
MMP-9 (<i>df</i> = 83)	3.0282	.0049	.2259	0.2979	.5867	.0028
α 2-macroglobulin (<i>df</i> = 84)	3.2930	.0026	.2387	0.6844	.4104	.0062
β 2-microglobulin (<i>df</i> = 84)	2.7265	.0099	.2067	0.1250	.7246	.0012
Complement C3 (<i>df</i> = 84)	3.6439	.0011	.2576	0.4767	.4918	.0042
Factor VII (<i>df</i> = 84)	2.8871	.0069	.2157	0.8406	.3618	.0078
Ferritin (<i>df</i> = 84)	3.2590	.0028	.2369	0.2037	.6529	.0019
Fibrinogen (<i>df</i> = 84)	3.0633	.0045	.2259	1.1197	.2930	.0103
TIMP-1 (<i>df</i> = 84)	2.8610	.0073	.2141	0.0118	.9139	.0001
IBP 1 (<i>df</i> = 80)	2.7557	.0097	.2160	0.7664	.3840	.0075
IBP 2 (<i>df</i> = 80)	2.8015	.0087	.2188	1.1756	.2815	.0115
IBP 3 (<i>df</i> = 80)	2.6679	.0119	.2106	0.3529	.5542	.0035
IBP 4 (<i>df</i> = 80)	2.8888	.0070	.2241	0.4249	.5164	.0041
IBP 5 (<i>df</i> = 80)	4.0282	.0005	.2872	0.6742	.4140	.0060
IBP 6 (<i>df</i> = 80)	3.0083	.0053	.2313	2.5325	.1155	.0243
<u>Global Efficiency</u>						
CRP (<i>df</i> = 82)	3.2080	.0032	.2384	0.6683	.4160	.0062
IL-8 (<i>df</i> = 61)	2.0604	.0539	.2127	0.3847	.5374	.0050
IL-18 (<i>df</i> = 84)	3.0422	.0047	.2246	0.5250	.4707	.0048
MCP-1 (<i>df</i> = 54)	2.1254	.0489*	.2395	2.2792	.1369	.0321
RANTES (<i>df</i> = 84)	3.0062	.0051	.2226	0.1570	.6929	.0015
ICAM-1 (<i>df</i> = 84)	3.0669	.0044	.2261	2.1672	.1447	.0200
VCAM-1 (<i>df</i> = 84)	3.3613	.0022	.2425	2.1106	.1500	.0190
MMP-3 (<i>df</i> = 84)	2.7762	.0090	.2091	0.0959	.7576	.0009
MMP-9 (<i>df</i> = 83)	2.9829	.0055	.2233	0.0079	.9292	.0001
α 2-macroglobulin (<i>df</i> = 84)	3.4700	.0017	.2484	1.9722	.1639	.0176
β 2-microglobulin (<i>df</i> = 84)	2.8451	.0076	.2132	0.8095	.3708	.0076
Complement C3 (<i>df</i> = 84)	3.6759	.0010	.2593	0.4853	.4879	.0043
Factor VII (<i>df</i> = 84)	2.7556	.0094	.2079	0.0213	.8843	.0002
Ferritin (<i>df</i> = 84)	3.2595	.0028	.2369	0.2732	.6025	.0025
Fibrinogen (<i>df</i> = 84)	2.9065	.0065	.2168	0.0118	.9138	.0001
TIMP-1 (<i>df</i> = 84)	2.9258	.0062	.2179	0.4423	.5079	.0001
IBP 1 (<i>df</i> = 80)	2.8237	.0082	.2202	1.1252	.2920	.0110
IBP 2 (<i>df</i> = 80)	2.6270	.0131	.2080	0.0003	.9870	.0000
IBP 3 (<i>df</i> = 80)	2.7186	.0106	.2137	0.5613	.4559	.0055
IBP 4 (<i>df</i> = 80)	2.8942	.0070	.2245	0.1355	.7138	.0013
IBP 5 (<i>df</i> = 80)	3.9247	.0006	.2819	0.2332	.6305	.0021
IBP 6 (<i>df</i> = 80)	2.6382	.0128	.2087	0.0544	.8162	.0005

Table B.2b (cont.) | F statistics from moderation analyses, FDR corrected: DMN efficiency, general intelligence; continued

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 82)	4.6812	.0001	.3135	0.0004	.9832	.0000
IL-8 (<i>df</i> = 61)	2.8719	.0089	.2736	1.0789	.3031	.0128
IL-18 (<i>df</i> = 84)	3.9482	.0005	.2733	0.3420	.5602	.0030
MCP-1 (<i>df</i> = 54)	1.9381	.0728	.2231	1.0929	.3005	.0157
RANTES (<i>df</i> = 84)	4.2677	.0002	.2890	0.4542	.5022	.0038
ICAM-1 (<i>df</i> = 84)	3.9221	.0006	.2720	1.3617	.2465	.0118
VCAM-1 (<i>df</i> = 84)	4.3578	.0002	.2933	1.5834	.2118	.0133
MMP-3 (<i>df</i> = 84)	3.7986	.0008	.2657	0.1820	.6708	.0016
MMP-9 (<i>df</i> = 83)	4.0626	.0004	.2814	0.5656	.4541	.0049
α 2-macroglobulin (<i>df</i> = 84)	4.4202	.0002	.2963	0.8943	.3470	.0075
β 2-microglobulin (<i>df</i> = 84)	3.7492	.0009	.2631	0.1078	.7434	.0009
Complement C3 (<i>df</i> = 84)	4.6436	.0001	.3066	0.7335	.3942	.0061
Factor VII (<i>df</i> = 84)	3.8211	.0007	.2668	0.7473	.3898	.0065
Ferritin (<i>df</i> = 84)	4.4664	.0002	.2984	0.6337	.4282	.0053
Fibrinogen (<i>df</i> = 84)	3.9724	.0005	.2745	0.5072	.4783	.0044
TIMP-1 (<i>df</i> = 84)	3.9862	.0005	.2752	0.9948	.3214	.0086
IBP 1 (<i>df</i> = 80)	3.6238	.0012	.2660	0.0205	.8866	.0002
IBP 2 (<i>df</i> = 80)	3.6333	.0012	.2665	0.3992	.5293	.0037
IBP 3 (<i>df</i> = 80)	3.5665	.0014	.2629	0.2162	.6432	.0020
IBP 4 (<i>df</i> = 80)	3.8026	.0008	.2755	0.7534	.3880	.0068
IBP 5 (<i>df</i> = 80)	5.6958	.0000	.3629	0.2531	.6163	.2531
IBP 6 (<i>df</i> = 80)	3.5563	.0014	.2623	0.2913	.5909	.0027

*Indicates overall models that did not survive FDR correction

**Table B.2c | F statistics from moderation analyses, FDR corrected:
DMN efficiency (IV), immediate memory (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 84)	2.6334	.0126*	.2005	0.0218	.8831	.0002
IL-8 (<i>df</i> = 61)	1.5092	.1728	.1652	0.2022	.6545	.0028
IL-18 (<i>df</i> = 86)	1.6350	.1267	.1320	0.0493	.8248	.0005
MCP-1 (<i>df</i> = 56)	1.5125	.1737	.1777	3.1477	.0815	.0462
RANTES (<i>df</i> = 86)	1.6905	.1122	.1359	0.0508	.8223	.0005
ICAM-1 (<i>df</i> = 86)	1.7771	.0926	.1419	1.0541	.3075	.0105
VCAM-1 (<i>df</i> = 86)	2.3210	.0264*	.1776	3.2364	.0755	.0310
MMP-3 (<i>df</i> = 86)	1.9497	.0627	.1535	0.8316	.3644	.0082
MMP-9 (<i>df</i> = 85)	1.6456	.1240	.1341	0.0224	.8813	.0002
α 2-macroglobulin (<i>df</i> = 86)	2.0460	.0502	.1599	0.0015	.9693	.0000
β 2-microglobulin (<i>df</i> = 86)	2.3358	.0254*	.1785	0.0003	.9853	.0000
Complement C3 (<i>df</i> = 86)	2.0395	.0510	.1595	0.3547	.5530	.0035
Factor VII (<i>df</i> = 86)	2.0689	.0476*	.1614	0.1680	.6829	.0016
Ferritin (<i>df</i> = 86)	2.1575	.0387*	.1672	0.5589	.4568	.0054
Fibrinogen (<i>df</i> = 86)	2.2936	.0281*	.1758	0.4522	.5031	.0043
TIMP-1 (<i>df</i> = 86)	2.0127	.0542	.1577	0.2171	.6425	.0021
IBP 1 (<i>df</i> = 82)	2.5541	.0154*	.1995	1.0343	.3122	.0101
IBP 2 (<i>df</i> = 82)	1.6351	.1275	.1376	0.0986	.7543	.0010
IBP 3 (<i>df</i> = 82)	1.9182	.0681	.1576	1.1662	.2833	.0120
IBP 4 (<i>df</i> = 82)	2.0684	.0483*	.1679	0.2577	.6131	.0026
IBP 5 (<i>df</i> = 82)	1.7520	.0988	.1460	1.1908	.2784	.0124
IBP 6 (<i>df</i> = 82)	1.8953	.0717	.1560	0.0435	.8350	.0004

*Indicates overall models that did not survive FDR correction

**Table B.2d | F statistics from moderation analyses, FDR corrected:
FPN efficiency (IV), immediate memory (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 84)	2.685	.011*	.204	1.063	.305	.010
IL-8 (<i>df</i> = 61)	1.484	.182	.163	0.142	.708	.002
IL-18 (<i>df</i> = 86)	1.589	.140	.129	0.232	.631	.002
MCP-1 (<i>df</i> = 56)	1.065	.401	.132	0.003	.957	.000
RANTES (<i>df</i> = 86)	1.817	.085	.145	1.551	.216	.015
ICAM-1 (<i>df</i> = 86)	1.881	.073	.149	2.305	.133	.023
VCAM-1 (<i>df</i> = 86)	1.762	.096	.141	0.092	.763	.001
MMP-3 (<i>df</i> = 86)	1.713	.107	.138	0.135	.714	.001
MMP-9 (<i>df</i> = 85)	2.212	.034*	.172	4.561	.036	.044
α 2-macroglobulin (<i>df</i> = 86)	2.029	.052	.159	0.285	.595	.003
β 2-microglobulin (<i>df</i> = 86)	2.305	.027*	.177	0.581	.448	.006
Complement C3 (<i>df</i> = 86)	1.914	.068	.151	0.274	.602	.003
Factor VII (<i>df</i> = 86)	1.960	.061	.154	0.239	.626	.002
Ferritin (<i>df</i> = 86)	2.243	.032*	.173	1.725	.193	.017
Fibrinogen (<i>df</i> = 86)	2.151	.039*	.167	0.529	.469	.005
TIMP-1 (<i>df</i> = 86)	1.957	.062	.154	0.654	.421	.006
IBP 1 (<i>df</i> = 82)	2.348	.025*	.186	0.237	.628	.002
IBP 2 (<i>df</i> = 82)	1.868	.076	.154	1.987	.162	.020
IBP 3 (<i>df</i> = 82)	1.872	.076	.154	1.102	.297	.011
IBP 4 (<i>df</i> = 82)	2.024	.054	.165	0.316	.576	.003
IBP 5 (<i>df</i> = 82)	1.560	.150	.132	0.014	.906	.000
IBP 6 (<i>df</i> = 82)	2.175	.038*	.175	2.190	.143	.022

*Indicates overall models that did not survive FDR correction

**Table B.2e | F statistics from moderation analyses, FDR corrected:
FPN efficiency (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 81)	2.727	.010	.212	0.382	.538	.004
IL-8 (<i>df</i> = 60)	1.688	.120	.184	0.083	.775	.001
IL-18 (<i>df</i> = 83)	2.634	.013	.202	1.695	.197	.016
MCP-1 (<i>df</i> = 53)	1.202	.316	.154	0.209	.650	.003
RANTES (<i>df</i> = 83)	2.998	.005	.224	0.096	.758	.001
ICAM-1 (<i>df</i> = 83)	2.390	.023	.187	0.005	.944	.000
VCAM-1 (<i>df</i> = 83)	2.413	.022	.189	0.002	.968	.000
MMP-3 (<i>df</i> = 83)	2.546	.016	.197	0.404	.527	.004
MMP-9 (<i>df</i> = 82)	2.895	.007	.220	0.340	.562	.003
α 2-macroglobulin (<i>df</i> = 83)	2.713	.010	.207	1.530	.220	.015
β 2-microglobulin (<i>df</i> = 83)	2.416	.021	.189	0.000	.985	.000
Complement C3 (<i>df</i> = 83)	3.060	.004	.228	0.298	.587	.003
Factor VII (<i>df</i> = 83)	2.535	.016	.196	0.135	.714	.001
Ferritin (<i>df</i> = 83)	3.126	.004	.232	0.450	.504	.004
Fibrinogen (<i>df</i> = 83)	2.631	.013	.202	0.048	.827	.000
TIMP-1 (<i>df</i> = 83)	2.394	.022	.188	0.243	.624	.002
IBP 1 (<i>df</i> = 79)	2.595	.014	.208	1.929	.169	.0193
IBP 2 (<i>df</i> = 79)	2.001	.056	.169	0.440	.509	.0046
IBP 3 (<i>df</i> = 79)	2.005	.056	.169	0.007	.932	.000
IBP 4 (<i>df</i> = 79)	2.027	.054	.170	0.000	.991	.000
IBP 5 (<i>df</i> = 79)	2.653	.012	.212	1.036	.312	.010
IBP 6 (<i>df</i> = 79)	2.103	.045*	.176	0.048	.828	.000
<u>Global Efficiency</u>						
CRP (<i>df</i> = 81)	2.629	.013	.206	0.464	.498	.004
IL-8 (<i>df</i> = 60)	1.563	.155	.172	0.003	.959	.000
IL-18 (<i>df</i> = 83)	2.488	.018	.193	1.783	.186	.017
MCP-1 (<i>df</i> = 53)	1.212	.310	.155	0.394	.533	.006
RANTES (<i>df</i> = 83)	2.630	.013	.202	0.021	.885	.000
ICAM-1 (<i>df</i> = 83)	2.242	.032	.178	0.081	.777	.001
VCAM-1 (<i>df</i> = 83)	2.266	.030	.179	0.032	.860	.000
MMP-3 (<i>df</i> = 83)	2.396	.022	.188	0.137	.712	.001
MMP-9 (<i>df</i> = 82)	2.781	.009	.213	0.548	.461	.005
α 2-macroglobulin (<i>df</i> = 83)	2.521	.017	.196	1.332	.252	.013
β 2-microglobulin (<i>df</i> = 83)	2.263	.031	.179	0.019	.891	.000
Complement C3 (<i>df</i> = 83)	3.038	.005	.226	1.238	.269	.012
Factor VII (<i>df</i> = 83)	2.429	.021	.190	0.288	.593	.003
Ferritin (<i>df</i> = 83)	2.845	.008	.215	0.026	.872	.000
Fibrinogen (<i>df</i> = 83)	2.452	.020	.191	0.004	.948	.000
TIMP-1 (<i>df</i> = 83)	2.211	.035	.176	0.013	.911	.000
IBP 1 (<i>df</i> = 79)	2.425	.021	.197	1.330	.252	.014
IBP 2 (<i>df</i> = 79)	1.961	.062	.166	0.919	.341	.010
IBP 3 (<i>df</i> = 79)	1.958	.063	.166	0.003	.956	.000
IBP 4 (<i>df</i> = 79)	1.999	.057	.168	0.152	.698	.002
IBP 5 (<i>df</i> = 79)	2.402	.022	.196	0.162	.688	.002
IBP 6 (<i>df</i> = 79)	2.010	.056	.169	0.029	.866	.000

*Indicates overall models that did not survive FDR correction

**Table B.2f | F statistics from moderation analyses, FDR corrected:
LN efficiency (IV), general intelligence (DV)**

	Overall Model			Interaction		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Local Efficiency						
CRP (<i>df</i> = 82)	3.134	.004	.234	0.160	.690	.002
IL-8 (<i>df</i> = 61)	2.387	.026	.238	0.096	.0758	.001
IL-18 (<i>df</i> = 84)	2.992	.005	.222	0.427	.515	.004
MCP-1 (<i>df</i> = 54)	1.725	.114	.204	1.253	.268	.018
RANTES (<i>df</i> = 84)	2.989	.005	.222	0.029	.865	.000
ICAM-1 (<i>df</i> = 84)	3.006	.005	.223	1.853	.177	.017
VCAM-1 (<i>df</i> = 84)	3.016	.005	.223	0.001	.970	.000
MMP-3 (<i>df</i> = 84)	2.793	.009	.210	0.266	.608	.002
MMP-9 (<i>df</i> = 83)	2.974	.006	.223	0.010	.922	.000
α 2-macroglobulin (<i>df</i> = 84)	3.161	.004	.231	0.092	.762	.001
β 2-microglobulin (<i>df</i> = 84)	2.847	.008	.213	0.910	.343	.008
Complement C3 (<i>df</i> = 84)	3.578	.001	.254	0.090	.765	.001
Factor VII (<i>df</i> = 84)	2.943	.006	.219	1.298	.258	.012
Ferritin (<i>df</i> = 84)	3.213	.003	.234	0.070	.792	.001
Fibrinogen (<i>df</i> = 84)	2.913	.006	.217	0.206	.651	.002
TIMP-1 (<i>df</i> = 84)	2.861	.007	.214	0.073	.787	.001
IBP 1 (<i>df</i> = 80)	2.725	.010	.214	0.601	.440	.006
IBP 2 (<i>df</i> = 80)	2.619	.013	.208	0.040	.842	.000
IBP 3 (<i>df</i> = 80)	3.122	.004	.238	3.250	.075	.031
IBP 4 (<i>df</i> = 80)	2.827	.008	.220	0.040	.841	.000
IBP 5 (<i>df</i> = 80)	3.851	.001	.278	0.023	.880	.000
IBP 6 (<i>df</i> = 80)	2.795	.009	.218	1.194	.278	.012
Global Efficiency						
CRP (<i>df</i> = 82)	3.173	.004	.236	0.106	.746	.001
IL-8 (<i>df</i> = 61)	2.268	.034	.229	0.342	.561	.004
IL-18 (<i>df</i> = 84)	3.002	.005	.222	0.460	.500	.004
MCP-1 (<i>df</i> = 54)	1.637	.136	.195	0.495	.484	.007
RANTES (<i>df</i> = 84)	3.005	.005	.222	0.034	.854	.000
ICAM-1 (<i>df</i> = 84)	3.041	.005	.225	2.040	.157	.019
VCAM-1 (<i>df</i> = 84)	3.022	.005	.224	0.044	.833	.000
MMP-3 (<i>df</i> = 84)	2.813	.008	.211	0.350	.555	.003
MMP-9 (<i>df</i> = 83)	3.118	.004	.231	0.750	.389	.007
α 2-macroglobulin (<i>df</i> = 84)	3.154	.004	.231	0.012	.915	.000
β 2-microglobulin (<i>df</i> = 84)	2.900	.007	.216	1.200	.277	.011
Complement C3 (<i>df</i> = 84)	3.636	.001	.257	0.194	.660	.002
Factor VII (<i>df</i> = 84)	2.906	.007	.217	1.015	.317	.010
Ferritin (<i>df</i> = 84)	3.375	.002	.243	0.945	.334	.008
Fibrinogen (<i>df</i> = 84)	2.995	.005	.222	0.690	.408	.006
TIMP-1 (<i>df</i> = 84)	2.940	.006	.219	0.547	.462	.005
IBP 1 (<i>df</i> = 80)	2.687	.011	.212	0.242	.624	.002
IBP 2 (<i>df</i> = 80)	2.632	.013	.208	0.051	.822	.000
IBP 3 (<i>df</i> = 80)	3.105	.004	.237	3.065	.084	.029
IBP 4 (<i>df</i> = 80)	2.903	.007	.225	0.407	.525	.004
IBP 5 (<i>df</i> = 80)	3.853	.001	.278	0.000	.999	.000
IBP 6 (<i>df</i> = 80)	2.983	.006	.230	2.320	.132	.022

**Table B.2f (cont.) | F statistics from moderation analyses, FDR corrected:
LN efficiency (IV), general intelligence (DV); continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 82)	3.261	.003	.241	0.966	.328	.009
IL-8 (<i>df</i> = 61)	2.016	.059	.209	0.106	.746	.001
IL-18 (<i>df</i> = 84)	2.994	.005	.222	0.347	.557	.003
MCP-1 (<i>df</i> = 54)	1.830	.091	.213	0.004	.949	.000
RANTES (<i>df</i> = 84)	3.393	.002	.244	2.258	.137	.203
ICAM-1 (<i>df</i> = 84)	2.754	.009	.208	0.089	.766	.001
VCAM-1 (<i>df</i> = 84)	3.189	.003	.233	0.936	.336	.008
MMP-3 (<i>df</i> = 84)	2.790	.009	.210	0.055	.815	.000
MMP-9 (<i>df</i> = 83)	3.024	.005	.226	0.212	.646	.002
α 2-macroglobulin (<i>df</i> = 84)	3.267	.003	.237	0.401	.528	.004
β 2-microglobulin (<i>df</i> = 84)	2.910	.006	.217	1.142	.288	.011
Complement C3 (<i>df</i> = 84)	3.581	.001	.254	0.083	.775	.001
Factor VII (<i>df</i> = 84)	2.770	.009	.209	0.060	.806	.001
Ferritin (<i>df</i> = 84)	3.386	.002	.244	1.004	.319	.009
Fibrinogen (<i>df</i> = 84)	3.267	.003	.237	2.319	.132	.021
TIMP-1 (<i>df</i> = 84)	2.882	.007	.215	0.001	.977	.000
IBP 1 (<i>df</i> = 80)	2.944	.006	.228	1.734	.192	.017
IBP 2 (<i>df</i> = 80)	3.067	.005	.235	2.559	.114	.024
IBP 3 (<i>df</i> = 80)	2.683	.012	.212	0.167	.684	.002
IBP 4 (<i>df</i> = 80)	2.990	.006	.230	0.836	.363	.008
IBP 5 (<i>df</i> = 80)	3.952	.001	.283	0.170	.681	.002
IBP 6 (<i>df</i> = 80)	2.710	.011	.213	0.357	.552	.004

All significant overall models remained significant after FDR correction

**Table B.2g | F statistics from moderation analyses, FDR corrected:
LN efficiency (IV), immediate memory (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 84)	2.517	.017*	.193	0.135	.714	.001
IL-8 (<i>df</i> = 61)	1.487	.181	.163	0.016	.900	.000
IL-18 (<i>df</i> = 86)	1.698	.110	.136	0.400	.529	.004
MCP-1 (<i>df</i> = 56)	1.593	.148	.185	3.275	.076	.048
RANTES (<i>df</i> = 86)	1.985	.058	.156	1.798	.184	.018
ICAM-1 (<i>df</i> = 86)	1.650	.123	.133	0.075	.786	.001
VCAM-1 (<i>df</i> = 86)	1.790	.090	.143	0.140	.709	.001
MMP-3 (<i>df</i> = 86)	1.832	.082	.146	0.005	.944	.000
MMP-9 (<i>df</i> = 85)	1.677	.116	.136	0.146	.703	.002
α 2-macroglobulin (<i>df</i> = 86)	2.122	.042*	.165	0.242	.624	.002
β 2-microglobulin (<i>df</i> = 86)	2.249	.031*	.173	0.014	.905	.000
Complement C3 (<i>df</i> = 86)	2.217	.034*	.171	1.512	.222	.015
Factor VII (<i>df</i> = 86)	2.284	.029*	.175	1.697	.196	.016
Ferritin (<i>df</i> = 86)	1.185	.036*	.169	0.813	.370	.008
Fibrinogen (<i>df</i> = 86)	2.342	.025*	.179	1.433	.235	.014
TIMP-1 (<i>df</i> = 86)	1.986	.058	.156	0.151	.698	.002
IBP 1 (<i>df</i> = 82)	2.289	.029*	.183	0.016	.899	.000
IBP 2 (<i>df</i> = 82)	1.949	.080	.153	1.230	.271	.013
IBP 3 (<i>df</i> = 82)	1.849	.080	.153	0.190	.664	.002
IBP 4 (<i>df</i> = 82)	2.130	.042*	.172	0.778	.380	.008
IBP 5 (<i>df</i> = 82)	1.629	.129	.137	0.157	.693	.002
IBP 6 (<i>df</i> = 82)	2.553	.016*	.199	4.698	.033	.046
<u>Global Efficiency</u>						
CRP (<i>df</i> = 84)	2.495	.018*	.192	0.265	.608	.003
IL-8 (<i>df</i> = 61)	1.504	.175	.165	0.157	.694	.002
IL-18 (<i>df</i> = 86)	1.825	.083	.145	1.247	.267	.012
MCP-1 (<i>df</i> = 56)	1.553	.160	.182	2.640	.110	.039
RANTES (<i>df</i> = 86)	1.976	.059	.155	1.700	.196	.017
ICAM-1 (<i>df</i> = 86)	1.645	.124	.133	0.030	.864	.000
VCAM-1 (<i>df</i> = 86)	1.757	.097	.140	0.015	.903	.000
MMP-3 (<i>df</i> = 86)	1.834	.082	.146	0.028	.867	.000
MMP-9 (<i>df</i> = 85)	1.781	.092	.144	0.862	.356	.009
α 2-macroglobulin (<i>df</i> = 86)	2.137	.041*	.166	0.299	.586	.003
β 2-microglobulin (<i>df</i> = 86)	2.210	.034*	.170	0.001	.979	.000
Complement C3 (<i>df</i> = 86)	2.164	.038*	.168	0.830	.365	.008
Factor VII (<i>df</i> = 86)	2.108	.044*	.164	0.447	.506	.004
Ferritin (<i>df</i> = 86)	2.118	.042*	.165	0.149	.700	.002
Fibrinogen (<i>df</i> = 86)	2.311	.027*	.177	1.018	.316	.010
TIMP-1 (<i>df</i> = 86)	1.963	.061	.154	0.184	.669	.002
IBP 1 (<i>df</i> = 82)	2.241	.032*	.179	0.092	.763	.001
IBP 2 (<i>df</i> = 82)	1.868	.076	.154	1.424	.236	.015
IBP 3 (<i>df</i> = 82)	1.813	.086	.150	0.015	.902	.000
IBP 4 (<i>df</i> = 82)	2.154	.040*	.174	0.718	.399	.007
IBP 5 (<i>df</i> = 82)	1.651	.123	.139	0.376	.541	.004
IBP 6 (<i>df</i> = 82)	1.986	.058	.162	0.748	.390	.008

*Indicates overall models that did not survive FDR correction

**Table B.2h | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), auditory memory (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 83)	2.954	.006*	.222	2.777	.099	.026
IL-8 (<i>df</i> = 61)	1.671	.124	.180	0.153	.697	.002
IL-18 (<i>df</i> = 85)	2.107	.044*	.166	0.070	.792	.001
MCP-1 (<i>df</i> = 55)	1.164	.337	.145	0.015	.904	.000
RANTES (<i>df</i> = 85)	2.683	.011*	.202	0.781	.379	.007
ICAM-1 (<i>df</i> = 85)	2.468	.019*	.188	1.728	.192	.016
VCAM-1 (<i>df</i> = 85)	2.143	.040*	.168	0.327	.569	.003
MMP-3 (<i>df</i> = 85)	2.254	.031*	.175	0.050	.824	.000
MMP-9 (<i>df</i> = 84)	2.443	.020*	.189	0.195	.660	.002
α 2-macroglobulin (<i>df</i> = 85)	2.616	.013*	.198	3.169	.079	.030
β 2-microglobulin (<i>df</i> = 85)	2.464	.019*	.188	0.061	.805	.001
Complement C3 (<i>df</i> = 85)	2.247	.032*	.174	0.223	.638	.002
Factor VII (<i>df</i> = 85)	2.206	.035*	.172	0.133	.716	.001
Ferritin (<i>df</i> = 85)	2.589	.014*	.196	2.793	.098	.026
Fibrinogen (<i>df</i> = 85)	2.690	.011*	.202	0.951	.332	.009
TIMP-1 (<i>df</i> = 85)	2.587	.014*	.196	1.194	.278	.011
IBP 1 (<i>df</i> = 81)	2.484	.018*	.197	0.172	.680	.002
IBP 2 (<i>df</i> = 81)	2.762	.010*	.214	0.095	.758	.001
IBP 3 (<i>df</i> = 81)	2.418	.021*	.193	0.503	.480	.005
IBP 4 (<i>df</i> = 81)	2.384	.023*	.191	0.151	.698	.002
IBP 5 (<i>df</i> = 81)	2.783	.009*	.216	3.634	.060	.035
IBP 6 (<i>df</i> = 81)	2.559	.015*	.202	1.772	.187	.018
<u>Global Efficiency</u>						
CRP (<i>df</i> = 83)	2.384	.023*	.187	1.588	.211	.016
IL-8 (<i>df</i> = 61)	1.246	.288	.140	0.013	.911	.000
IL-18 (<i>df</i> = 85)	1.686	.114	.137	0.022	.881	.000
MCP-1 (<i>df</i> = 55)	0.941	.491	.120	0.253	.617	.004
RANTES (<i>df</i> = 85)	2.138	.041*	.168	0.002	.964	.000
ICAM-1 (<i>df</i> = 85)	2.000	.056	.158	1.497	.224	.015
VCAM-1 (<i>df</i> = 85)	1.864	.076	.149	0.904	.344	.009
MMP-3 (<i>df</i> = 85)	1.863	.076	.149	0.002	.969	.000
MMP-9 (<i>df</i> = 84)	1.938	.065	.156	0.003	.954	.000
α 2-macroglobulin (<i>df</i> = 85)	2.291	.028*	.177	3.546	.063	.034
β 2-microglobulin (<i>df</i> = 85)	2.159	.039*	.169	0.244	.623	.002
Complement C3 (<i>df</i> = 85)	1.8395	.081	.148	0.113	.738	.001
Factor VII (<i>df</i> = 85)	1.900	.070	.152	0.759	.386	.008
Ferritin (<i>df</i> = 85)	1.831	.082	.147	0.595	.443	.006
Fibrinogen (<i>df</i> = 85)	2.118	.043*	.166	0.121	.729	.001
TIMP-1 (<i>df</i> = 85)	2.107	.044*	.166	0.404	.527	.004
IBP 1 (<i>df</i> = 81)	2.163	.039*	.176	0.070	.792	.001
IBP 2 (<i>df</i> = 81)	2.283	.029*	.184	0.039	.844	.000
IBP 3 (<i>df</i> = 81)	2.032	.053	.167	0.860	.356	.009
IBP 4 (<i>df</i> = 81)	1.910	.070	.159	0.001	.978	.000
IBP 5 (<i>df</i> = 81)	1.973	.060	.163	1.215	.274	.013
IBP 6 (<i>df</i> = 81)	1.872	.076	.156	0.451	.504	.005

**Table B.2h (cont.) | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), auditory memory (DV); continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 83)	2.414	.021*	.189	0.701	.405	.007
IL-8 (<i>df</i> = 61)	1.303	.259	.146	1.145	.289	.016
IL-18 (<i>df</i> = 85)	1.806	.087	.145	0.008	.930	.000
MCP-1 (<i>df</i> = 55)	1.271	.278	.156	0.595	.444	.009
RANTES (<i>df</i> = 85)	2.551	.015*	.194	1.997	.161	.019
ICAM-1 (<i>df</i> = 85)	1.996	.056	.158	0.867	.354	.009
VCAM-1 (<i>df</i> = 85)	1.886	.073	.151	0.140	.710	.001
MMP-3 (<i>df</i> = 85)	1.963	.061	.156	0.608	.438	.006
MMP-9 (<i>df</i> = 84)	1.973	.060	.158	0.074	.786	.001
α 2-macroglobulin (<i>df</i> = 85)	2.135	.041*	.167	2.045	.156	.020
β 2-microglobulin (<i>df</i> = 85)	2.648	.012*	.200	2.165	.145	.020
Complement C3 (<i>df</i> = 85)	2.036	.052	.161	0.001	.923	.000
Factor VII (<i>df</i> = 85)	1.880	.074	.150	0.020	.888	.000
Ferritin (<i>df</i> = 85)	2.258	.031*	.175	2.048	.156	.020
Fibrinogen (<i>df</i> = 85)	2.658	.012*	.200	2.194	.142	.021
TIMP-1 (<i>df</i> = 85)	2.113	.043*	.166	0.015	.902	.000
IBP 1 (<i>df</i> = 81)	2.263	.031*	.183	0.647	.423	.006
IBP 2 (<i>df</i> = 81)	2.117	.043*	.173	0.005	.944	.000
IBP 3 (<i>df</i> = 81)	2.437	.020*	.194	3.006	.087	.030
IBP 4 (<i>df</i> = 81)	2.141	.041*	.174	0.000	.984	.000
IBP 5 (<i>df</i> = 81)	2.481	.018*	.197	4.321	.041	.043
IBP 6 (<i>df</i> = 81)	1.859	.078*	.155	0.027	.870	.000

*Indicates overall models that did not survive FDR correction

**Table B.2i | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 81)	2.864	.007	.220	0.004	.947	.000
IL-8 (<i>df</i> = 60)	1.700	.117	.185	0.474	.494	.006
IL-18 (<i>df</i> = 83)	3.021	.005	.226	2.921	.091	.027
MCP-1 (<i>df</i> = 53)	1.261	.284	.160	0.531	.469	.008
RANTES (<i>df</i> = 83)	2.910	.006	.219	0.053	.819	.000
ICAM-1 (<i>df</i> = 83)	2.666	.012	.204	0.521	.472	.005
VCAM-1 (<i>df</i> = 83)	2.727	.010	.208	0.746	.390	.007
MMP-3 (<i>df</i> = 83)	2.767	.009	.210	0.000	.990	.000
MMP-9 (<i>df</i> = 82)	3.224	.003	.239	0.812	.370	.008
α 2-macroglobulin (<i>df</i> = 83)	2.699	.011	.206	0.295	.589	.003
β 2-microglobulin (<i>df</i> = 83)	2.813	.008	.213	1.330	.252	.013
Complement C3 (<i>df</i> = 83)	3.284	.003	.240	0.179	.674	.002
Factor VII (<i>df</i> = 83)	2.738	.010	.209	0.247	.620	.002
Ferritin (<i>df</i> = 83)	3.250	.003	.238	0.272	.604	.002
Fibrinogen (<i>df</i> = 83)	2.803	.008	.213	0.135	.715	.001
TIMP-1 (<i>df</i> = 83)	2.728	.010	.208	1.069	.304	.010
IBP 1 (<i>df</i> = 79)	2.813	.008	.222	0.981	.325	.010
IBP 2 (<i>df</i> = 79)	2.350	.025	.192	0.533	.468	.005
IBP 3 (<i>df</i> = 79)	2.827	.008	.223	2.571	.113	.025
IBP 4 (<i>df</i> = 79)	2.584	.015	.207	0.877	.352	.009
IBP 5 (<i>df</i> = 79)	2.880	.007	.226	0.246	.621	.002
IBP 6 (<i>df</i> = 79)	2.497	.018	.202	0.278	.600	.003
<u>Small World Propensity</u>						
CRP (<i>df</i> = 81)	2.561	.015	.202	0.086	.770	.001
IL-8 (<i>df</i> = 60)	1.574	.152	.174	0.052	.820	.001
IL-18 (<i>df</i> = 83)	2.217	.034	.176	0.012	.912	.000
MCP-1 (<i>df</i> = 53)	1.195	.320	.153	0.092	.763	.002
RANTES (<i>df</i> = 83)	2.566	.015	.198	0.015	.904	.000
ICAM-1 (<i>df</i> = 83)	2.700	.011	.206	3.137	.080	.030
VCAM-1 (<i>df</i> = 83)	2.612	.013	.201	2.295	.134	.022
MMP-3 (<i>df</i> = 83)	2.375	.024	.186	0.005	.945	.000
MMP-9 (<i>df</i> = 82)	2.743	.010	.211	0.001	.970	.000
α 2-macroglobulin (<i>df</i> = 83)	2.352	.025	.185	0.262	.610	.003
β 2-microglobulin (<i>df</i> = 83)	2.296	.028	.181	0.245	.622	.002
Complement C3 (<i>df</i> = 83)	2.992	.005	.224	0.940	.335	.009
Factor VII (<i>df</i> = 83)	2.455	.019	.191	0.471	.494	.005
Ferritin (<i>df</i> = 83)	3.113	.004	.231	1.813	.182	.017
Fibrinogen (<i>df</i> = 83)	2.640	.012	.203	1.238	.269	.012
TIMP-1 (<i>df</i> = 83)	2.356	.025	.185	0.981	.325	.010
IBP 1 (<i>df</i> = 79)	2.367	.024	.193	0.612	.436	.006
IBP 2 (<i>df</i> = 79)	1.911	.070	.162	0.200	.656	.002
IBP 3 (<i>df</i> = 79)	2.005	.056	.169	0.021	.886	.000
IBP 4 (<i>df</i> = 79)	2.032	.053	.171	0.291	.591	.003
IBP 5 (<i>df</i> = 79)	2.393	.023	.195	0.000	.986	.000
IBP 6 (<i>df</i> = 79)	2.194	.036	.182	0.622	.433	.006

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table B.2j | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 82)	3.294	.003	.243	0.507	.479	.005
IL-8 (<i>df</i> = 61)	2.012	.060	.209	0.001	.980	.000
IL-18 (<i>df</i> = 84)	3.558	.001	.253	3.076	.083	.027
MCP-1 (<i>df</i> = 54)	1.622	.140	.194	0.599	.442	.009
RANTES (<i>df</i> = 84)	3.143	.004	.230	0.096	.758	.001
ICAM-1 (<i>df</i> = 84)	2.882	.007	.215	0.126	.723	.001
VCAM-1 (<i>df</i> = 84)	3.387	.002	.244	1.200	.277	.011
MMP-3 (<i>df</i> = 84)	2.918	.006	.218	0.079	.780	.001
MMP-9 (<i>df</i> = 83)	3.179	.003	.234	0.022	.883	.000
α 2-macroglobulin (<i>df</i> = 84)	3.423	.002	.246	0.902	.345	.008
β 2-microglobulin (<i>df</i> = 84)	2.844	.008	.213	0.000	.988	.000
Complement C3 (<i>df</i> = 84)	3.750	.001	.263	0.167	.684	.002
Factor VII (<i>df</i> = 84)	2.871	.007	.215	0.006	.938	.000
Ferritin (<i>df</i> = 84)	3.435	.002	.246	0.585	.446	.005
Fibrinogen (<i>df</i> = 84)	3.006	.005	.223	0.000	.984	.000
TIMP-1 (<i>df</i> = 84)	3.015	.005	.223	0.236	.629	.002
IBP 1 (<i>df</i> = 80)	2.923	.006	.226	0.476	.492	.005
IBP 2 (<i>df</i> = 80)	2.881	.007	.224	0.294	.589	.003
IBP 3 (<i>df</i> = 80)	2.902	.007	.225	0.374	.542	.004
IBP 4 (<i>df</i> = 80)	3.098	.004	.236	0.333	.566	.003
IBP 5 (<i>df</i> = 80)	4.142	.000	.293	0.259	.612	.002
IBP 6 (<i>df</i> = 80)	2.862	.008	.222	0.093	.761	.001
<u>Global Efficiency</u>						
CRP (<i>df</i> = 82)	3.481	.002	.254	1.049	.309	.010
IL-8 (<i>df</i> = 61)	2.018	.059	.209	0.000	.997	.000
IL-18 (<i>df</i> = 84)	3.540	.001	.252	2.796	.098	.025
MCP-1 (<i>df</i> = 54)	1.888	.081	.219	2.234	.141	.032
RANTES (<i>df</i> = 84)	3.132	.004	.230	0.002	.960	.000
ICAM-1 (<i>df</i> = 84)	2.893	.007	.216	0.144	.706	.001
VCAM-1 (<i>df</i> = 84)	3.226	.003	.235	0.672	.414	.006
MMP-3 (<i>df</i> = 84)	2.945	.006	.219	0.059	.809	.000
MMP-9 (<i>df</i> = 83)	3.210	.003	.236	0.052	.820	.000
α 2-macroglobulin (<i>df</i> = 84)	3.278	.003	.238	0.211	.647	.002
β 2-microglobulin (<i>df</i> = 84)	2.859	.007	.214	0.007	.934	.000
Complement C3 (<i>df</i> = 84)	3.675	.001	.259	0.068	.795	.001
Factor VII (<i>df</i> = 84)	2.880	.007	.215	0.001	.975	.000
Ferritin (<i>df</i> = 84)	3.353	.002	.242	0.121	.728	.001
Fibrinogen (<i>df</i> = 84)	3.003	.005	.222	0.057	.811	.000
TIMP-1 (<i>df</i> = 84)	2.989	.005	.222	0.175	.677	.002
IBP 1 (<i>df</i> = 80)	3.061	.005	.234	.577	.450	.006
IBP 2 (<i>df</i> = 80)	2.953	.006	.228	0.226	.636	.002
IBP 3 (<i>df</i> = 80)	3.053	.005	.234	0.784	.378	.008
IBP 4 (<i>df</i> = 80)	3.209	.003	.243	0.731	.395	.007
IBP 5 (<i>df</i> = 80)	4.301	.000	.301	0.573	.451	.005
IBP 6 (<i>df</i> = 80)	2.948	.006	.228	0.198	.658	.002

**Table B.2j (cont.) | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), general intelligence (DV); continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 82)	3.286	.003	.243	0.290	.592	.003
IL-8 (<i>df</i> = 61)	2.063	.054	.213	0.022	.884	.000
IL-18 (<i>df</i> = 84)	3.084	.004	.227	0.130	.720	.001
MCP-1 (<i>df</i> = 54)	1.530	.169	.185	0.002	.965	.000
RANTES (<i>df</i> = 84)	3.231	.003	.235	0.387	.536	.004
ICAM-1 (<i>df</i> = 84)	3.252	.003	.236	2.343	.130	.021
VCAM-1 (<i>df</i> = 84)	3.214	.003	.234	0.473	.494	.004
MMP-3 (<i>df</i> = 84)	2.920	.006	.218	0.066	.797	.001
MMP-9 (<i>df</i> = 83)	3.357	.002	.244	0.049	.826	.000
α 2-macroglobulin (<i>df</i> = 84)	3.325	.002	.240	0.046	.830	.000
β 2-microglobulin (<i>df</i> = 84)	2.944	.006	.219	0.456	.501	.004
Complement C3 (<i>df</i> = 84)	3.767	.001	.264	0.689	.409	.006
Factor VII (<i>df</i> = 84)	2.890	.007	.216	0.002	.967	.000
Ferritin (<i>df</i> = 84)	3.528	.002	.252	0.968	.328	.009
Fibrinogen (<i>df</i> = 84)	3.230	.003	.235	1.275	.262	.012
TIMP-1 (<i>df</i> = 84)	3.039	.005	.224	0.241	.624	.002
IBP 1 (<i>df</i> = 80)	3.039	.005	.233	0.449	.505	.004
IBP 2 (<i>df</i> = 80)	2.968	.006	.229	0.000	.985	.000
IBP 3 (<i>df</i> = 80)	2.950	.006	.228	0.007	.933	.000
IBP 4 (<i>df</i> = 80)	3.152	.004	.240	0.430	.514	.004
IBP 5 (<i>df</i> = 80)	4.187	.000	.295	0.089	.767	.001
IBP 6 (<i>df</i> = 80)	2.974	.006	.229	0.246	.624	.002

All significant overall models remained significant after FDR correction

**Table B.2k | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), immediate memory (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 84)	2.886	.007*	.216	1.954	.166	.018
IL-8 (<i>df</i> = 61)	1.838	.087	.194	0.168	.683	.002
IL-18 (<i>df</i> = 86)	1.699	.110	.136	0.176	.676	.002
MCP-1 (<i>df</i> = 56)	1.053	.408	.131	0.011	.917	.000
RANTES (<i>df</i> = 86)	1.862	.076	.148	0.759	.386	.008
ICAM-1 (<i>df</i> = 86)	1.978	.059	.155	2.155	.146	.021
VCAM-1 (<i>df</i> = 86)	1.882	.073	.149	0.338	.562	.003
MMP-3 (<i>df</i> = 86)	1.877	.074	.149	0.001	.981	.000
MMP-9 (<i>df</i> = 85)	1.807	.087	.145	0.443	.508	.004
α 2-macroglobulin (<i>df</i> = 86)	2.438	.020*	.185	1.744	.190	.016
β 2-microglobulin (<i>df</i> = 86)	2.472	.018*	.187	1.132	.290	.011
Complement C3 (<i>df</i> = 86)	2.225	.033*	.172	1.554	.216	.015
Factor VII (<i>df</i> = 86)	2.380	.023*	.181	2.329	.131	.022
Ferritin (<i>df</i> = 86)	2.201	.035*	.170	0.350	.556	.003
Fibrinogen (<i>df</i> = 86)	2.506	.017*	.189	1.659	.201	.016
TIMP-1 (<i>df</i> = 86)	2.184	.036*	.169	1.110	.295	.011
IBP 1 (<i>df</i> = 82)	2.494	.018*	.196	0.599	.441	.006
IBP 2 (<i>df</i> = 82)	1.860	.078	.154	0.158	.692	.002
IBP 3 (<i>df</i> = 82)	2.152	.040*	.174	1.488	.226	.015
IBP 4 (<i>df</i> = 82)	2.319	.027*	.184	0.921	.340	.009
IBP 5 (<i>df</i> = 82)	1.793	.090	.149	0.269	.605	.003
IBP 6 (<i>df</i> = 82)	2.203	.035*	.177	0.134	.716	.001
<u>Global Efficiency</u>						
CRP (<i>df</i> = 84)	2.548	.016*	.195	0.335	.564	.003
IL-8 (<i>df</i> = 61)	1.585	.148	.172	0.005	.944	.000
IL-18 (<i>df</i> = 86)	1.607	.135	.130	0.236	.628	.002
MCP-1 (<i>df</i> = 56)	1.115	.367	.137	0.154	.697	.002
RANTES (<i>df</i> = 86)	1.650	.123	.133	0.001	.976	.000
ICAM-1 (<i>df</i> = 86)	1.951	.063	.154	2.700	.104	.027
VCAM-1 (<i>df</i> = 86)	1.815	.085	.144	0.259	.612	.003
MMP-3 (<i>df</i> = 86)	1.817	.085	.145	0.192	.662	.002
MMP-9 (<i>df</i> = 85)	1.768	.095	.143	0.989	.323	.010
α 2-macroglobulin (<i>df</i> = 86)	2.536	.016*	.191	2.831	.096	.027
β 2-microglobulin (<i>df</i> = 86)	2.678	.011*	.199	2.799	.098	.026
Complement C3 (<i>df</i> = 86)	2.110	.043*	.164	1.440	.234	.014
Factor VII (<i>df</i> = 86)	2.554	.015*	.192	4.176	.044	.039
Ferritin (<i>df</i> = 86)	2.026	.053	.159	0.079	.780	.001
Fibrinogen (<i>df</i> = 86)	2.249	.031*	.173	0.792	.376	.008
TIMP-1 (<i>df</i> = 86)	2.009	.055	.158	0.445	.507	.004
IBP 1 (<i>df</i> = 82)	2.435	.020*	.192	0.119	.731	.001
IBP 2 (<i>df</i> = 82)	1.767	.096	.147	0.205	.652	.002
IBP 3 (<i>df</i> = 82)	2.125	.042*	.172	2.051	.156	.021
IBP 4 (<i>df</i> = 82)	2.094	.046*	.170	0.292	.590	.003
IBP 5 (<i>df</i> = 82)	1.655	.122	.139	0.000	.996	.000
IBP 6 (<i>df</i> = 82)	2.006	.056	.164	0.267	.607	.003

**Table B.2k (cont.) | F statistics from moderation analyses, FDR corrected:
SMN efficiency (IV), immediate memory (DV); continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 84)	2.733	.010*	.206	0.002	.967	.000
IL-8 (<i>df</i> = 61)	1.542	.162	.168	0.095	.759	.001
IL-18 (<i>df</i> = 86)	1.848	.079	.147	0.428	.515	.004
MCP-1 (<i>df</i> = 56)	1.169	.334	.143	0.661	.420	.010
RANTES (<i>df</i> = 86)	2.055	.049*	.160	1.242	.268	.012
ICAM-1 (<i>df</i> = 86)	1.783	.091	.142	0.012	.913	.000
VCAM-1 (<i>df</i> = 86)	2.227	.033*	.172	1.163	.284	.011
MMP-3 (<i>df</i> = 86)	2.009	.055	.158	0.450	.504	.004
MMP-9 (<i>df</i> = 85)	1.986	.058	.158	0.652	.422	.006
α 2-macroglobulin (<i>df</i> = 86)	2.289	.028*	.176	0.159	.691	.002
β 2-microglobulin (<i>df</i> = 86)	2.719	.010*	.202	0.546	.462	.005
Complement C3 (<i>df</i> = 86)	2.261	.030*	.174	0.015	.903	.000
Factor VII (<i>df</i> = 86)	2.238	.032*	.172	0.787	.378	.008
Ferritin (<i>df</i> = 86)	3.200	.003*	.229	5.162	.026	.046
Fibrinogen (<i>df</i> = 86)	2.567	.015*	.193	0.584	.447	.006
TIMP-1 (<i>df</i> = 86)	2.223	.033*	.171	0.334	.565	.003
IBP 1 (<i>df</i> = 82)	2.593	.014*	.202	0.005	.944	.000
IBP 2 (<i>df</i> = 82)	1.882	.074	.155	0.156	.694	.002
IBP 3 (<i>df</i> = 82)	2.488	.018*	.195	3.170	.079	.031
IBP 4 (<i>df</i> = 82)	2.501	.018*	.196	0.116	.734	.001
IBP 5 (<i>df</i> = 82)	2.218	.034*	.178	2.659	.107	.027
IBP 6 (<i>df</i> = 82)	2.288	.029*	.182	1.064	.305	.011

*Indicates overall models that did not survive FDR correction

**Table B.2m | F statistics from moderation analyses, FDR corrected:
DAN efficiency (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 81)	2.799	.009	.216	0.071	.790	.001
IL-8 (<i>df</i> = 60)	1.858	.084	.198	1.509	.224	.020
IL-18 (<i>df</i> = 83)	2.490	.018	.194	1.356	.248	.013
MCP-1 (<i>df</i> = 53)	1.482	.186	.183	2.264	.138	.035
RANTES (<i>df</i> = 83)	2.609	.014	.201	0.001	.976	.000
ICAM-1 (<i>df</i> = 83)	2.517	.017	.195	1.552	.216	.015
VCAM-1 (<i>df</i> = 83)	2.669	.012	.205	2.100	.151	.020
MMP-3 (<i>df</i> = 83)	2.460	.019	.192	0.079	.780	.001
MMP-9 (<i>df</i> = 82)	3.093	.004	.232	2.408	.125	.023
α 2-macroglobulin (<i>df</i> = 83)	2.366	.024	.186	0.017	.896	.000
β 2-microglobulin (<i>df</i> = 83)	2.382	.023	.187	0.066	.798	.001
Complement C3 (<i>df</i> = 83)	3.180	.003	.235	2.043	.157	.019
Factor VII (<i>df</i> = 83)	2.456	.019	.191	0.258	.613	.002
Ferritin (<i>df</i> = 83)	2.908	.007	.219	0.283	.596	.003
Fibrinogen (<i>df</i> = 83)	2.524	.016	.196	0.037	.847	.000
TIMP-1 (<i>df</i> = 83)	2.336	.026	.184	0.367	.546	.004
IBP 1 (<i>df</i> = 79)	2.384	.024	.194	0.001	.973	.000
IBP 2 (<i>df</i> = 79)	2.108	.045*	.176	1.439	.234	.015
IBP 3 (<i>df</i> = 79)	2.073	.048*	.174	0.476	.492	.005
IBP 4 (<i>df</i> = 79)	2.234	.033	.184	1.359	.247	.014
IBP 5 (<i>df</i> = 79)	2.434	.021	.198	0.087	.768	.001
IBP 6 (<i>df</i> = 79)	2.137	.042*	.178	0.289	.591	.003

*Indicates overall models that did not survive FDR correction

**Table B.2n | F statistics from moderation analyses, FDR corrected:
DAN efficiency (IV), general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 82)	3.976	.000	.280	0.116	.734	.001
IL-8 (<i>df</i> = 61)	2.639	.015	.257	1.400	.241	.017
IL-18 (<i>df</i> = 84)	3.808	.001	.266	2.500	.118	.022
MCP-1 (<i>df</i> = 56)	1.771	.103	.208	0.408	.526	.006
RANTES (<i>df</i> = 84)	3.409	.002	.245	0.006	.939	.000
ICAM-1 (<i>df</i> = 84)	3.228	.003	.235	0.305	.582	.003
VCAM-1 (<i>df</i> = 84)	3.917	.001	.272	2.778	.099	.024
MMP-3 (<i>df</i> = 84)	3.266	.003	.237	0.200	.656	.002
MMP-9 (<i>df</i> = 83)	3.509	.002	.253	0.912	.342	.008
α 2-macroglobulin (<i>df</i> = 84)	3.620	.001	.256	0.099	.753	.001
β 2-microglobulin (<i>df</i> = 84)	3.216	.003	.234	0.052	.820	.000
Complement C3 (<i>df</i> = 84)	3.988	.000	.275	0.539	.465	.005
Factor VII (<i>df</i> = 84)	3.443	.002	.247	1.558	.215	.014
Ferritin (<i>df</i> = 84)	3.690	.001	.260	0.212	.646	.002
Fibrinogen (<i>df</i> = 84)	3.370	.002	.243	0.052	.820	.000
TIMP-1 (<i>df</i> = 84)	3.289	.003	.238	0.076	.783	.001
IBP 1 (<i>df</i> = 80)	3.192	.003	.242	0.449	.505	.004
IBP 2 (<i>df</i> = 80)	3.115	.004	.238	0.381	.539	.004
IBP 3 (<i>df</i> = 80)	3.085	.004	.236	0.063	.803	.001
IBP 4 (<i>df</i> = 80)	3.252	.003	.245	0.021	.884	.000
IBP 5 (<i>df</i> = 80)	4.501	.000	.310	0.505	.479	.004
IBP 6 (<i>df</i> = 80)	3.052	.005	.234	0.037	.847	.000

All significant overall models remained significant after FDR correction

**Table B.2p | F statistics from moderation analyses, FDR corrected:
DAN efficiency (IV), task switching (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 83)	1.871	.076	.153	0.974	.326	.010
IL-8 (<i>df</i> = 61)	1.638	.133	.177	1.425	.237	.019
IL-18 (<i>df</i> = 84)	2.141	.041*	.169	0.009	.926	.000
MCP-1 (<i>df</i> = 55)	1.556	.160	.185	0.482	.490	.007
RANTES (<i>df</i> = 84)	2.024	.053	.162	0.580	.449	.006
ICAM-1 (<i>df</i> = 84)	2.729	.010*	.206	0.008	.931	.000
VCAM-1 (<i>df</i> = 84)	1.995	.057	.160	0.764	.384	.008
MMP-3 (<i>df</i> = 84)	1.834	.082	.149	0.391	.534	.004
MMP-9 (<i>df</i> = 83)	1.829	.083	.150	0.700	.405	.007
α 2-macroglobulin (<i>df</i> = 84)	2.017	.054	.161	0.565	.454	.006
β 2-microglobulin (<i>df</i> = 84)	1.899	.071	.153	0.304	.583	.003
Complement C3 (<i>df</i> = 84)	1.863	.077	.151	0.112	.739	.001
Factor VII (<i>df</i> = 84)	1.797	.089	.146	0.068	.796	.001
Ferritin (<i>df</i> = 84)	1.857	.078	.150	0.561	.456	.006
Fibrinogen (<i>df</i> = 84)	1.991	.057	.159	0.705	.403	.007
TIMP-1 (<i>df</i> = 84)	2.125	.042*	.168	0.188	.666	.002
IBP 1 (<i>df</i> = 81)	1.909	.070	.159	0.374	.543	.004
IBP 2 (<i>df</i> = 81)	2.403	.022*	.192	1.991	.162	.020
IBP 3 (<i>df</i> = 81)	2.003	.056	.165	0.022	.884	.000
IBP 4 (<i>df</i> = 81)	1.957	.062	.162	0.570	.453	.006
IBP 5 (<i>df</i> = 81)	2.248	.032*	.182	2.593	.111	.026
IBP 6 (<i>df</i> = 81)	2.149	.040*	.175	0.420	.519	.004

*Indicates overall models that did not survive FDR correction

**Table B.2q | F statistics from moderation analyses, FDR corrected:
VAN efficiency (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 81)	3.058	.005	.232	3.118	.081	.030
IL-8 (<i>df</i> = 60)	2.013	.060	.212	2.325	.133	.030
IL-18 (<i>df</i> = 83)	2.625	.013	.202	2.722	.103	.026
MCP-1 (<i>df</i> = 53)	1.172	.333	.150	0.103	.750	.002
RANTES (<i>df</i> = 83)	2.566	.015	.198	0.009	.923	.000
ICAM-1 (<i>df</i> = 83)	2.279	.030	.180	0.348	.557	.003
VCAM-1 (<i>df</i> = 83)	2.276	.030	.180	0.077	.782	.001
MMP-3 (<i>df</i> = 83)	2.380	.023	.187	0.007	.935	.000
MMP-9 (<i>df</i> = 82)	2.694	.011	.208	0.021	.884	.000
α 2-macroglobulin (<i>df</i> = 83)	2.323	.027	.183	0.077	.782	.001
β 2-microglobulin (<i>df</i> = 83)	2.302	.028	.182	0.273	.603	.003
Complement C3 (<i>df</i> = 83)	2.850	.008	.216	0.081	.777	.001
Factor VII (<i>df</i> = 83)	2.389	.023	.187	0.007	.933	.000
Ferritin (<i>df</i> = 83)	2.842	.008	.215	0.062	.803	.001
Fibrinogen (<i>df</i> = 83)	2.457	.019	.192	0.030	.864	.000
TIMP-1 (<i>df</i> = 83)	2.219	.034	.176	0.058	.811	.001
IBP 1 (<i>df</i> = 79)	2.239	.033	.185	0.002	.961	.000
IBP 2 (<i>df</i> = 79)	1.968	.061	.166	0.953	.332	.010
IBP 3 (<i>df</i> = 79)	1.980	.060	.167	0.154	.695	.002
IBP 4 (<i>df</i> = 79)	1.986	.059	.168	0.073	.788	.001
IBP 5 (<i>df</i> = 79)	2.394	.023	.195	0.214	.644	.002
IBP 6 (<i>df</i> = 79)	2.150	.040	.179	0.959	.330	.010

All significant overall models remained significant after FDR correction

**Table B.2r | F statistics from moderation analyses, FDR corrected:
VAN efficiency (IV), general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Small World Propensity</u>						
CRP (<i>df</i> = 82)	3.759	.001	.268	3.953	> .05	.035
IL-8 (<i>df</i> = 61)	2.206	.039	.224	0.434	.513	.006
IL-18 (<i>df</i> = 84)	2.942	.006	.219	0.035	.852	.000
MCP-1 (<i>df</i> = 54)	1.654	.132	.197	0.585	.448	.009
RANTES (<i>df</i> = 84)	3.108	.004	.228	0.790	.377	.007
ICAM-1 (<i>df</i> = 84)	2.725	.010	.206	0.061	.806	.001
VCAM-1 (<i>df</i> = 84)	3.020	.005	.223	0.053	.819	.000
MMP-3 (<i>df</i> = 84)	2.753	.010	.208	0.001	.981	.000
MMP-9 (<i>df</i> = 83)	2.987	.005	.224	0.091	.764	.001
α 2-macroglobulin (<i>df</i> = 84)	3.202	.003	.234	0.335	.564	.003
β 2-microglobulin (<i>df</i> = 84)	2.784	.009	.210	0.506	.479	.005
Complement C3 (<i>df</i> = 84)	3.680	.001	.260	0.717	.400	.006
Factor VII (<i>df</i> = 84)	2.741	.010	.207	0.008	.928	.000
Ferritin (<i>df</i> = 84)	3.230	.003	.235	0.153	.697	.001
Fibrinogen (<i>df</i> = 84)	3.195	.003	.233	1.969	.164	.018
TIMP-1 (<i>df</i> = 84)	2.999	.005	.222	0.953	.332	.009
IBP 1 (<i>df</i> = 80)	2.634	.013	.208	0.011	.916	.000
IBP 2 (<i>df</i> = 80)	2.668	.012	.211	0.356	.552	.004
IBP 3 (<i>df</i> = 80)	2.611	.014	.207	0.002	.966	.000
IBP 4 (<i>df</i> = 80)	3.047	.005	.234	1.377	.244	.013
IBP 5 (<i>df</i> = 80)	3.862	.001	.279	0.066	.798	.001
IBP 6 (<i>df</i> = 80)	2.635	.013	.209	0.169	.682	.002

All significant overall models remained significant after FDR correction

**Table B.2s | F statistics from moderation analyses, FDR corrected:
VAN efficiency (IV), immediate memory (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Local Efficiency</u>						
CRP (<i>df</i> = 84)	2.516	.017*	.193	0.269	.605	.003
IL-8 (<i>df</i> = 61)	1.554	.158	.169	0.436	.511	.006
IL-18 (<i>df</i> = 86)	1.717	.106	.138	0.426	.516	.004
MCP-1 (<i>df</i> = 56)	1.156	.342	.142	0.302	.585	.005
RANTES (<i>df</i> = 86)	1.789	.090	.143	0.007	.932	.000
ICAM-1 (<i>df</i> = 86)	1.664	.119	.134	0.082	.776	.001
VCAM-1 (<i>df</i> = 86)	2.062	.048*	.161	1.765	.188	.017
MMP-3 (<i>df</i> = 86)	2.126	.042*	.165	1.860	.176	.018
MMP-9 (<i>df</i> = 85)	2.406	.022*	.185	5.094	.027	.049
α 2-macroglobulin (<i>df</i> = 86)	3.155	.004*	.227	6.519	.012	.059
β 2-microglobulin (<i>df</i> = 86)	2.284	.029*	.175	0.079	.779	.001
Complement C3 (<i>df</i> = 86)	2.067	.048*	.161	0.144	.706	.001
Factor VII (<i>df</i> = 86)	2.834	.008*	.209	5.175	.025	.048
Ferritin (<i>df</i> = 86)	2.316	.027*	.177	1.491	.225	.014
Fibrinogen (<i>df</i> = 86)	2.255	.031*	.173	0.076	.784	.001
TIMP-1 (<i>df</i> = 86)	2.040	.051	.160	0.201	.655	.002
IBP 1 (<i>df</i> = 82)	2.272	.030*	.181	0.132	.717	.001
IBP 2 (<i>df</i> = 82)	1.953	.063	.160	1.782	.186	.018
IBP 3 (<i>df</i> = 82)	2.038	.052	.166	1.811	.182	.018
IBP 4 (<i>df</i> = 82)	2.002	.056	.163	0.109	.742	.001
IBP 5 (<i>df</i> = 82)	1.934	.066	.159	2.304	.133	.024
IBP 6 (<i>df</i> = 82)	2.084	.047*	.169	0.961	.330	.010

*Indicates overall models that did not survive FDR correction

B. 3 *Peripheral Biomarkers and White Matter Structure*

**Table B.3a | F statistics from moderation analyses, FDR corrected:
global white matter (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Radial Diffusion</u>						
CRP (<i>df</i> = 97)	2.710	.010	.183	0.278	.599	.002
IL-8 (<i>df</i> = 73)	1.628	.132	.151	0.012	.912	.000
IL-18 (<i>df</i> = 99)	2.893	.006	.190	3.214	.076	.026
RANTES (<i>df</i> = 99)	3.026	.004	.196	1.506	.223	.012
ICAM-1 (<i>df</i> = 99)	2.892	.006	.189	0.075	.785	.001
VCAM-1 (<i>df</i> = 99)	2.706	.010	.180	1.390	.241	.012
MMP-3 (<i>df</i> = 99)	2.914	.006	.191	0.597	.442	.005
α 2-macroglobulin (<i>df</i> = 99)	2.674	.011	.178	0.108	.743	.001
Complement C3 (<i>df</i> = 99)	3.277	.002	.209	1.109	.295	.009
Factor VII (<i>df</i> = 99)	3.112	.004	.201	2.092	.151	.017
Ferritin (<i>df</i> = 99)	3.535	.001	.222	0.022	.881	.000
IBP 1 (<i>df</i> = 94)	2.983	.005	.202	1.214	.273	.010
IBP 2 (<i>df</i> = 94)	2.193	.035	.157	0.124	.726	.001
IBP 3 (<i>df</i> = 94)	2.711	.010	.188	0.555	.458	.005
IBP 4 (<i>df</i> = 94)	3.018	.005	.204	2.233	.138	.019
IBP 5 (<i>df</i> = 94)	3.137	.004	.211	1.555	.216	.013
IBP 6 (<i>df</i> = 94)	2.886	.006	.197	1.084	.300	.009

*Indicates overall models that did not survive FDR correction; significant interactions are in bold

**Table B.3b | F statistics from moderation analyses, FDR corrected:
global white matter (IV), general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Radial Diffusion</u>						
CRP (<i>df</i> = 98)	4.582	.000	.272	0.634	.428	.005
IL-8 (<i>df</i> = 74)	3.301	.003	.263	0.210	.648	.002
IL-18 (<i>df</i> = 100)	4.774	.000	.276	0.636	.427	.005
RANTES (<i>df</i> = 100)	4.505	.000	.265	0.174	.677	.001
ICAM-1 (<i>df</i> = 100)	4.769	.000	.276	2.458	.120	.018
VCAM-1 (<i>df</i> = 100)	5.145	.000	.292	3.356	.070	.024
MMP-3 (<i>df</i> = 100)	4.976	.000	.285	2.801	.097	.020
α 2-macroglobulin (<i>df</i> = 100)	4.964	.000	.284	0.896	.346	.006
Complement C3 (<i>df</i> = 100)	4.847	.000	.279	0.316	.575	.002
Factor VII (<i>df</i> = 100)	4.951	.000	.284	3.178	.078	.023
Ferritin (<i>df</i> = 100)	4.642	.000	.271	0.000	.988	.000
IBP 1 (<i>df</i> = 95)	4.730	.000	.285	2.924	.091	.022
IBP 2 (<i>df</i> = 95)	4.172	.000	.260	0.039	.843	.000
IBP 3 (<i>df</i> = 95)	4.678	.000	.283	3.032	.085	.023
IBP 4 (<i>df</i> = 95)	4.634	.000	.281	1.212	.274	.009
IBP 5 (<i>df</i> = 95)	5.398	.000	.312	1.143	.288	.008
IBP 6 (<i>df</i> = 95)	4.173	.000	.260	0.006	.938	.000
<u>Fractional Anisotropy</u>						
CRP (<i>df</i> = 98)	4.310	.000	.260	0.124	.725	.001
IL-8 (<i>df</i> = 74)	3.158	.004	.254	0.108	.743	.001
IL-18 (<i>df</i> = 100)	4.622	.000	.270	1.050	.308	.008
RANTES (<i>df</i> = 100)	4.337	.000	.258	0.003	.954	.000
ICAM-1 (<i>df</i> = 100)	4.543	.000	.267	2.059	.154	.015
VCAM-1 (<i>df</i> = 100)	4.859	.000	.280	2.805	.097	.020
MMP-3 (<i>df</i> = 100)	4.720	.000	.274	2.318	.131	.017
α 2-macroglobulin (<i>df</i> = 100)	4.835	.000	.279	0.947	.333	.007
Complement C3 (<i>df</i> = 100)	4.689	.000	.273	0.060	.807	.000
Factor VII (<i>df</i> = 100)	4.721	.000	.274	2.754	.100	.020
Ferritin (<i>df</i> = 100)	4.507	.000	.265	0.013	.910	.000
IBP 1 (<i>df</i> = 95)	4.483	.000	.274	2.515	.116	.019
IBP 2 (<i>df</i> = 95)	4.002	.000	.252	0.034	.855	.000
IBP 3 (<i>df</i> = 95)	4.387	.000	.270	2.329	.130	.018
IBP 4 (<i>df</i> = 95)	4.432	.000	.272	0.810	.370	.006
IBP 5 (<i>df</i> = 95)	5.136	.000	.302	0.747	.390	.006
IBP 6 (<i>df</i> = 95)	4.016	.000	.253	0.060	.808	.000

All significant overall models remained significant after FDR correction; significant interactions are in bold

**Table B.3c | F statistics from moderation analyses, FDR corrected:
genu of the corpus callosum (IV), fluid intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Axial Diffusion</u>						
CRP (<i>df</i> = 97)	2.198	.034	.154	0.336	.563	.003
IL-8 (<i>df</i> = 73)	1.332	.242	.127	0.056	.813	.001
IL-18 (<i>df</i> = 99)	1.930	.064	.135	0.004	.951	.000
RANTES (<i>df</i> = 99)	2.498	.016	.168	0.001	.976	.000
ICAM-1 (<i>df</i> = 99)	2.226	.032	.152	0.006	.938	.000
VCAM-1 (<i>df</i> = 99)	2.007	.053	.140	0.050	.824	.000
MMP-3 (<i>df</i> = 99)	2.198	.034	.151	0.026	.873	.000
α 2-macroglobulin (<i>df</i> = 99)	2.322	.025	.158	0.552	.459	.005
Complement C3 (<i>df</i> = 99)	2.709	.010	.180	0.051	.823	.000
Factor VII (<i>df</i> = 99)	2.278	.028	.155	0.281	.597	.002
Ferritin (<i>df</i> = 99)	3.298	.002	.210	2.678	.105	.021
IBP 1 (<i>df</i> = 94)	2.226	.032	.159	0.215	.644	.002
IBP 2 (<i>df</i> = 94)	1.795	.088	.132	0.324	.573	.003
IBP 3 (<i>df</i> = 94)	2.128	.040*	.153	0.412	.522	.004
IBP 4 (<i>df</i> = 94)	2.727	.010	.188	3.334	.071	.029
IBP 5 (<i>df</i> = 94)	2.802	.008	.193	2.558	.113	.022
IBP 6 (<i>df</i> = 94)	2.067	.047*	.150	0.206	.651	.002
<u>Radial Diffusion</u>						
CRP (<i>df</i> = 97)	2.360	.023	.163	0.140	.709	.001
IL-8 (<i>df</i> = 73)	1.505	.170	.142	0.017	.898	.000
IL-18 (<i>df</i> = 99)	2.617	.012	.175	3.462	.066	.029
RANTES (<i>df</i> = 99)	2.750	.009	.182	0.899	.345	.007
ICAM-1 (<i>df</i> = 99)	2.515	.016	.169	0.001	.974	.000
VCAM-1 (<i>df</i> = 99)	2.442	.019	.165	1.681	.198	.014
MMP-3 (<i>df</i> = 99)	2.498	.016	.168	0.525	.470	.004
α 2-macroglobulin (<i>df</i> = 99)	2.416	.020	.163	0.269	.605	.002
Complement C3 (<i>df</i> = 99)	2.950	.005	.192	0.898	.346	.007
Factor VII (<i>df</i> = 99)	2.621	.012	.175	0.927	.338	.008
Ferritin (<i>df</i> = 99)	3.195	.003	.205	0.178	.674	.001
IBP 1 (<i>df</i> = 94)	2.613	.013	.182	1.403	.239	.012
IBP 2 (<i>df</i> = 94)	1.901	.069	.139	0.141	.708	.001
IBP 3 (<i>df</i> = 94)	2.308	.026	.164	0.209	.649	.002
IBP 4 (<i>df</i> = 94)	2.478	.018	.174	0.897	.346	.008
IBP 5 (<i>df</i> = 94)	2.812	.008	.193	1.858	.176	.016
IBP 6 (<i>df</i> = 94)	2.412	.020	.170	1.135	.290	.010

All significant overall models remained significant after FDR correction

**Table B.3d | F statistics from moderation analyses, FDR corrected:
genu of the corpus callosum (IV), general intelligence (DV)**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
<u>Axial Diffusion</u>						
CRP (<i>df</i> = 98)	4.060	.000	.249	0.073	.788	.001
IL-8 (<i>df</i> = 74)	3.444	.002	.271	2.462	.121	.024
IL-18 (<i>df</i> = 100)	4.225	.000	.253	0.305	.582	.002
RANTES (<i>df</i> = 100)	4.199	.000	.252	0.008	.927	.000
ICAM-1 (<i>df</i> = 100)	4.078	.000	.246	0.973	.326	.007
VCAM-1 (<i>df</i> = 100)	4.373	.000	.259	0.894	.347	.007
MMP-3 (<i>df</i> = 100)	4.122	.000	.248	0.629	.430	.005
α 2-macroglobulin (<i>df</i> = 100)	4.556	.000	.267	0.485	.488	.004
Complement C3 (<i>df</i> = 100)	4.651	.000	.271	0.826	.366	.006
Factor VII (<i>df</i> = 100)	4.220	.000	.252	1.479	.227	.011
Ferritin (<i>df</i> = 100)	4.352	.000	.258	1.458	.230	.011
IBP 1 (<i>df</i> = 95)	4.073	.000	.255	1.459	.230	.011
IBP 2 (<i>df</i> = 95)	3.817	.001	.243	0.023	.879	.000
IBP 3 (<i>df</i> = 95)	4.113	.000	.257	1.902	.171	.015
IBP 4 (<i>df</i> = 95)	4.223	.000	.262	0.632	.429	.005
IBP 5 (<i>df</i> = 95)	5.070	.000	.299	1.109	.295	.008
IBP 6 (<i>df</i> = 95)	3.838	.001	.244	0.063	.803	.001
<u>Radial Diffusion</u>						
CRP (<i>df</i> = 98)	4.091	.000	.250	0.007	.933	.000
IL-8 (<i>df</i> = 74)	3.039	.005	.247	0.001	.993	.000
IL-18 (<i>df</i> = 100)	4.406	.000	.261	1.312	.255	.010
RANTES (<i>df</i> = 100)	4.277	.000	.255	0.454	.502	.003
ICAM-1 (<i>df</i> = 100)	4.278	.000	.255	1.894	.172	.014
VCAM-1 (<i>df</i> = 100)	4.515	.000	.265	2.057	.155	.015
MMP-3 (<i>df</i> = 100)	4.323	.000	.257	1.632	.204	.012
α 2-macroglobulin (<i>df</i> = 100)	4.528	.000	.266	0.437	.510	.003
Complement C3 (<i>df</i> = 100)	4.509	.000	.265	0.213	.645	.213
Factor VII (<i>df</i> = 100)	4.598	.000	.269	3.393	.068	.025
Ferritin (<i>df</i> = 100)	4.270	.000	.255	0.160	.690	.001
IBP 1 (<i>df</i> = 95)	4.288	.000	.265	2.748	.101	.021
IBP 2 (<i>df</i> = 95)	3.900	.000	.247	0.697	.406	.006
IBP 3 (<i>df</i> = 95)	4.029	.000	.253	1.544	.217	.012
IBP 4 (<i>df</i> = 95)	4.138	.000	.258	0.408	.524	.003
IBP 5 (<i>df</i> = 95)	4.790	.000	.287	0.223	.638	.002
IBP 6 (<i>df</i> = 95)	3.949	.000	.250	0.913	.342	.007

**Table B.3d (cont.) | F statistics from moderation analyses, FDR corrected:
genu of the corpus callosum (IV), general intelligence (DV); continued**

	<u>Overall Model</u>			<u>Interaction</u>		
	<i>F</i>	<i>p</i>	<i>R</i> ²	<i>F</i>	<i>p</i>	ΔR^2
Fractional Anisotropy						
CRP (<i>df</i> = 98)	3.953	.000	.244	0.000	.996	.000
IL-8 (<i>df</i> = 74)	2.960	.006	.242	0.078	.781	.001
IL-18 (<i>df</i> = 100)	4.368	.000	.259	2.098	.151	.016
RANTES (<i>df</i> = 100)	4.148	.000	.249	0.318	.574	.002
ICAM-1 (<i>df</i> = 100)	4.060	.000	.245	1.462	.230	.011
VCAM-1 (<i>df</i> = 100)	4.366	.000	.259	2.035	.157	.015
MMP-3 (<i>df</i> = 100)	4.230	.000	.253	1.970	.164	.015
α 2-macroglobulin (<i>df</i> = 100)	4.450	.000	.262	0.576	.450	.004
Complement C3 (<i>df</i> = 100)	4.400	.000	.260	0.002	.964	.000
Factor VII (<i>df</i> = 100)	4.459	.000	.263	3.482	.065	.026
Ferritin (<i>df</i> = 100)	4.127	.000	.248	0.165	.686	.001
IBP 1 (<i>df</i> = 95)	4.162	.000	.260	2.791	.098	.022
IBP 2 (<i>df</i> = 95)	3.754	.001	.240	0.544	.463	.004
IBP 3 (<i>df</i> = 95)	3.833	.001	.244	1.132	.290	.009
IBP 4 (<i>df</i> = 95)	4.031	.000	.253	0.269	.605	.002
IBP 5 (<i>df</i> = 95)	4.690	.000	.283	0.204	.653	.002
IBP 6 (<i>df</i> = 95)	3.886	.000	.247	1.266	.263	.010

*Indicates overall models that did not survive FDR correction; significant interactions are in bold