Investigating Visual Function and Cortical Structure in Groups with (or at Risk for) Alzheimer's Dementia

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Abstract

Investigating Visual Function and Cortical Structure in Groups with (or at Risk for) Alzheimer's Dementia

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Poor sensory performance is cross-sectionally associated with poorer cognition and increases risk for cognitive decline and Alzheimer's dementia (AD). The purpose of this study was to characterize the degree of visual impairment in individuals with (or at risk for) dementia and explore the effects of this sensory-cognitive relationship on brain structure.

Using the Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND) dataset, we analyzed vision and imaging data from three diagnostic groups: individuals with subjective cognitive decline (SCD; N = 53), mild cognitive impairment (MCI; N = 102), and mild AD (N = 45). We characterized used ANCOVAs to determine whether visual performance on reading acuity and contrast sensitivity differed as a function of clinical diagnosis. Cortical thickness and volume were extracted using FreeSurfer, and hierarchical regression analyses were done to determine whether visual performance predicted brain structure (i.e., cortical thickness and volume) beyond diagnostic group membership.

We found that the AD group performed significantly worse on reading acuity and contrast sensitivity compared to the SCD and MCI groups, which did not differ from each other. Despite our independent findings that visual performance differs across diagnostic groups and that group membership predicted cortical structure, our results demonstrate that visual performance does not predict cortical structure above and beyond clinical diagnosis. Our findings support the hypothesis that atrophy in underlying visual areas and pathways is responsible for the functional vision deficits observed in AD.

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Sensory loss and cognitive decline are common age-related conditions that have a detrimental effect on functional independence and quality of life. Previous literature identifies sensory loss as one factor that increases the risk for cognitive decline and developing Alzheimer's dementia (AD; Livingston et al., 2017) and is associated with reduced physiological integrity and degeneration in the aging brain (Albers et al., 2015). The goal of our research was to characterize visual function in different clinical populations with (or at risk for) dementia, as well as explore the effects of this sensory-cognitive relationship on cortical structure in sensory regions. In this thesis, I will review previous research that has examined cross-sectional and longitudinal relationships between visual impairment and cognitive decline in healthy and clinical populations. Several hypotheses have been suggested to explain this sensory-cognitive relationship, such as the common-cause hypothesis (i.e., a third common factor associated with aging causes both sensory and cognitive decline) and the sensory deprivation hypothesis (i.e., prolonged sensory decline leads to cognitive deterioration through functional and structural changes in the brain). Evidence for each hypothesis will be presented to elucidate our rationale for investigating the effect of the visual-cognitive relationship on brain structure.

Introduction to Alzheimer's Dementia

AD is an increasingly common age-related neurodegenerative disease with profound personal and economic costs. It is classified as a severe level of impairment marked by cognitive deficits and deterioration in daily functioning and independence. AD is one of the leading causes of death and disability and is expected to affect more than 100 million globally by 2050. In Canada alone, the number of individuals living with dementia is estimated to increase from

564 000 in 2016 to 937 000 by 2031 (Alzheimer Society of Canada, 2016). Moreover, the combined healthcare and caregiver costs for AD are expected to rise from $10.4 billion in 2016 to $16.6 billion by 2031 (Alzheimer Society of Canada, 2016). Given these staggering costs, the identification of at-risk individuals and prevention of AD has become a priority worldwide.

Identification of at-risk or intermediate states in the progression of disease pathology is crucial in AD prevention. Early stages of dementia include objective and/or subjective declines in cognitive function beyond that associated with typical aging, although these conditions do not always convert to future dementia. Mild cognitive impairment (MCI) represents a prodromal state of objectively impaired cognitive function that overlaps normal age-related cognitive decline and the onset of AD, with the estimated prevalence ranging between 10-20% of individuals older than 65 years of age (Petersen, 2011). Compared to AD, there is preservation of functional independence in MCI individuals. Although not all MCI individuals progress to dementia, the general rate for progression is 10% per year in high-risk clinical populations and can be heightened by other factors, such as degree of cognitive impairment at baseline or genetic and neuroimaging biomarkers (Petersen, 2011). A preclinical stage to MCI and AD is subjective cognitive decline (SCD) in individuals who are clinically healthy, but express concern over a self-perceived decline in cognitive function without evidence of objective cognitive impairment on standardised cognitive testing or interference in daily functioning (Jessen et al., 2014; Jessen et al., 2020).

Prevalence and Burden of Sensory Loss

Prevalence of Visual Impairment in Normative Aging Populations

While the most prominent deficits in early cognitive decline and dementia are associated with cognitive impairment (e.g., memory loss), sensory deficits (e.g., hearing and vision loss) are prevalent in MCI and AD patients (see Albers et al., 2015 for a review). Rapid population aging is associated with increased prevalence rates for visual impairment globally. In 2019, the World Health Organization (WHO) estimated that out of the 2.2 billion of the world's population are estimated to have a visual impairment. Specifically, an estimated 188 million had mild vision impairment (visual acuity worse than 6/12 but 6/18 or better; 217 million had moderate or severe vision impairment (visual acuity worse than 6/18 but 3/60 or better), and 36 million people were blind (reported visual acuity worse than 3/60; Bourne et al., 2017). Rates of moderate and severe vision impairment are estimated to increase to 237.1 million people in 2020 and 587.6 million people in 2050. Rates for blindness are also expected to rapidly increase and project to 38.5 million by 2020 and 115 million by 2050.

In the same prevalence study, individuals 50 years or older had the highest burden of vision impairment, representing globally 86% of blind individuals, 80% of individuals with moderate to severe vision impairment, and 74% of individuals with mild vision impairment (Bourne et al., 2017). These impairments were largely due to unaddressed refractive error and cataracts; however, other important causes of vision loss in aging populations include eye-related diseases such as age-related macular degeneration (AMD), diabetic retinopathy, and glaucoma (Pascoloni et al., 2011).

In Canada, vision loss also presents as a widespread problem. As reported in the Cost of Vision Loss Summary Report in 2009, 817 000 Canadians are currently living with some form of vision loss, leading to national healthcare costs of over $30 billion per year (Cruess, Gordon, Bellan, Mitchell & Pezzullo, 2011). This prevalence rate is expected to increase within the next

25 years, with the number of cases with vision loss doubling after 40 years of age and tripling after 75 years of age. In a recent study using data from the Canadian Longitudinal Study on Aging, which assessed data from approximately 30 000 Canadians 45-85 years of age, mild and moderate vision loss (in terms of acuity) was prevalent among 19.8% and 2.4% of males and 23.9% and 2.6% of females, respectively, with vision loss increasing steadily with age (Mick et al., 2020).

Prevalence of Visual Impairment in Populations with AD

Along with advancing age, memory problems have been identified as one factor associated with higher odds of visual impairment (Aljied, Aubin, Buhrmann, Sabeti, & Freeman, 2018). In a large Canadian database of 30 097 people between 45-85 years old, individuals with visual impairment also reported problems with memory with 10% of this group reporting having previously been diagnosed with dementia or AD (Aljied et al., 2018). Similarly, it has been demonstrated that older individuals often have both cognitive and visual impairments. For example, visual impairment was reported in 50 (37.3%) of 150 residents with a diagnosis of dementia residing in a long-term care facility (Chriqui, Law, Kergoat, Leclerc, & Kergoat, 2017). In another study, the prevalence of visual impairment (measured by visual acuity worse than 6/12) was 32.5% in 708 patients with dementia aged 60-89 years (Bowen et al., 2016). Therefore, the well-established association between cognition and visual function, as well as the prevalence of vision deficits in dementia populations, compels further examination of the role of sensory loss on cognitive outcomes.

Functional Burden of Visual Impairment

Visual impairment has a profound impact on the preservation of daily functioning and independence. In fact, Canadians with vision loss experience 2-5 times more difficulty with daily

activities of living and report greater social dependence and medication errors (Gordon, Cruess, Bellan, Mitchell, & Pezzullo, 2011). Visual impairment is also associated with twice the risk of falls (Harwood, 2001; Kulmala et al., 2009) and mortality (McCarty et al., 2001), increased risk for frailty (Swenor, Lee, Tian, Varadaraj, & Bandeen-Roche, 2020), as well as four times the risk for serious hip fractures and early admission to nursing homes (Vu, Keeffe, McCarty & Taylor, 2005). Specifically, individuals with age-related maculopathy or glaucoma have demonstrated mobility difficulties, especially with driving and balance (Scilley et al 2002; Popescu et al 2011). Finally, Whitson et al (2007) found that participants with comorbid visual and cognitive impairment were at a greater risk of disability in activities of daily living compared to individuals with just visual or cognitive impairment alone.

Other consequences of visual impairment include social isolation and reduced communication and participation in leisure activities, an increase in depressive symptoms, as well as poor quality of life (Hassell, Lamoureux, & Keeffe, 2006; Han, Lee, Jung, & Park, 2018). Regardless of the degree of vision loss, individuals with vision complaints report poor quality of life with concern about worsening eyesight and coping with everyday life (Hassell et al., 2006). Moreover, limited mobility and household activity due to poor vision can negatively impact overall subjective well-being (Xiang et al., 2020). Compared to healthy controls, patients with AMD or glaucoma participated in fewer cognitive activities per month and were at a higher risk of disability if they had coexisting visual and cognitive impairment, with each eye-related condition contributing additively to the risk (Varin et al., 2017). Together, these studies demonstrate the impact of poor vision on day-to-day functioning and overall quality of life.

Sensory Function and Cognitive Decline

Review of the Sensory-Cognitive Relationship

Early studies have reported that sensory functioning can be a strong predictor of individual differences in cognitive functioning in late life (Lindenberger & Baltes, 1994). More specifically, visual and auditory acuity predicted a significant amount of age-related variance in performance on cognitive tests. Beyond changes in cognitive functioning, sensory impairment has been linked with an increased risk for dementia (Brenowitz, Kaup, Lin, & Yaffe, 2019; Luo et al., 2018). This sensory-cognitive relationship has been supported by recent longitudinal studies that have found that changes in hearing (Gates, Anderson, Feeney, McCurry, & Larson, 2008; Lin et al., 2011) and vision (Zheng et al., 2018, Fischer et al., 2016) may precede a diagnosis of AD and can serve as risk factors for cognitive impairment with advancing age.

There is well-established literature on the relationship between hearing and cognition. Hearing loss (HL) is one of the most prevalent sensory deficits in older adults, and multiple longitudinal studies have identified a relationship between age-related hearing loss or central auditory function and the risk of dementia five to 10 years later in individuals who were cognitively normal or had mild memory impairment without dementia at baseline (Gates, Beiser, Rees, D'Agostino, & Wolf, 2002; Gates, Anderson, McCurry, Feenery, & Larson, 2011). Moreover, auditory function has been associated with performance on cognitive tasks. In one prospective study with cognitively healthy participants from the Baltimore Longitudinal Study of Aging, hearing loss was independently associated with non-verbal and verbal measures of cognition over six years (Lin et al., 2011). These findings have profound implications for determining the role of HL in cognitive decline and the development of AD, moreover; the HL-cognitive link has provided a greater understanding of the larger relationship between sensory loss and cognitive decline.

However, the link between sensory impairment and cognitive function is not unique to just one sensory system (i.e., limited to hearing, Albers et al., 2015). There is also a growing body of empirical evidence supporting associations between visual function and cognitive impairment (Lin et al., 2004; Anstey, Luszcz, & Sanchez, 2001; Spierer, Fischer, Barak & Belkin, 2016; Chen, Bhattacharya, & Pershing, 2017; Reyes-Ortiz et al., 2005; Swenor et al., 2018; Zheng et al., 2018; Mine et al., 2016). In one longitudinal study that investigated the association between sensory impairment (hearing, sensory, or dual) and cognitive decline in women aged 69 years or older, Lin et al. (2004) found that combined hearing and vision impairment and vision impairment alone were at higher risk for cognitive decline relative to hearing impairment alone. Hearing impairment was defined as the inability to hear a tone of 40 dB or greater at 2,000 Hz frequency in the better ear, and visual impairment was defined as having corrected binocular vision worse than 20/40. Cognitive decline was measured by the amount of change in scores on a modified version of the Mini-Mental State Examination (3MS) from baseline to follow-up (4.4 years) that exceeded the average change in scores by at least one standard deviation. Lin et al (2004) found that combined visual and hearing impairment had the greatest risk for cognitive (odds ratio (OR): 2.19) and functional (OR = 1.87) decline, followed by vision impairment alone (OR for cognitive decline = 1.78, functional decline = 1.79) and hearing impairment alone (OR for cognitive decline = 1.38, functional decline = 1.10). In another study with a similar methodological design and cognitively healthy persons over the age of 70, Anstey et al. (2001) found that a two-year decline in visual acuity, but not hearing, had a significant effect on visual memory decline. Together, these studies demonstrate a link between visual impairment and cognitive decline that is independent of having another sensory impairment (e.g., HL).

The Vision-Cognition Relationship among Persons with no Eye Disease who are Cognitively Normal at Baseline

Associations between Visual Function and Cognitive Performance in Cognitively and Visually Healthy Individuals. Previous findings support a vision-cognition relationship, in that poor performance on psychophysical measures of vision (e.g., impairments in visual acuity, contrast sensitivity, color vision, motor perception, or visuospatial processing) has been cross-sectionally associated with poor cognition in healthy older adults (see Albers et al., 2015; Tzekov & Mullan, 2014 for a review). In normative populations that are cognitively healthy, multiple studies have demonstrated associations between poorer performance on visual tests with poorer cognitive function. For example, better visual function (as measured by visual acuity) was associated with better cognitive performance on the Mini-Mental State Exam (MMSE; Spierer et al., 2016; Mine et al., 2016). In fact, Mine et al. (2016) found that individuals with mild visual impairment had 2.4 times odds (cross-sectionally) of having cognitive impairment compared to individuals without visual impairment, controlling for age, sex, and education. In another study, Chen et al. (2017) found that both distance and self-reported visual impairment (as measured by visual acuity) was associated with lower scores on other measures of cognitive function (i.e., the Digit Symbol Substitution test) in healthy respondents aged 60 years or older even after accounting for demographics and socio-economic status.

Longitudinal Associations between Visual Function and Risk for Cognitive Decline. Poor performance on visual measures at baseline have also been associated longitudinally with poor global cognition (e.g., MMSE scores) or cognitive decline at follow-up assessments (Reyes-Ortiz et al., 2005; Lin et al., 2004; Swenor et al., 2018; Zheng et al., 2018; but see Hong, Mitchell, Burlutsky, Liew, & Wang, 2016 for conflicting findings). For example, Reyes-Ortiz et

al. (2005) found that near vision impairment at baseline was associated with cognitive decline (i.e., a drop in MMSE performance) at a 2-year follow-up assessment in Mexican Americans aged 65 years or older. These findings have been supported by other studies that assessed cognitive decline as a function of change in global cognition scores using the MMSE (Lin et al., 2004; Swenor et al., 2018; Zheng et al., 2018). For example, Zheng et al. (2018) measured visual acuity and global cognition (MMSE) in 2520 older adults registered in the Salisbury Eye Evaluation Study at baseline and four different time points. Results from their study demonstrated that visual impairment was associated with declining cognitive function both cross-sectionally and longitudinally over time, with worsening vision having a stronger association with declining cognition. Moreover, individuals with poor visual acuity, CS, and stereo acuity at baseline presented greater decline on cognitive scores (MMSE) over 9 years, with the hazard ratio for incident cognitive impairment being the highest for the group with poor visual acuity at baseline (Swenor et al., 2018). On other cognitive tasks besides the MMSE, Anstey et al. (2001) found that performance decline in visual acuity was associated with visual memory decline (but not with processing speed or verbal ability) over two years in the Longitudinal Study of Aging. Moreover, Valentijn et al. (2005) found that a change in visual acuity was associated with a change in scores on some tasks measuring auditory memory, processing speed, and executive function. This particular finding supports an association between sensory acuity and cognitive performance across multiple domains, both cross-sectionally and longitudinally. Overall, this literature provides substantive evidence that worse vision in older adults may be adversely associated with cognitive function over time.

Cross-sectional and Longitudinal Associations between Visual Function and Risk for Dementia. Visual impairment has been established as a risk factor for dementia both cross-

sectionally and longitudinally at follow-up assessments. In cross-sectional studies, for example, Uhlmann et al. (1991) found that the risk of dementia associated with near-vision impairment remained significant, even after adjusting for other risk factors such as family history of dementia, depression, medication, and hearing impairment. Moreover, Uhlmann et al. (1991) found that both near- and far-vision impairment (visual acuity) were significantly associated with poorer cognitive function on the MMSE, even after excluding vision-dependent items on the MMSE. Despite the association between visual impairment and the risk and clinical severity of dementia, their findings did not support an increased relative risk for cognitive dysfunction with greater visual impairment (i.e., a dose-response relationship). Low visual acuity has also been identified as one risk factor for MCI in individuals aged 70-90 years (Sachdev et al., 2012).

The link between visual impairment and risk for dementia has also been established longitudinally in multiple studies (Fischer et al., 2016; Davies-Kershaw et al., 2018; Ward et al., 2018; Naël et al., 2019; Elyashiv, Shabtai, & Belkin, 2014; Rogers & Langa, 2010; Hajek et al., 2016). For example, Davies-Kershaw et al (2018) found that healthy individuals aged 50-69 who had moderate and severe visual impairment at baseline were 2 and 4 times as likely, respectively, to have dementia at a 10-year follow-up compared to those who reported normal vision at baseline. When age-related eye diseases were entered into the hazards model, individuals in the same age group were still at greater risk of developing dementia, although this was no longer statistically significant. Rogers and Langa (2010) also established the link between untreated poor vision and risk for cognitive decline and AD, more specifically, participants with excellent vision at baseline presented a 63% reduced risk of dementia over 8.5 years on average, whereas patients with poor vision at baseline (who also did not visit an ophthalmologist) had a nine-fold risk of developing AD and a five-fold risk for cognitive impairment without dementia. In a

similar study with a wider age range (individuals aged 53-102 years), poorer visual acuity at baseline was correlated with a higher risk for dementia and worse global cognitive scores over 10 years (Elyashiv et al., 2014). However, Elyashiv et al. (2014) did not report the aetiology of visual impairment among their participants. Finally, Ward et al. (2018) demonstrated that poor contrast sensitivity at baseline not only predicted reduced cognitive performance, but also development of MCI or dementia over a decade later in older women. Specifically, the risk for dementia doubled in women who performed in the lowest quartile for contrast sensitivity at baseline. Moreover, the association between contrast sensitivity and MCI/AD remained even after excluding women with base- line self-reported glaucoma or AMD. Thus far, these results support a directional pattern of the relationship between visual impairment and cognitive decline, in that poor visual function at baseline can predict development of cognitive decline and dementia over time.

In another longitudinal study with multiple follow-up assessments, Fischer et al. (2016) found that visual impairment was independently associated with risk of cognitive impairment (as indicated by a <24/30 score on the MMSE or history of dementia). However, it is important to note that despite this independent association between visual function and cognitive impairment, 81% of all individuals with visual impairment at baseline did not develop cognitive impairment at follow-up assessments. Therefore, although we can hypothesize that individuals with AD may present with and have a history of mild vision deficits or visual impairment, it may not always be the case that individuals with visual impairment progress to clinical MCI or AD diagnoses.

The Vision-Cognition Relationship among Persons with Eye Disease who are Cognitively Normal at Baseline

Diagnosed visual impairment and eye-related diseases have likewise been shown to be associated with cognitive function. For example, Jefferis et al. (2012) found a relationship between visual impairment and poor MMSE scores with older adults aged 85 years or older who were registered as sight impaired by a consultant ophthalmologist. More specifically, individuals with registered sight impairment scored worse compared to healthy controls on MMSE items that both did and did not require vision, suggesting that poor vision may impact cognition in a domain-general manner (i.e., on both auditory and visual tasks). In multiple studies measuring visual impairment as a function of an AMD diagnosis (Clemons, Rankin, & McBee, 2006; Pham, Kifley, Mitchell, & Wang, 2006), individuals with AMD were more likely to demonstrate lower global cognition scores on the MMSE compared to healthy controls, even after excluding visual items from the MMSE. Among other cognitive functions, visuospatial function, verbal memory, and visual memory were impaired in AMD compared to healthy controls (Woo et al., 2012). Notably, Woo et al. (2012) found poorer cognitive function in AMD patients compared to healthy controls even after adjusting for age and visual acuity, suggesting that cognitive impairment in AMD patients is not exclusively due to poor vision and may be attributable to neurodegenerative changes in the brain. Moreover, Zhu et al. (2019) noted that participants with any degree of AMD had a higher prevalence of subjective cognitive complaints relative to participants without AMD.

Patients with other eye-related diseases such as cataracts, glaucoma, and diabetic retinopathy have also demonstrated lower global cognitive scores (e.g., on the MMSE; Harrabi et al., 2014; Ong et al., 2012) and on specific cognitive tests of auditory working memory and

encoding (e.g., Digit Span, Logical Memory; Varin et al., 2019) compared to healthy controls with normal vision. These findings indicate that cognitive impairment in populations with visual deficits or eye-related diseases extends across multiple cognitive domains and is not exclusive to visuospatial function or visual memory. Moreover, these findings further support the visual-cognitive relationship, in that they elucidate an established link between cognitive decline and clinical visual impairment (i.e., diagnosed or registered visual deficits) over and above poor performance on psychophysical measures of visual function. Finally, the connection between eye-related diseases and cognitive decline compels further investigation on associations and shared mechanisms between eye-related diseases and development of dementia.

The Vision-Cognition Relationship among Persons with no Eye Disease who are Cognitively Impaired at Baseline

Cross-sectional Associations between Visual Function and Cognitive Decline. Cross-sectional findings have demonstrated that clinical populations with MCI and AD demonstrate poorer performance on visual measures compared to healthy older adults. For example, AD individuals demonstrate worse performance on measures of psychophysical visual function compared to healthy controls, such as visual acuity (Uhlmann, Larson, Koepsell, Rees, & Duckert, 1991), contrast sensitivity (Hutton, Morris, Elias, & Poston, 1993; Rizzo, Anderson, Dawson, & Nawrot, 2000; Nissen et al., 1985), spatial orientation (Henderson, Mack, & Williams, 1989), figure copying, colour vision/discrimination, and stereopsis (Cronin-Golomb, Rizzo, Corkin, & Growdon, 1991a; Kiyosawa et al., 1989; Pache et al., 2003; Salamone et al., 2009), general perceptual organization and visuospatial perception (Kurylo, Corkins, & Growdon, 1994; Mandal, Joshi, & Saharan, 2012), and motion and depth perception (Mendez & Cherrier, 1996; Rizzo & Nawrot, 1998). For example, Uhlmann et al. (1991) found more deficits

in near- and far-visual acuity in AD cases compared to healthy controls. They also found a significant correlation between the degree of visual impairment and severity of cognitive dysfunction in AD patients, even after adjusting for family history of dementia, depression, drug use, and hearing impairment.

Other studies have also been conducted comparing visual function across clinical groups with varying degrees of AD pathology. More specifically, Marquie et al. (2019) found that individuals with dementia demonstrated worse visual acuity compared to SCD and MCI groups when controlling for age, sex, and education. In fact, patients with dementia were 3.4 and 1.6 times more likely to present poorer visual acuity compared to the SCD and MCI groups, respectively. Additionally, there were no group differences in previously diagnosed eye-related disorders (e.g., open-angle glaucoma, age-related macular degeneration) that are the leading causes of vision loss. In another study comparing across diagnostic groups, both MCI and AD groups demonstrated greater contrast sensitivity deficits compared to individuals with cognitive complaints or healthy controls, while the group with cognitive complaints performed intermediately between the MCI cognitively healthy controls (Risacher et al., 2013). Risacher et al. (2013) also demonstrated a significant association between performance on contrast sensitivity and on cognitive tasks of general cognition (MMSE) and auditory memory. Overall, these studies support the vision-cognition relationship in demonstrating that visual deficits are a feature of AD and AD-related changes; moreover, review of this literature suggests that AD (and possibly MCI) individuals are likely to perform worse on various visual domains compared to preclinical groups with less cognitive impairment and cognitively healthy controls.

Mechanisms Underlying the Sensory-Cognitive Relationship

Despite growing evidence for a link between visual impairment and cognition, the underlying mechanisms are still unclear. Several theories have been suggested to explain the relationship between sensory and cognitive decline, which often overlap and interrelate in complex ways. However, only a few hypotheses have been explored in studies assessing the specific link between vision and cognition.

One theory is the common-cause hypothesis, which suggests that a common factor associated with aging causes both sensory and cognitive decline through widespread neural degeneration, such as the presence of eye-related diseases (Lindenberger & Baltes, 1994; Baltes & Lindenberger, 1997). Another theory is of the social isolation hypothesis, which posits that social variables mediate the sensory-cognitive link, such that visual impairment negatively influences cognitive function through limiting social participation and communication (Clemons et al., 2006; Verghese et al., 2006; Zheng et al., 2018). For example, poor vision can reduce ability to participate in mental and physical activities that promote brain stimulation and well-being, which can be a risk factor for cognitive decline. Another hypothesis that has been presented in vision-cognition research is the information degradation hypothesis, which is that degraded perceptual inputs can lead to both errors in basic perceptual processing and higher-order cognitive processes (Lindenberger & Baltes, 1994; Monge & Madden, 2016; Valentijn et al., 2005). This theory has been supported by Monge & Madden (2016), who found that manipulation of the quality of visual input signals could affect performance on cognitive tasks. Finally, the sensory deprivation hypothesis posits that prolonged sensory decline gradually leads to cognitive deterioration due to neurophysiological changes in the brain (Lindenberger &

Baltes, 1994). However, the effect of the relationship between visual impairment and cognitive decline on brain structure remains largely understudied.

Evidence for the Common-Cause Hypothesis

In support of the common-cause hypothesis, individuals with AD often have concomitant diagnoses with age-related eye diseases (Albers et al., 2015). Moreover, previous findings suggest a bidirectional relationship between development of AD and eye-related disease, such that AD individuals are at a higher risk for developing age-related eye diseases and individuals with eye-related diseases also present cognitive impairment and risk for AD. Finally, besides the fact that age is a principal risk factor for both AD and eye-related diseases, these conditions often share similar neuropathological pathways (see Albers et al., 2015; Ikram, Cheung, Wong, & Chen, 2012; Kusne, Wolf, Townley, Conway, & Peyman, 2017 for a review). Given this overlap, the following paragraphs will discuss similarities in clinical and neuropathological presentations in common ophthalmic conditions and AD.

Clinical Associations between AD and AMD

In a comprehensive meta-analysis of 21 studies investigating the association between AD and AMD, Rong et al. (2019) found that patients with dementia or AD were at risk for AMD. This meta-analysis emphasized the association between dementia/AD and AMD across multiple cross-sectional, case-control and cohort studies. Moreover, patients with AMD had poorer cognitive functions when compared with healthy controls with no visual impairment; however, this was mostly for studies that adopted vision-dependent cognitive function tests. In the opposite direction (e.g., development of AD following diagnosis of AMD), a retrospective cohort study by Choi, Jahng, Park, and Jee (2019) demonstrated that compared to non-AMD patients, AMD patients had a higher risk for AD and Parkinson's disease even among those with healthy

lifestyle behaviours. Klaver et al. (1999) similarly found an increased risk of incident AD over two years if subjects had AMD at baseline. Within AMD populations, Woo et al., (2012) also found that AMD patients with poor visual acuity (<20/100) had a six-fold higher risk for developing MCI compared to other AMD subjects with good or moderate visual acuity (>20/100). However, it is also important to consider that other studies have found no elevated risk of developing AD following AMD (Keenan, Goldacre, Goldacre, & Hyman, 2014) and no association between AD and AMD (Williams et al., 2015).

Shared Features between AD and AMD

A shared prominent neuropathologic feature between AD and AMD are extracellular amyloid deposits, which have been detected in early AMD drusen and AD senile plaques (see Ohno-Matsui, 2011 for a review on parallel findings between AD and AMD). In fact, amyloid proteins have been implicated in initiating the inflammatory cascade that leads to drusen formation and atrophy in the retina, which are present in both AD and AMD individuals (Johnson et al., 2002). Moreover, neurofibrillary tangles are a common shared condition in both AD and AMD. Although plaques and tangles can also be present in many cognitively healthy individuals, amyloid beta plaques and neurofibrillary tangles have been found at different levels of the visual system in AD persons, ranging from subcortical areas such as the lateral geniculate nucleus (i.e., the relay centre that projects information from retinal ganglion cells to higher-order cortical areas) and cortical regions associated with visual function (e.g., primary and associative visual cortices; Albers et al., 2015; Ikram et al., 2012). Leuba and Sani (1995) also demonstrated that neuropathology (i.e., neuritic plaques and tangles) in the visual association cortex occurred later in disease progression, demonstrating that atrophy in visual-related cortical areas may only be observed at later stages of AD. Contrary to Leuba and Sani's (1995) findings, McKee et al.

(2006) presented that all subjects with mild cognitive or suspected AD had dense tangles and neuritic plaques in the visual association cortex; therefore, they suggest that neuropathology may occur early in vision-processing brain regions prior to their occurrence in the hippocampus. Therefore, similar pathology between AD and AMD at various levels of the visual pathway and related structures may explain poor vision function in AD.

Clinical Associations between AD and Glaucoma

Previous findings demonstrate an increased incidence rate of glaucoma in patients who have AD (Bayer & Ferrari, 2002; Tamura et al., 2006). In fact, the occurrence rate of glaucoma in 112 AD patients was 25.9% compared to 5.2% in cognitively healthy controls (Bayer & Ferrari, 2002). In one retrospective population-based cohort study Lin, Hazzard, & Blazer (2016) established a higher incidence rate of AD among patients with primary open-angle glaucoma (2.85) compared to controls without primary open-angle glaucoma (1.98). Moreover, Lin et al. (2016) found that a diagnosis of primary open-angle glaucoma predicted development of AD in elderly patients aged 60 years or older. In Taiwanese older adults, glaucoma is associated with 1.5-fold increased odds for developing AD (Lai, Lin, & Liao, 2017). In contrast to these studies, Kessing, Lopez, Andersen, & Kessing (2007) found no increased risk for developing AD in patients with glaucoma.

Shared Features between AD and Glaucoma

Beyond age, AD shares similar retinal features with glaucoma, such as thinning of the retinal nerve fiber layer (RNFL), a loss of retinal ganglion cells, and optic nerve degeneration (Valenti, 2011; Hinton, Sadun, Blanks, & Miller, 1986; Bambo et al., 2014; Lu et al., 2010; Kirbas, Turkyilmaz, Anlar, Tufekci, & Durmus, 2013). It has been hypothesized that both conditions share a similar process: oxidative stress contributes to deterioration of retinal ganglion

cells, which may progressively lead to thinning of the RNFL and optic nerve (Valenti, 2011). Given these similarities, glaucoma has been identified as an early (non-memory) manifestation of AD in older people (Lai et al., 2017). This is because retinal abnormalities and pathology that are common in patients with glaucoma are observed early in AD, with noticeable patterns in RNFL loss, narrow veins and decreased blood flow in retinal veins (Berisha, Feke, Trempe, McMeel, & Schepens, 2007; Blanks, Hinton, Sadun, & Miller, 1989; Blanks, Torigoe, Hinton, & Blanks, 1996a; Blanks et al., 1996b). In a recent meta-analysis of 11 imaging studies (optical coherence tomography), AD patients had a significant reduction in mean RNFL and in all four retinal quadrants around the macula (Coppola et al., 2015). Compared to age-matched healthy controls, retinas of AD patients present widespread axonal degeneration in the optic nerves and a profound reduction in the number of retinal ganglion cells (Hinton et al., 1986). Abnormal RNFL thickness have also been observed in MCI groups and in early AD patients with normal visual function (Kesler, Vakhapova, Korczyn, Naftaliev, & Neudorfer, 2011; Paquet et al., 2007; Lu et al., 2010). These studies indicate that pathological changes in the retina occur early in AD progression and may have diagnostic relevance in early identification and prevention. It is also important to note that RNFL thickness in AD is linked to reductions in retinal ganglion cells and optic nerve axons, which are critical in transferring visual information to the brain (Kusne et al., 2017). Therefore, there is strong evidence for prominent involvement of the retina and related structures in AD, which may explain poor perceptual processing and visual function in AD.

Evidence for the Sensory Deprivation Hypothesis

In addition to ocular and vascular abnormalities, there is evidence of functional and structural changes in visual-processing brain regions as a result of normal aging. Previous literature shows that there is a general age-related thinning in early visual areas, including V1

(Jorge, Canário, Quental, Bernardes, & Castelo-Branco, 2020; Salat et al., 2004; Fjell et al., 2009; McGinnis, Brickhouse, Pascual, & Dickerson, 2011; but also see Thambisetty, 2008; Lemaitre, Goldman, & Sambataro, 2012 for evidence that does not support age-related changes in V1). A more recent study by Griffis, Burge, and Visscher (2016) further presented that age-dependent cortical thickness occurred specifically in the anterior portions of V1 that correspond with peripheral vision; therefore, age-related changes in cortical thickness may be unique to specific regions and not all aspects of visual function may be affected in normal aging. Supporting this, the authors hypothesize that cortical changes in areas of peripheral vision may mirror normal, age-related functional decline in complex visual tasks requiring peripheral vision. Spear (1993) has similarly hypothesized that age-related neural changes (e.g., damage to the parvocellular pathway) are associated with a functional reduction in visual acuity. Therefore, age-related structural changes in brain areas involved in sensory processing (i.e., vision-related areas) may potentially contribute to decline in visual function.

Although sparse, the link between visual function and cortical changes in clinical populations with visual impairment has also been investigated in functional and structural studies of the brain. For example, there is EEG evidence of disrupted communication within brain visual networks and damage to the visual pathway in partially blind patients (Bola, Gall, & Sabel, 2015). There is also evidence of decline in functional activity in the visual cortex in patients with early glaucoma, however; this reduction in activity may also be influenced by structural degeneration in the visual cortex (Murphy et al., 2016). With their findings, Murphy et al. (2016) demonstrate that functional abnormalities in the brain may be present before substantial vision loss can be detected.

Multiple studies have found reduced cortical thickness and volume in regions associated with visual processing in groups with profound visual impairment (e.g., patients with glaucoma, AMD, central vision loss, visual field deficits, and monocular blindness) compared to healthy controls (Burge et al., 2016; Boucard et al., 2009; Plank et al., 2011; Chen et al., 2013; Prins, Jansonius, & Cornelissen, 2017; Hernowo et al., 2014). For example, there are findings on reduced thickness and gray matter volume in the primary visual cortex and occipital cortices in patients with AMD and glaucoma compared to healthy controls (Burge et al., 2016; Boucard et al., 2009). Volumetric reductions in the optic nerves, the chiasm, the lateral geniculate bodies, the primary visual cortex have also been found in patients with AMD (Hernowo et al., 2014). Finally, Lou et al. (2013) found that improved visual input following cataract surgery led to an increase in gray matter volume in visual association areas, indicative of cortical plasticity and restoration of impaired vision in the visual cortex. Although these studies do not investigate cognitive decline, these findings may be interpreted using the sensory deprivation hypothesis, in that poor visual input can lead to long-term changes in visual pathways and related structural areas. More broadly, these findings provide first insights on the relationship between visual impairment and structural decline and pinpoint which specific brain regions may be implicated with visual impairment.

Finally, the impact of the vision-cognition relationship on brain structure and the interaction between sensory loss, cognitive decline, and brain integrity has only been explored in a handful of studies. Early studies by Cronin-Golomb et al. (1991a) and Rizzo et al. (2000) attributed poor performance on visual measures in AD patients to involvement of the primary visual and association cortex. In a study with MCI and AD participants, Nishioka, Poh, and Sun (2015) found that MCI and AD patients demonstrated white matter damage in the optic nerves

and tracts as a result of a disrupted visual pathway between the eye and the brain. Finally, in ten patients with posterior cortical atrophy, referred to as the visual variant of AD, there was loss of both white and gray matter volume in the occipital lobe (Millington et al., 2017). While these findings with various methodologies and populations hint at a possible visual-cognitive-brain relationship, there is not enough literature to form and establish any strong conclusions on the impact of combined sensory-cognitive issues on cortical changes in thickness and volume.

Rationale

As evidenced, it remains largely unknown what the effects of the sensory-cognitive relationship are on brain structure. Second, while there is some previous research on the relationship between visual impairment and structural atrophy in the brain, these studies do not investigate the role of cognition in the sensory-brain relationship. Therefore, the purpose of our study was to target the interactive sensory-cognitive-brain relationship by 1) characterizing visual impairment in older adults with (or at risk for) dementia and 2) investigating the role of this sensory-cognitive relationship on brain structure.

Objectives and Hypotheses

In the current study, we analyzed data from the Comprehensive Assessment of Neurodegeneration and Dementia (COMPASS-ND) to assess three diagnostic groups: SCD (N = 53), MCI (N = 102), and mild AD (N = 45). The COMPASS-ND dataset is the clinical study of the Canadian Consortium on Neurodegeneration in Aging (CCNA), a national initiative aimed towards understanding neurodegenerative diseases, working towards prevention, and improving quality of life for individuals living with dementia (Chertkow et al., 2019). The COMPASS-ND study aims to identify clinical, experimental, genetic, and imaging markers for a wide range of dementias to target collaborative prevention and intervention.

First Objective

Our first objective was to characterize the degree and frequency of visual impairment in a large Canadian sample of older adults with (or at risk for) dementia. Measures of reading acuity (ability to discern sentences at a given distance) and contrast sensitivity (ability to distinguish an object from its background) were used to assess visual functioning in both eyes. Comparisons between diagnostic groups using ANOVAs were then calculated to investigate whether performance on visual measures differed as a function of clinical diagnosis, controlling for age, sex, and education. We also examined whether the sensory-cognitive relationship was confounded by prevalence of eye-related diseases across all three diagnostic groups. Based on shared neuropathological mechanisms between AD and age-related eye diseases, as well as the cross-sectional and longitudinal findings linking visual impairment with cognitive decline and dementia, we hypothesized that visual function would differ across diagnostic groups (i.e., the AD group will likely have poorer vision compared to the other preclinical groups), over and above age.

Second Objective

Our second objective was to assess the interaction between visual function, diagnostic group membership, and cortical structure. We used T1-weighted MRI images from the COMPASS-ND dataset and FreeSurfer to extract cortical thickness and volume from brain regions of interest associated with visual processing (controlling for age, sex, education, and total intracranial volume).

Nine ROIs were selected bilaterally based on anatomical location and involvement in visual perception and processing: the calcarine sulcus, the cuneus gyrus, occipital pole, middle occipital gyrus, lunate sulcus (marks transition between visual areas V1 and V2), parieto-

occipital sulcus, superior occipital gyrus, and the inferior occipital sulcus, and the anterior occipital sulcus (close to occipito-temporal junction, but connected with parieto-occipital sulcus and calcarine fissure). First, our ROIs were based on their involvement in processing reading acuity and contrast sensitivity and further supported by the cortical anatomy of the visual pathway. Although the we used a more complex measure of high-level reading acuity, basic grating acuity has been associated with low-level perception in the primary visual cortex (synonymous with V1; Duncan & Boynton, 2003). Contrast sensitivity is also processed in low-level regions like V1, along with V2, V3, and V5, as well as higher-order processing areas like the lateral occipital complex (Avidan et al., 2002). Given the role of the primary visual cortex in processing both acuity and contrast sensitivity (i.e., our measures of visual function), we selected ROIs that occupy the primary visual cortex, including the calcarine region and the medial surface of the occipital lobe, which extends to both the parietal-occipital sulcus and the occipital pole (Wichmann & Müller-Forell, 2004). Moreover, as secondary visual cortices are also implicated in processing reading acuity and contrast sensitivity, we included regions that surround or are connected to the primary visual cortex (e.g., the cuneus, the superior occipital gyrus, the inferior occipital gyrus, and the anterior occipital sulcus).

Second, ROIs were based on previous publications that have used similar region-of-interest analysis methods and selected visual-based regions to assess cortical thickness and volume in individuals with severe visual impairments or blindness (Burge et al., 2016; Boucard et al., 2009; Plank et al., 2011; Prins et al., 2011; Hernowo et al., 2014). Common ROIs selected by these studies and ours include the calcarine sulcus (and surrounding regions including the anterior and posterior banks), the occipital pole, the parieto-occipital sulcus, superior occipital and inferior occipital gyri, and the middle occipital regions. Like these studies, we selected

posterior regions (e.g., occipital lobe) and anterior regions (e.g., parieto-occipital sulcus) given their approximate location and closeness to the superior and inferior banks of the calcarine sulcus (i.e., V1).

Hierarchical regression analyses were done to determine whether visual function (i.e., performance on vision measures) predicted brain structure (i.e., cortical thickness and volume) beyond diagnostic group membership. For this objective, although we predicted that group membership would alone explain a large portion of variance in cortical structure, we hypothesized that worse performance on reading acuity and contrast sensitivity would additionally predict reduced cortical thickness and volume based on previous results on strong relationships between visual deficits and cortical atrophy in vision-related brain areas. Support of these hypotheses may provide novel evidence for the sensory deprivation hypothesis in older adults with (or at risk for) dementia.

Methods

Participants

The first and second waves of COMPASS-ND data were used to assess sensory and neuroimaging data from 200 older adults (SCD N = 53, MCI N = 102, AD N = 45). General inclusion criteria for participants included sufficient proficiency in English or French to undergo self-report and neuropsychological assessment, geographical accessibility to the study site, and the presence of a study partner who interacted with the participant weekly and could participate if required. Participants also had to be younger than 85 years and have demonstrated subjective or objective cognitive impairment.

General exclusion criteria included: participants with other significant known chronic brain diseases unrelated to AD or Parkinson's disease (e.g., moderate-severe chronic static leukoencephalopathy with previous traumatic injury), multiple sclerosis, a serious developmental handicap, malignant tumors, and other rarer brain illnesses; participants with on-going alcohol or drug abuse, participants without study partners, participants without sufficient proficiency in English or French, individuals unable to undergo MRI scanning, and severely impaired participants with a score of ≤ 13 in the Montréal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) or with a symptomatic stroke within the previous year were excluded (Chertkow et al., 2019). The COMPASS-ND study was approved by the Jewish General Research Ethics Board. Written informed consent was obtained from all participants.

From the first and second data releases (total N = 409) of the COMPASS-ND data, 208 participants were identified that satisfied the criteria for SCD (N = 55), MCI (N = 105), and AD (N = 48) following the clinical visit. Eight participants were excluded in total. Five participants were excluded due to missing MRI data or clinical data, one participant was an outlier based on brain volume (+/- 3 standard deviations (SD) compared to group average), and two participants

were outliers based on performance on visual measure, leaving a final sample of 53 SCD participants, 102 MCI participants, and 45 AD participants.

SCD Criteria

Participants who were diagnosed with SCD were selected based on the following criteria: 1) self-experienced persistent decline in cognitive capacities in comparison with a previously normal status, unrelated to an acute event (Jessen et al., 2020; Jessen et al., 2014); 2) normal age- and education- adjusted performance on standard cognitive tests including a word list recall score of >5 on the Consortium to Establish a Registry for Alzheimer's Disease (Morris et al., 1989), a score on the Weschler Memory Scale (WMS-III) Logical Memory II (i.e., delayed recall; Weschler, 1987) above ADNI education-adjusted cut-offs, and a score of ≥ 26 on the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005); 3) a score of 0 on the Clinical Dementia Rating (CDR; Hughes, Berg, Danziger, Coben, & Martin, 1982). Other SCD exclusion criteria include: surgery within the last 2 months, history of intercranial surgery, regular use of benzodiazepines, comorbid condition that is likely to result in death within three years, and age being less than 60 years.

MCI Criteria

Participants who were diagnosed with MCI were selected based on the following criteria: 1) concern regarding a change in cognition from previous levels based on the participant's or an informant's report (Albert et al., 2011); 2) impairment in one or more cognitive domains that is greater than what would be expected for the patient's age and education: WMS-III Logical Memory II score below education-adjusted ADNI cutoffs, CERAD word list recall score less than 6, global CDR score > 0, and MoCA score between 13-24; 3) assigned a CDR score of ≤ .5 to not be given a diagnosis of dementia; and 4) have preservation of independence in functional

abilities by having a score greater than 14/23 on the Lawton-Brody Instrumental Activities of Daily Living (IADL) scale. Participants must also have an absence of diffuse subcortical cerebrovascular disease to be classified as MCI.

AD Criteria

Participants who were diagnosed with AD were selected based on the following criteria: 1) gradual and progressive change in memory and/or other cognitive functions over more than six months based on the participant's and/or informant's report; 2) objective evidence of significant decline in at least 2 cognitive domains by satisfying 2 or more of the following: WMS-III Logical Memory II score below ADNI cut-offs, a CERAD word list recall score of <6, MoCA score between 13-24 inclusive (with at least one point lost in a non-memory task), and a "yes" response to whether the participant has had any changes in personality or behaviour; 3) evidence of impairment of functional abilities by responding "yes" to whether cognitive deficits interfere with independence in everyday activities (e.g., paying bills, managing medications). There must also be no evidence for another concurrent and active neurological disease, a non-neurological medical comorbidity, or use of medication that could have a substantial effect on cognition.

Measures of Visual Function

MNRead Acuity Charts

The MNRead Acuity Charts measure reading acuity, the ability to discern sentences at a given distance, by assessing reading performance depending on various font sizes (Mansfield, Legge, Luebker, & Cunningham, 1994). For this task, participant read sentences on a chart, which was held by the participant with a distance of 40 cm at a 45-degree angle from the participant's

eyes to the chart. Participants were instructed to read the sentences on the chart aloud starting from the top until they could not read any words in a sentence using both eyes.

Reading acuity was operationalized as the smallest print size at which the participant can read the entire sentence without making significant errors (measured to the nearest 0.1 logMAR). Reading acuity was measured as the logMAR of the last sentence the participant was able to read. A more precise calculation was determined based on the number of sentences correctly read and errors made (e.g., words read incorrectly or missed). Per the MNRead scoring instructions, the formula for calculating reading acuity is as follows: [acuity = 1.4 – (amount of all sentences read x 0.1) + (total amount of errors x 0.01)].

The MARS Contrast Sensitivity Test

The MARS Contrast Sensitivity Test was used to assess contrast sensitivity, the ability to distinguish an object from its background, by measuring resolution of the eyes in processing letters at different spatial frequencies (Dougerty, Flom, & Bullimore, 2005). For this task, participants must read letters on a chart, which was held by the participant with a distance of 50 cm at a 45-degree angle from the participant's eyes to the chart. Participants were instructed to read the letters from the left to the right of each line, from the top to the bottom of the chart using both eyes. Testing was discontinued when the participant made two consecutive errors.

Contrast sensitivity was operationalized as the final correct letter read by the participant. Per the MARS manual, the logCS was calculated by identifying the value at the lowest contrast letter prior to two incorrectly identified letters and subtracting it by the number of errors prior to the final correct letter. There was one missing case for this measure in the MCI group, which was dealt with using mean substitution.

MRI Data Acquisition and Analyses

MRI Data Acquisition

T1-weighted images were obtained using 3T scanners from different COMPASS-ND sites across Canada following the Canadian Dementia Imaging Protocol (CDIP), which is a harmonized and validated protocol for MRI data acquisition available for GE, Philips, and Siemens scanners (Duchesne et al., 2019). Parameters for the acquisition of 3D T1-weighted images differed depending on the scanner type and version (see https://www.cdip-pcid.ca/ for details on all parameters). The T1-weighted images were then processed using the Civet pipeline (version 1.1.11) at McGill University to extract cortical volumes (gray matter in left and right frontal, temporal, occipital, parietal lobes) and conduct structural image analysis (Ad-Dab'bagh et al., 2006; Zijdenbos, Forghani, & Evans, 2002).

Cortical reconstruction and segmentation of the T1-weighted images were further performed using FreeSurfer (version 6.0, documented online and freely available on http://freesurfer.net/). The FreeSurfer pipeline performs surface-based morphometry (SBM) using several processing steps described extensively in previous literature (Dale, Fischl, & Sereno, 1999; Fischl & Dale, 2000; Fischl et al., 2004). The fully automated pipeline generates individual cortical surface models with high spatial precision on a web-based analysis software called CBrain. Five participants (2 MCI, 3 AD) were excluded due to preprocessing errors. All brain scans were then manually checked for segmentation precision, with no further participants removed.

Regions-of-interest Analyses

Following the preprocessing procedure, the cortex was further parcellated into regions of interest (ROIs) using the Destrieux cortical atlas (Destrieux, Fischl, Dale, & Halgren, 2010), which segments the cortex into gyral and sulcal regions on the basis of anatomical landmarks and

curvature and convexity. For example, the occipital lobe can be divided into areas such as the parieto-occipital sulcus, anterior occipital sulcus, occipital pole, calcarine sulcus, and so forth, which allows for the extraction of cortical thickness and cortical volume at each vertex of the occipital area. Cortical thickness is estimated as the minimal distance between gray or white matter and the tessellated pial surface at each location in the brain (Fischl & Dale, 2000). This calculation has previously been validated against histological analysis and manual measurements and has been shown to be reliable in healthy older adults (Liem et al., 2015). Cortical volume is the product of both thickness and surface area. Cortical thickness and volume were analyzed for selected ROIs (defined by the Destrieux atlas) using standard procedures for ROI extraction in FreeSurfer.

Our ROIs were selected based on the specific vision-related areas examined by other studies that have investigated the relationship between profound visual impairment and structural decline, or areas that were associated with processing of reading acuity and contrast sensitivity. For more information regarding justification and choice of ROIs, please refer to our objectives and rationale section.

Aside from visual-related regions, we also looked at cortical thickness and volume in the precentral and postcentral gyri in the motor cortex. As motor areas tend to be relatively spared in early stages of AD (see Mann, 1991; Baron et al., 2001; Fox et al., 2001; Whitwell, 2010 for a review), these regions served as control areas to compare any significant effects we saw for visual-based ROIs. This would determine whether our findings between diagnostic groups were specific to visual-based regions of the brain and not just a result of generalized atrophy throughout the brain.

Statistical Analyses

Data analyses were completed using R and RStudio (Version 3.6.0). Data were first assessed for missing data, data entry errors, and out of range outliers (+/- 3 SD). Assumptions of normality (using histograms, skewness and kurtosis values, and statistical normality tests including the Kolmogorov-Smirnov and Shapiro-Wilk) and homogeneity of variance (Levene's Test) were also checked. We used age, sex, and education as covariates in all statistical analyses based on group differences (see Table 1). In analyses involving cortical structure, we also included intracranial volume (ICV) as a covariate in order to control for potential differences in premorbid brain volume between groups (Voevodskaya et al., 2014). Along with basic demographic analyses (i.e., age, sex, education) between groups, we conducted Chi-squared tests for independence to determine whether comorbid eye-related disease or visual deficits were significantly related to diagnostic group membership (see Table 1 for all Chi-square results).

To assess our first objective, the diagnostic groups were first compared in their performance on the vision measures (i.e., reading acuity and contrast sensitivity) using one-way ANCOVAs. For pairwise comparisons, we conducted post-hoc tests with Bonferroni adjustment for multiple comparisons and calculated Cohen's *d* to estimate effect size between groups. To address our second objective, we conducted hierarchical (sequential) regression models to determine whether visual performance predicted cortical structure over and above group membership. For each outcome variable (cortical volume and cortical thickness), a family of four hierarchical regressions were conducted for each of the 9 ROIs in each hemisphere. All regressions had the same predictor variables entered at the same step for all four models. All continuous predictors (age, years of education, ICV, reading acuity scores, contrast sensitivity scores) were scaled across the overall sample for ease in interpretation. For predictors with multiple levels (sex,

diagnostic group), SCD women were used as the referent group. Pairwise comparisons between the MCI and AD groups were also done for each regression to assess group-specific relationships between visual performance and brain structure. In the first model, demographic predictors of age, sex, education, and total ICV were used to predict thickness or volume in each ROI. In the second model, diagnostic group was added as a predictor as previous literature has established that cortical structure differs based on diagnostic group (Dickerson et al., 2009; Gili et al., 2010; Kiuchi et al., 2014). In the third model, both reading acuity and contrast sensitivity scores were added as variables of interest to determine if performance on visual tests predicted a significant amount of additional variance in cortical thickness and volume. Based on limited theoretical and logical rationale for whether reading acuity or contrast sensitivity would explain more variance in cortical structure, both measures were entered in the third model simultaneously. In the fourth and final model, diagnostic group was set to interact with reading acuity and contrast sensitivity scores to determine whether the relationship between visual performance and cortical structure differed by group (i.e., whether the interaction between visual performance and group explained variance beyond the separate main effects of visual performance and diagnostic group in Models 2-3). Analysis of the best predictive model and influence of each predictor in explaining the variance in cortical structure was done primarily by running an ANOVA between the four models with an alpha level of .05; moreover, R_2 change and Akaike Information Criterion (AIC; lowest AIC score is the best model across all ranked models; Bozdogan, 1987) values were also examined to determine the influence of each predictor on cortical structure.

Results

There were two outliers (+/3 SD) identified for reading acuity (i.e., 1 in the MCI group, 1 in the SCD group) and no outliers for cortical structure in all ROIs. Assumptions of normality (skewness and kurtosis per guidelines by Kline, 2016) were met for all variables. Assumptions of homogeneity of variance were met for most outcome variables, except for left parieto-occipital sulcus thickness. We ran a non-parametric Kruskal-Wallis test to assess this violation, which indicated a statistically significant difference in left parieto-occipital thickness between the three independent groups. Mann-Whitney U tests were also conducted to determine the significant main effect between independent groups on this variable.

Table 1 lists the demographics and descriptives on visual measures for each diagnostic group. There were significant group differences for age, sex, and education, which were used as covariates in all further analyses. The AD group was significantly older, with fewer years of education, compared to the SCD and MCI groups. Moreover, there was a significant difference in sex over the diagnostic groups, such that the AD group was largely male (66.6%) and the SCD group was largely female (77.5%; see Table 1). There were also significant group differences for visual field loss and AMD between diagnostic groups. For visual field loss, the AD group had the highest percentage of visual field deficits, followed by the MCI group. For AMD, the AD group had the greatest percentage of AMD cases followed by the SCD group, which was followed by the MCI group. Results from these post-hoc tests assessing violation of homogeneity in variance indicated a statistically significant difference in left parieto-occipital sulcus thickness between SCD and MCI groups, as well as SCD and AD groups. However, this was not corrected as the difference in cortical thickness between the SCD group and the MCI and AD groups may be inherently meaningful.

Diagnostic Group Comparisons in Visual Function

Figure 1 shows a categorical distribution of performance on both vision measures across the entire sample. Most participants demonstrated normal reading acuity and contrast sensitivity (92% of SCD, 90% of MCI, 64% of AD) compared to low reading acuity and normal contrast sensitivity (2% of SCD, 1% of MCI, 2% of AD), normal reading acuity and moderate-severe contrast sensitivity (6% of SCD, 9% of MCI, 27% of AD), and low reading acuity and moderate-severe contrast sensitivity (0% of SCI, 0% of MCI, 7% of AD). For each visual measure, 98% of SCD, 99% of MCI, and 91% of AD had normal reading acuity and 94% of SCD, 91% of MCI, and 67% of AD had normal contrast sensitivity.

There was a significant difference between diagnostic groups in reading acuity performance ($F(2,200) = 3.59$, $p < .01$; see Figure 2) and in contrast sensitivity performance ($F(2,200) = 10.29$, $p < .01$; see Figure 3). Post-hoc tests demonstrated that the AD group (.21 ± .03) performed significantly worse on reading acuity compared to the SCD (.10 ± .03, $p = .01$, $d = -3.67$) and MCI groups (.13 ± .02, $p = .02$, $d = -3.41$), with no statistically significant difference between the SCD and MCI groups ($p = 1.00$, $d = -1.26$). Post-hoc tests also showed that the AD group (1.58 ± .02) performed significantly worse on contrast sensitivity compared to the SCD (1.71 ± .02, $p < .01$, $d = 6.5$) and MCI groups (1.70 ± .02, $p < .01$, $d = 6.00$), with no statistically significant difference between the SCD and MCI groups ($p = 1.00$, $d = .5$).

Predicting Cortical Structure by Diagnostic Group and Visual Performance

To preview the results, our hierarchal regressions demonstrated that visual performance did not explain more variance in vision-related cortical structure in both hemispheres beyond group membership (see Tables 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38,

40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72 for thickness and volume in the left and right hemisphere of all nine ROIs).

Left Hemisphere

Having controlled for age, sex, education, and total ICV, and holding SCD women as the as reference group, we found that group membership (Model 2) explained a significant amount of variance in cortical structure and was selected as the best predictive model for most areas compared to Models 3 and 4.

Cortical Volume. Group membership was selected as the best predictive model for multiple areas, including the left inferior occipital gyrus (an additional 3.8% of variance; SCD > AD; see Tables 2-3), the left cuneus (an additional 3.8% of variance; SCD > AD; see Tables 6-7), the left middle occipital gyrus (an additional 2.4% of variance; SCD > AD; see Tables 10-11), and the left parieto-occipital sulcus (an additional 6.7% of variance; SCD, MCI > AD; see Tables 34-35). In no cases did Models 3 and 4 (i.e., visual performance) significantly account for greater than 1.5% of variance in cortical volume, in any of the nine ROIs.

Cortical Thickness. Group membership was selected as the best predictive model for multiple areas, including the left inferior occipital gyrus (an additional 6.8% of variance; SCD > AD; see Tables 4-5), the left middle occipital gyrus (an additional 3% of variance; SCD > AD; see Tables 12-13), the left lunate sulcus (an additional 4.8% of variance; SCD, MCI > AD; see Tables 16-17), the left occipital pole (an additional 2.9% of variance; SCD > MCI, AD; see Tables 24-25), the left calcarine sulcus (an additional 2.2% of variance; SCD > MCI, AD; see Tables 28-29), the left anterior occipital sulcus (an additional 7.5% of variance; SCD, MCI > AD; see Tables 32-33), and the left parieto-occipital sulcus (an additional 3.8% of variance; SCD, MCI > AD; see Tables 36-37). In no cases did Models 3 and 4 (i.e., visual performance)

significantly account for, in any of the 9 ROIs, greater than 1.1% of variance in cortical thickness.

Right Hemisphere

Similar to regressions in the left hemisphere, group membership (Model 2) was identified as the best predictive model for most areas.

Cortical Volume. Group membership was selected as the best predictive model for cortical volume in the right cuneus (an additional 2.8% of variance; SCD, MCI > AD; see Tables 42-43), the right middle occipital gyrus (an additional 3.4% of variance; SCD, MCI > AD; see Tables 46-47), the right occipital pole (an additional 8.3% of variance; SCD, MCI > AD; see Tables 58-59), and the right parieto-occipital sulcus (an additional 5.7% of variance; SCD, MCI > AD; see Tables 70-71). In no cases did Models 3 and 4 (i.e., visual performance) significantly account for, in any of the 9 ROIs, greater than 1.3% of variance in cortical volume.

Cortical Thickness. Group membership was selected as the best predictive model for cortical thickness in the right lunatus sulcus (an additional 5.2% of variance; SCD, MCI > AD; see Tables 52-53), the right superior occipital gyrus (an additional 2.2% of variance; SCD > AD; see Tables 56-57), the right occipital pole (an additional 2.9% of variance; SCD > AD; see Tables 60-61), the right calcarine sulcus (an additional 5.8% of variance; SCD > AD; see Tables 64-65), and the right parieto-occipital sulcus (an additional 5.7% of variance; SCD > AD; see Tables 72-73). In no cases did Models 3 and 4 (i.e., visual performance) significantly account for, in any of the 9 ROIs, greater than 1.3% of variance in cortical thickness.

Group Differences in Cortical Structure in Motor Areas

Our results demonstrated no significant differences across or between groups for the precentral and postcentral gyri (see Tables 74-77 for results on cortical volume and thickness in

the left precentral and postcentral gyri and Tables 78-81 for results on cortical volume and thickness in the right precentral and postcentral gyri).

Discussion

The goal of our study was to characterize visual function in individuals with or at risk for dementia and explore the effects of this sensory-cognitive relationship on brain structure. Our findings indicate that older adults with dementia (AD) present significantly worse visual functioning compared to older adults at risk for dementia (SCD and MCI groups). Despite our findings that visual performance differs across diagnostic groups and that group membership predicted cortical structure, our results demonstrate that visual performance does not predict cortical structure above and beyond group membership. Although previous literature has established that AD participants demonstrate poor visual performance, we are the first to characterize and explore visual function for all three diagnostic groups with varying clinical pathology. Moreover, our findings provide new insights into the sensory-cognitive-brain relationship and are the first to investigate vision and the sensory deprivation hypothesis in older adults with or at risk for dementia.

Visual Performance in Older Adults with AD

We assessed whether visual performance on measures of reading acuity and contrast sensitivity differed across groups. We found that the AD group demonstrated both poorer reading acuity and contrast sensitivity compared to the SCD and MCI groups, even when controlling for age, sex, and education. There were no significant differences between the MCI and SCD groups; moreover, visual function in the SCD and MCI groups were mostly within the normal range, which characterizes visual function in pre-clinical groups at risk for dementia. First, these results suggest that vision impairment may only be evident in later stages of AD progression. Second, 91% of AD had normal reading acuity and 67% of AD had normal contrast sensitivity. Although the AD group demonstrates reliably poorer performance on measures of reading acuity

and contrast sensitivity compared to the other two groups, the majority of AD individuals perform within the normal range on both measures. This suggests that their visual difficulties, overall, are not severe or of clinical significance. Moreover, our observed deficits in reading acuity and contrast sensitivity in AD may indicate AD-related changes associated with neuropathologic and/or functional changes in the retina and/or visual processing pathways.

We do not believe that our findings on visual function were driven by presence of co-morbid diseases or other visual deficits. Although there was a significant group differences of AMD diagnosis (the MCI group had a higher percentage of cases compared to the SCD and AD groups), our results on visual function follow a different pattern (the SCD and MCI groups had better visual performance compared to the AD group; see Table 1). There was also a group difference in visual field deficits (the SCD group had a lower percentage of visual deficits than the MCI group, which had a lower percentage of visual deficits than the AD group; see Table 1); however, the difference between SCD and MCI groups is small (0% in SCD, and 1% in MCI) and is likely unreliable. Moreover, classification of visual field deficits was based only on one clinical test done during the COMPASS-ND neurology exam and did not comprehensively assess true visual field function. Therefore, this suggests that the relationship between diagnostic group membership and visual function is not confounded by presence of concurrent eye-related diseases or visual deficits. In support of our results, other studies have also indicated no group differences among SCD, MCI, and AD in previously diagnosed eye-related disorders (Marquie et al., 2019).

Previously, cross-sectional research has found worse performance for visual acuity (Uhlmann et al., 1991; Rizzo et al., 2000) and contrast sensitivity (Hutton et al., 1993; Rizzo et al., 2000; Nissen et al., 1985; Bassi, Solomon, & Young, 1993) in clinical AD groups compared

to healthy controls. Our finding that the AD group demonstrated poorer reading acuity compared to the SCD and MCI groups supports a recent study by Marquie et al. (2019), who also found that AD patients present worse visual acuity compared to SCD and MCI groups. In another study, Risacher et al. (2013) demonstrated that both AD and MCI groups demonstrate poor contrast sensitivity compared to individuals with cognitive complaints (SCD). This is somewhat in contrast with our findings, as both SCD and MCI groups were similar in performance on both measures of reading acuity and contrast sensitivity. This difference may be due to few reasons. First, our AD and MCI groups were similar in age (~76 years) and significantly older than the SCD group in the Risacher et al (2013) study, whereas the SCD and MCI groups were similar in age (SCD age = ~70 years, MCI = ~71 years) and significantly younger than the AD group in our study. Second, Risacher et al (2013) used a complex measure of visual field contrast sensitivity that evaluated 55 regions in each eye, which provided comprehensive analysis of contrast sensitivity thresholds, overall contrast sensitivity in each eye, and standard deviation to indicate how it deviates from age-adjusted norms. In comparison, we used the MARS Contrast Sensitivity test, which assesses letter contrast sensitivity at low retinal spatial frequencies on a chart. Variability in both the type of contrast sensitivity measure and the complexity of the measure itself could have contributed to differences in our findings and those of Risacher et al. (2013).

Finally, our findings demonstrate a consistent pattern across both visual measures and diagnostic groups (AD has reliably worse visual performance than SCD and MCI), suggesting that the AD group has significantly poor vision function compared to pre-clinical groups with less AD pathology. It is possible that any difference in visual deficits between SCD and MCI groups may be unobservable or subtle, especially when compared to larger reductions in visual

function with more prominent clinical pathology (AD). This is substantiated by other cross-sectional studies that associate poor visual function with AD pathology (Marquie et al., 2019; Risacher et al., 2013) and poor cognitive function quantified by MMSE scores (Zheng et al., 2018; Spierer et al., 2016; Mine et al., 2016) and other neuropsychological tests (Chen et al., 2017). Therefore, our study adds to previous literature by characterizing visual performance on multiple visual measures for all three diagnostic groups with or at risk for dementia.

Group Membership Predicts Variance in Cortical Structure for Multiple ROIs

Based on our hierarchical regression analyses, we found that group membership predicted cortical structure for multiple ROIs in each hemisphere beyond the baseline model predictors of age, sex, education, and ICV. In general, the AD group showed reduced cortical volume compared to the SCD group in the left inferior occipital gyrus and middle occipital gyrus, and in cortical thickness in the left inferior occipital gyrus and middle occipital gyrus, and the right superior occipital gyrus, calcarine sulcus, and parieto-occipital sulcus. Moreover, the AD group showed reduced cortical volume compared to both the SCD and MCI groups in the left-parieto occipital sulcus and the right cuneus middle occipital gyrus, occipital pole, and parieto-occipital sulcus, and in cortical thickness in the left anterior occipital sulcus and parieto-occipital sulcus and the right lunatus sulcus. Finally, both the MCI and AD groups showed reduced cortical thickness compared to the SCD group in the and between the SCD group left occipital pole and calcarine sulcus. These results present that overall, the AD group demonstrates more cortical atrophy in multiple vision-related ROIs compared to the SCD and MCI groups.

Reduced cortical integrity in AD individuals has been previously substantiated by multiple studies. Cortical atrophy has been supported as a neurological marker of increasing AD pathology (Mouton, Martin, Calhoun, Dal Forno, & Price, 1998; Obara, Meyer, Mortel, &

Muramatsu, 1994). Relevant to our study, there have been some findings demonstrating cortical degeneration in visual-related regions in AD groups. AD patients present degeneration in the primary visual cortex and secondary visual association cortices (Brewer & Barton, 2014; Armstrong, 1996; Lewis et al., 1987; McKee et al., 2006), as well as of subcortical regions comprising parts of the visual pathway (e.g., lateral geniculate nucleus; Leuba & Saini, 1995) and degeneration of the optic nerve and retinal ganglion cells (Hinton et al., 1986; Danesh-Meyer, Birch, Ku, Carroll, & Gamble, 2006; Berisha et al., 2007). Other findings present different patterns of atrophy in early-and late-onset individuals with AD. Whereas AD individuals with early-onset have atrophy in the neocortex and occipital lobe (sparing the primary but not the secondary visual cortex), those with a late-onset have diffuse loss that is prominent in the medial-temporal area (Frisoni et al., 2007). Together, these studies substantiate our finding of atrophy in visual-related ROIs in the AD group.

Although the current consensus is that primary sensory and motor areas are left relatively spared or affected at later stages of AD, previous literature and histology studies have found AD pathologies in the primary visual cortex and visual association areas (Leuba & Saini, 1995; Lewis et al., 1987; McKee et al., 2006). In fact, McKee et al.'s (2006) findings indicate that posterior visual areas can be affected even in the early stages of AD. In comparison, there is substantive evidence to establish that the motor cortex is often less affected in advanced stages of AD compared to the medial-temporal lobe and surrounding parietal-temporal-occipital association areas (Mann, 1991; Baron et al., 2001; Fox et al., 2001; Whitwell, 2010). To our knowledge, our study is the first to assess differences in cortical atrophy between clinical groups in both the primary motor and vision areas. Similar to previous findings, we found significant group differences in multiple visual-related ROIs while there were no group differences in the

precentral and postcentral gyrus (i.e., motor areas). This suggests that cortical atrophy is specific to the visual cortex and not simply a result of generalized atrophy throughout the brain in AD individuals. Finally, given these neurodegenerative changes in visual areas for AD individuals, it may not be surprising that we also found higher-order visual deficits involving reading acuity and contrast sensitivity in the AD group.

Visual Performance does not Predict Cortical Structure beyond Group Membership

With our hierarchal regression analyses, we found that there were no ROIs in which visual performance or the interaction between visual performance and group membership significantly accounted for variance in cortical integrity once we accounted for age, sex, education, ICV, and group membership alone. Thus, visual function or the visual-cognitive association do not predict cortical thickness and volume over and above group membership, in contrast to our hypothesis.

Our findings support two independent links, in that there is a link between 1) vision and group membership and 2) between group membership and cortical integrity, with no independent or direct link between visual status and cortical integrity. Despite poorer performance on reading acuity and contrast sensitivity in AD, our study has demonstrated that it is not visual status that drives the cortical atrophy patterns we see in visual ROIs in AD individuals. Similarly, we can conclude that although the AD group does have cortical atrophy in the visual cortex and related association areas, it is not visual status or visual performance that is largely contributing to this atrophy.

Our findings provide insight on the sequence and pathological mechanisms at play behind the vision-cognition-brain relationship. Whereas the sensory deprivation hypothesis posits that sensory impairment leads to changes in brain structure and consequent development of AD, our

results instead support a hypothesis in a different direction, such that neuropathology due to AD contributes to atrophy in vision-related brain regions that affects functional visual performance. This may explain why visual performance was poorer in the AD groups compared to other groups with less cognitive pathology, although it did not specifically predict cortical atrophy in vision-related brain regions. Perhaps then, deficits or changes in visual performance may also be explained by the measure being used, especially when adequate performance on that specific measure (e.g., contrast sensitivity) requires integrity of the underlying visual areas that are affected by AD pathology. Moreover, it is possible that the visual measure itself (e.g., reading acuity) may require optimal cognitive function to perform adequately. Although oral reading is thought to be relatively preserved at least during early stages of AD (Friedman, Ferguson, Robinson, & Sunderland, 1992; Strain, Patterson, Graham, & Hodges, 1998), others have found that reading and understanding meaning of written words are impaired in individuals with AD due to difficulties with visual processing and analysis of linguistic stimuli (Glosser et al., 2000). To address this in our study, we briefly tested and found that reading deficits (measured by neuropsychological tasks of sentence and word reading) did not significantly explain performance on our vision measures of reading acuity and contrast sensitivity.

There is enough evidence in our findings to retain the common-cause hypothesis. The common-cause hypothesis traditionally suggests that one or more underlying factors contribute to the development of both sensory and cognitive impairment, more specifically, a common factor contributes to both visual and cognitive decline. Our findings did not support a causal relationship between a) greater cortical atrophy in AD and b) poor visual performance in AD, and instead suggest that there are other factors beyond visual status are contributing to cortical atrophy in vision-specific brain regions. One such factor could be AD neuropathology (e.g.,

neurofibrillary tangles, amyloid beta deposits, inflammation) at various levels of the visual pathway (e.g., retina, optic nerve, subcortical regions, cortical regions associated with visual function; Leuba & Sani, 1995; Ikram et al., 2012; McKee et al., 2006), which may contribute to both poor visual function and accelerated cortical atrophy in vision-related brain regions. Risacher et al. (2013) have similarly hypothesized that the observed visual deficits in individuals with MCI and AD reflect neuropathological changes in the retina and central visual processing pathways. To further support our theory, tau and amyloid pathology have been associated with increased neurodegeneration and rates of region-specific cortical atrophy in both cognitively normal older adults and in individuals with MCI and AD (see Bejanin et al., 2017; Chételat et al., 2012 for examples). However, it remains critical to note that our study did not assess measures of neuropathology across different levels of the visual system, and our conclusions remain speculative at best until further research is completed.

The pathological mechanisms underlying changes in contrast sensitivity and other low-level visual measures in AD have been previously discussed. Cronin-Golomb et al. (1991a), Cronin-Golomb et al. (1991b) and Leuba and Sani (1995) hypothesized that atrophy or lesions in the primary and associative visual cortex were responsible for the psychophysical visual deficits (e.g., in contrast sensitivity) observed in AD individuals, and that the pattern of performance on vision measures may elucidate the location and extent of underlying cortical atrophy that contributes to visual dysfunction in AD. In conjunction with atrophy in the cortex, other researchers have attributed visual problems to pathological changes or abnormalities in peripheral structures such as the optic nerve and retina (Gilmore & Whitehouse, 1995; Hinton et al., 1986; Sadun & Bassi, 1990; Bassi et al., 1993; Risacher et al., 2013). Overall, based both on previous literature and our findings, we can conclude that 1) cortical atrophy associated with

group membership drives visual performance, 2) deficits or changes in visual performance are pronounced when the measure relies on the integrity of underlying visual areas that are affected by AD pathology, and that 3) one area of future research is to assess the mechanisms and extent to which both cortical and retinal (e.g., degeneration of visual pathways, the optic nerve) pathology contribute to behavioural visual deficits in AD.

Limitations

Although our MCI group had a substantial sample size, we need additional data to obtain greater power and less variability in results for the SCD and AD groups. It is possible that smaller sample sizes for the SCD and AD groups could contribute to null effects or small effects that do not reach statistical significance although in the right direction. Increasing our sample size in these two groups will allow better estimates of effect size, especially with FreeSurfer analyses. Another limitation regarding our sample size is the skewed sex ratio of the SCD (78% women) and AD (33% women). This may not be representative of the population, especially given the fact that AD is more prevalent in women than men (see Baum, 2005 for a review).

Other shortcomings involve the scope and extent of the measures that were available in the COMPASS-ND dataset. One limitation is that we used a complex measure of reading acuity compared to a basic-level assessment of visual acuity, such as grating acuity. Reading acuity is a functional test of reading performance that measures not only threshold size, but also involves components of reading such as fluency, speed, and comprehension (Colenbrander, 2005; Xiong et al., 2018). It is also possible that high-contrast reading acuity may be too robust as a visual skill to be sensitive to subtle cortical changes, compared to low-contrast acuity (grey on white). Moreover, it is important to remember that we only used two visual measures to determine visual function in our participants. Although their relationship with cortical structure in visual-based

ROIs remains largely understudied, domains of color vision, depth perception, basic-level visual acuity, or visuospatial processing have all been implicated clinically in AD individuals and may contribute to stronger associations with atrophy in vision-related areas. To obtain a more comprehensive characterization of visual function in our participants, we could have measured peripheral vision (e.g., a complex measure of visual field deficits), retinal thickness, or amyloid deposits in the retina. There were also were no structural data in the COMPASS-ND dataset for important visual areas like the superior colliculus and pulvinar, which have been implicated as pathological structures underlying visual deficits in AD individuals (Iseki et al., 1989; Rizzo et al., 2000).

Finally, our study only assessed cross-sectional data. In order to clarify the direction of the vision-cognitive relationship and its influence on cortical structure, longitudinal data are needed (which are currently being collected in the COMPASS-ND study). Although our study is the first to assess the visual-cognition-brain relationship in multiple groups with varying cognitive function, longitudinal data will be critical in revealing core directions or causal relationships between visual impairment, cognitive decline, and brain structure.

Implications and Future Directions

These data give first insights into the frequency and degree of visual impairment in clinical groups with or at risk for dementia in the COMPASS-ND dataset, allowing us to explore the relationship between vision, cognition, and cortical structure in our participants. Given that we found poorer visual performance in the AD group compared to the SCD and MCI groups, and that visual impairment and cognitive decline are major health issues for older adults, our research supports efforts of targeting and treating poor vision (e.g., regular ophthalmological assessments) in preclinical stages of AD and AD to optimize visual function.

Future studies will be helpful in clarifying which specific visual measures (e.g., contrast sensitivity) are useful in predicting early MCI or AD and are promising tools for dementia screening. Moreover, deficits in contrast sensitivity can also lead to degraded visual input and consequently contribute to functional impairment, such as difficulties with mobility and navigating around obstacles, and greater risk for falls (see Cormack et al., 2000 for a review). Research investigating functional impairment caused by visual deficits can potentially have profound clinical implications. For example, we can ascertain the relationship between visual function and activities of daily living across the diagnostic groups in order to assess and improve quality of life.

Our study adds to previous sensory-cognitive literature and provides novel insight on the mechanisms underlying the sensory-cognitive-brain relationship; more specifically, the association between functional visual impairment in AD and structural atrophy in the visual system. It would be useful to further determine patterns and rates of atrophy present in the primary visual cortex and secondary visual association areas, and consequently ascertain how atrophy in vision-related areas contributes to neurodegeneration and acceleration in functional

visual deficits, above and beyond changes in hippocampal and medial-temporal areas. Moreover, additional research needs to be done to determine the pathological substrates underlying changes or deficits in visual function; more specifically, future research should delineate whether visual deficits are attributable to structural atrophy in central vision areas as a consequence of AD pathogenesis, pathological changes in peripheral structures like the retina and optic nerve that affect visual input, or deterioration and pathology in both.

More research also needs to be done to determine which clinical or neuropathologic factors accelerate cortical atrophy in vision-related areas in AD to facilitate identification of biomarkers that increase both visual and cognitive decline. With additional longitudinal data from the COMPASS-ND dataset, we may be able to identify visual impairment as a possible risk factor associated with developing AD or determine whether improving visual function is a promising opportunity for dementia prevention. Such studies will facilitate development of strategies and novel interventions that provide ways to detect and improve visual deficits to further reduce risk for cognitive decline and improve quality of life.

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Tables

Table 1

Basic Demographics and Descriptives on Vision Variables and Counts of Eye-Related Diseases and Visual Deficits for SCD, MCI, and AD Groups

Demographics	SCD (N = 53)		MCI (N = 102)		AD (N = 45)		F/X_2 Statistics		
	Mean	±SD	Mean	±SD	Mean	±SD	F	Post-hoc	X_2
Age (years)	70.34	6.99	71.29	6.31	74.24	7.79	4.34*	SCD, MCI> AD	-
Education (years)	16.95	3.16	15.67	3.98	14.88	3.79	3.96*	SCD, MCI> AD	-
Female (%)	77.5		46.1		33.3		-	-	21.34**
Vision Variables									
MNRead Acuity (logMAR[1])	.11	.14	.12	.17	.22	.21	3.59**	SCD, MCI > AD	-
MARS CS (log CS_2)	1.73	.13	1.70	.15	1.57	.18	10.29**	SCD, MCI > AD	-
Eye-Related Disease	SCD (N)		MCI (N)		AD (N)				
Diabetes Type I (%)	0		2		0		-	-	1.94
Diabetes Type II (%)	2		11		3		-	-	2.50
Cataracts (%)	20		41		18		-	-	.12
Glaucoma (%)	3		5		2		-	-	.08
Age-related macular degeneration (%)	3		4		7		-	-	6.82*
Visual field loss (%)	0		1		3		-	-	6.62*

Note. * p = <.05, ** p = <.01

[1] controlling for age and sex; logMAR = logarithm of the minimum angle of resolution; lower score indicates better performance; logMAR < .30 (equivalent of better than 20/40) = normal acuity. logMAR .30 to .50 (20/40 to 20/60) = moderate visual impairment

[2] controlling for age and sex; higher score indicates better performance; < 1 log CS = severe impairment, 1-1.5 log CS = moderate impairment, > 1.5 log CS = normal for age 60+

Table 2

Regression Models for the Volume of the Left Inferior Occipital Gyrus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	9.53	38.47	-66.34 – 85.39	33.93	38.50	-42.01 – 109.87	38.7	40.09	-40.37 – 117.77	39.69	40.92	-41.03 – 120.42
Sex	75.46	80.2	-82.71 – 233.62	139.09	81.87	-22.38 – 300.57	153.29	82.53	-9.5 – 316.08	155.79	84.96	-11.83 – 323.4
Education	105.3**	38.55	29.26 – 181.33	83.5*	38.43	7.69 – 159.3	85.59*	38.5	9.66 – 161.53	81.37*	39.38	3.67 – 159.06
ICV	88.4*	39.86	9.78 – 167.02	98.49*	39.19	21.19 – 175.79	101.01*	39.25	23.59 – 178.44	100.96*	40.76	20.55 – 181.37
Group (MCI)				-150.95	93.38	-336.31– 34.40	-154.33	94.17	-340.07 – 31.4	-139.82	105.17	-347.31 – 67.67
Group (AD)				370.41**	117.04	-601.25 – -139.56	365.78**	122.12	-606.65 – -124.9	301.17*	132.1	-561.79 – - 40.55
RA							55.21	43.73	-31.05 – 141.46	105.05	100.07	-92.38 – 302.47
CS							50.07	47.08	-42.80 – 142.94	9.37	99.9	-187.72 – 206.47
Group x Vision												
MCI x RA										-39.21	118.71	-267.12 – 201.29
AD x RA										-68.11	142.37	-349.01 – 212.78
MCI x CS										14.94	118.36	-218.59 – 248.44
AD x CS										94.02	140.89	-183.94 – 371.99
Adjusted R_2		.05			.09			.09			.07	
AIC		3091.47			3085.19			3087.19			3097.39	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 4.97$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = .94$, $p = .39$)

Table 3

Pairwise Comparisons between Groups in Volume of the Left Inferior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2956	77.1	2804 – 3108	
MCI	2805	52.6	2701– 2909	
AD	2585	82.1	2424 – 2747	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	151	94.0	1.61	.25
SCD – AD	370	117.0	3.17	.01
MCI – AD	219	97.3	2.26	.06

Note. Results are averaged over the levels of sex.

Table 4

Regression Models for the Thickness of the Left Inferior Occipital Gyrus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.00	.01	-.03 – .03	.01	.01	-.01 – .04	.02	.01	-.01 – .05	.02	.01	-.01 – .05
Sex	-.02	.03	-.08 – .04	.01	.03	-.05 – .07	.02	.03	-.04 – .07	.02	.03	-0.04 – .08
Education	.04*	.01	.01 – .06	.03	.01	-.00 – .05	.03	.01	-.00 – .05	.02	.01	-.00 – .05
ICV	.01	.01	-.02- .04	.01	.01	-0.02 – .04	.01	.01	-.02 – .04	.01	.01	-.02 – .04
Group (MCI)				-.07*	.03	-.14 – -.00	-.07*	.03	-.14 – -.00	-.07	.04	-.14 – .01
Group (AD)				-.17***	.04	-.25 – -.09	-0.16***	.04	-.25 – -.07	-.16***	.05	-.25 – -.07
RA							.02	.02	-.01 – .05	.04	.04	-.03 – .11
CS							.03	.02	-.01 – .06	.02	.04	-.05 – .09
Group x Vision												
MCI x RA										-.02	.04	-.1 – .07
AD x RA										-.04	.05	-.14 – .06
MCI x CS										.00	.04	-.08 – .08
AD x CS										-.03	.05	-.13 – .07
Adjusted R_2		.01			.08			.09			.08	
AIC		-73.80			-86.10			-84.68			-75.75	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 8.12$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = 1.22$, $p = .3$)

Table 5

Pairwise Comparisons between Groups in Thickness of the Left Inferior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.39	.03	2.34 – 2.45	
MCI	2.32	.02	2.29 – 2.36	
AD	2.33	.03	2.16 – 2.28	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.07	.03	2.03	.11
SCD – AD	.17	.04	4.02	.00
MCI – AD	.10	.03	2.88	.01

Note. Results are averaged over the levels of sex.

Table 6

Regression Models for the Volume of the Left Cuneus

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-18.08	37.5	-92.04 – 55.89	2.24	37.83	-72.38 – 76.86	12.64	39.46	-65.19 – 90.47	17.83	40.38	-61.84 – 97.49
Sex	38.49	78.19	-115.71 –192.68	85.8	80.45	-72.87 – 244.46	83.86	81.24	-76.38 – 244.10	84.81	83.84	-80.60 – 250.22
Education	66.74	37.59	-7.39 – 140.87	49.82	37.77	-24.67 – 124.31	50.87	37.89	-23.87 – 125.61	54.44	38.36	-22.23 – 131.11
ICV	94.08*	38.86	17.43 – 170.72	102.49**	38.51	26.53 – 178.45	102.84**	38.64	26.63 – 179.06	104.08*	40.22	24.73 – 183.43
Group (MCI)				-93.05	92.34	-275.18– 89.08	-87.03	92.69	-269.86 – 95.79	-111.89	103.78	-316.64 – 92.86
Group (AD)				-294.34**	115.01	-521.18 – -67.51	-258.27*	120.20	-495.37 – -21.8	-235.06	130.36	-492.25 – - 22.13
RA							-29.43	43.04	-114.33 – 55.48	-62.4	98.75	-257.22 – 132.43
CS							22.76	46.35	-68.66 – 114.17	-36.68	98.58	-231.18 – 157.82
Group x Vision												
MCI x RA										81.31	117.15	-149.81 – 312.43
AD x RA										8.51	140.5	-268.69 – 285.70
MCI x CS										81.64	116.80	-140.80 – 312.08
AD x CS										70.91	139.03	-241.51 – 162.4
Adjusted R_2		.03			.05			.05			.03	
AIC		3081.26			3078.17			3080.87			3092.09	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 3.38$, $p = .04$); Model 3 not better than Model 2 ($F(2, 191) = .61$, $p = .4$)

Table 7

Pairwise Comparisons between Groups in Volume of the Left Cuneus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2931	75.7	2782 – 3081	
MCI	2838	51.7	2736 – 2940	
AD	2637	80.6	2782 – 2796	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	93.1	92.3	1.01	.57
SCD – AD	294.3	115.0	2.56	.03
MCI – AD	201.3	95.6	2.11	.09

Note. Results are averaged over the levels of sex.

Table 8

Regression Models for the Thickness of the Left Cuneus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-.00	.01	-.02 – .02	.00	.01	-.02 – .02	-.00	.01	-.02 – .02	-.00	.01	-.02 – .02
Sex	-.02	.02	-.07 – .02	-.02	.02	-.06 – .03	-.02	.02	-.07 – .02	-.02	.02	-0.06 – .03
Education	.01	.01	-.01 – .03	.01	.01	-.02 – .03	.00	.01	-.02 – .03	.00	.01	-.02 – .02
ICV	-.00	.01	-.02 – .02	.00	.01	-.02 – .02	-.00	.01	-.02 – .02	.00	.01	-.02 – .02
Group (MCI)				-.01	.03	-.06 – .04	-.01	.03	-.06 – .04	-.01	.03	-.07 – .04
Group (AD)				-.04	.03	-.11 – .02	-.04	.03	-.11 – .02	-.04	.04	-.11 – .03
RA							-.02	.01	-.05 – .00	-.03	.03	-.08 – .03
CS							-.02	.01	-.04 – .01	-.03	.03	-.08 – .03
Group x Vision												
MCI x RA										.02	.03	-.05 – .08
AD x RA										-.02	.04	-.1 – .05
MCI x CS										.01	.03	-.05 – .06
AD x CS										.01	.04	-.06 – .07
Adjusted R_2		-.01			-.01			.00			-.02	
AIC		-200.67			-198.73			-199.03			-188.58	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = .99$, $p = .37$) and Model 3 ($F(2,191) = 2.04$, $p = .13$) not better than Model 1.

Table 9

Pairwise Comparisons between Groups in Thickness of the Left Cuneus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	1.88	.02	1.83 – 1.92	
MCI	1.86	.01	1.82 – 1.89	
AD	1.83	.02	1.79 – 1.88	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.01	.03	.56	.84
SCD – AD	.04	.03	1.38	.26
MCI – AD	.03	.03	1.12	.51

Note. Results are averaged over the levels of sex.

Table 10

Regression Models for the Volume of the Left Middle Occipital Gyrus

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-98.95*	49.21	-196.0 – -1.9	-70.74	49.52	-168.42 – 26.93	-44.75	51.17	-145.69 – 56.19	-50.46	52.33	-61.84 – 97.49
Sex	22.37	102.51	-179.96 – 224.71	74.66	105.30	-133.03 – 282.35	98.47	105.36	-109.35 – 306.29	108.21	108.65	-80.60 – 250.22
Education	47.12	49.32	-50.15 – 144.38	26.53	49.44	-70.98 – 124.03	32.21	49.15	-64.73 – 129.14	22.85	50.36	-22.23 – 131.11
ICV	65.98	51.00	-34.60 – 166.55	77.71	50.41	-21.72 – 177.14	83.07	50.11	-15.77 – 181.91	82.65	52.12	24.73 – 183.43
Group (MCI)				-51.94	120.88	-290.35– 186.46	-48.57	120.21	-258.68 – 188.54	-22.73	134.49	-316.64 – 92.86
Group (AD)				-375.63*	150.54	-672.55 – -78.71	-308.13*	155.89	-615.63 – -.64	-345.43*	168.93	-492.25 – - 22.13
RA							56.90	55.82	-114.33 – 55.48	60.48	127.97	-257.22 – 132.43
CS							132.08*	60.11	13.52 – 250.64	115.29	127.76	-231.18 – 157.82
Group x Vision												
MCI x RA										-37.8	151.81	-337.32 – 261.71
AD x RA										-6.24	182.08	-365.47 – 352.98
MCI x CS										12.98	151.36	-285.65 – 311.61
AD x CS										18.25	180.18	-337.23 – 373.73
Adjusted R_2		.01			.04			.06			.04	
AIC		3189.93			3185.87			3184.87			3195.78	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 3.94$, $p = .02$); Model 3 not better than Model 2 ($F(2, 191) = 2.36$, $p = .10$)

Table 11

Pairwise Comparisons between Groups in Volume of the Left Middle Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	4333	99.1	4137 – 4528	
MCI	4281	67.6	4148 – 4414	
AD	3957	105.6	3749 – 4165	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	51.9	121	.43	.90
SCD – AD	375.6	151	2.50	.04
MCI – AD	323.7	125	2.59	.03

Note. Results are averaged over the levels of sex.

Table 12

Regression Models for the Thickness of the Left Middle Occipital Gyrus

Variable	Model 1			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.01	.01	-.02 – .03	.01	.01	-.01 – .04	.02	.01	-.01 – .04	.02	.01	-.01 – .04
Sex	-.03	.02	-.08 – .01	-.02	.02	-.07 – .03	-.02	.03	-.07 – .03	-.03	.03	-0.08 – .03
Education	.02	.01	-.00 – .04	.02	.01	-.01 – .04	.02	.01	-.01 – .04	.02	.01	-.01 – .04
ICV	-.01	.01	-.04 – .01	-.01	.01	-.04 – .01	-.01	.01	-.04 – .01	-.01	.01	-.04 – .01
Group (MCI)				-.02	.03	-.08 – .03	-.02	.03	-.08 – .03	-.03	.03	-.09 – .04
Group (AD)				-.10**	.04	-.17 – -.03	-.09*	.04	-.16 – -.01	-.10*	.04	-.18 – -.02
RA							.00	.01	-.03 – .03	.05	.03	-.01 – .11
CS							.01	.01	-.02 – .04	.04	.03	-.02 – .1
Group x Vision												
MCI x RA										-.06	.04	-.13 – .01
AD x RA										-.06	.04	-.14 – .03
MCI x CS										-.02	.04	-.1 – .05
AD x CS										-.05	.04	-.14 – .03
Adjusted R_2		.02			.05			.05			.04	
AIC		-148.57			-152.88			-149.74			-140.67	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 4.02$, $p = .02$); Model 3 not better than Model 2 ($F(2, 191) = .40$, $p = .67$)

Table 13

Pairwise Comparisons between Groups in Thickness of the Left Middle Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.44	.02	2.4 – 2.49	
MCI	2.42	.02	2.39 – 2.45	
AD	2.35	.03	2.3 – 2.4	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.02	.03	.87	.66
SCD – AD	.10	.04	2.71	.02
MCI – AD	.07	.03	2.42	.04

Note. Results are averaged over the levels of sex.

Table 14

Regression Models for the Volume of the Left Middle Occipital Lunatus Sulcus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-1.51	23.56	-47.98 – 44.95	6.52	24.03	-40.87 – 53.91	9.99	24.82	-38.96 – 58.94	9.12	25.05	-40.31 – 58.54
Sex	19.82	49.12	-77.06 – 116.69	37.32	51.09	-63.44 – 138.09	51.46	51.09	-49.32 – 152.23	47.20	52.02	-55.42 – 149.83
Education	46.55	23.61	-.02 – 93.12	40.12	23.99	-7.18 – 87.43	42.06	23.83	-4.95 – 89.06	42.48	24.11	-5.09 – 90.05
ICV	70.01**	24.42	21.86 – 118.17	73.34**	24.46	25.10 – 121.59	75.77**	24.3	27.84 – 123.70	90.98***	24.95	41.75 – 140.21
Group (MCI)				-29.90	58.65	-145.57– 85.77	-33.91	58.29	-148.89 – 81.07	-15.27	64.39	-142.31 – 111.76
Group (AD)				-113.39	73.04	-257.45 – -30.67	-113.02	75.60	-262.13 – -36.09	-112.79	80.88	-272.35 – 46.78
RA							57.48*	27.07	4.09 – 110.88	-96.54	61.27	-24.33 – 217.41
CS							46.42	29.15	-11.07 – 103.91	-62.52	61.16	-58.16 – 183.19
Group x Vision												
MCI x RA										-23.19	72.68	-166.58 – 120.21
AD x RA										-161.87	87.17	-333.85 – 10.11
MCI x CS										-7.76	72.46	-150.73 – 135.31
AD x CS										2.36	86.26	-167.83 – 172.54
Adjusted R_2		.04			.05			.06			.07	
AIC		2895.33			2896.58			2895.37			2901.15	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 1.36$, $p = .26$) and Model 3 ($F(2,191) = 2.53$, $p = .08$) not better than Model 1.

Table 15

Pairwise Comparisons between Groups in Volume of the Left Middle Occipital Lunatus Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	1312	48.1	1217 – 1407	
MCI	1282	32.8	1218 – 1347	
AD	1199	51.2	1098 – 1300	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	29.9	58.6	.51	.87
SCD – AD	113.4	73	1.44	.27
MCI – AD	83.5	60.7	1.38	.36

Note. Results are averaged over the levels of sex.

Table 16

Regression Models for the Thickness of the Left Middle Occipital Lunatus Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.02	.01	-.00 – .04	.03*	.01	.00 – .05	.03*	.01	.01 – .06	.03**	.01	.01 – .06
Sex	-.06*	.02	-.11 – -.01	-.04	.03	-.09 – .01	-.04	.03	-.09 – .01	-.04	.03	-0.09 – .01
Education	.02*	.01	.00 – .05	.02	.01	-.01 – .04	.02	.01	-.01 – .04	.02	.01	-.01 – .04
ICV	.01	.01	-.02 – .03	.01	.01	-.01 – .04	-.01	.01	-.01 – .04	.02	.01	-.01 – .04
Group (MCI)				-.05	.03	-.1 – .01	-.04	.03	-.1 – .01	-.04	.03	-.1 – .02
Group (AD)				-.12**	.04	-.19 – -.05	-.11**	.04	-.19 – -.04	-.13***	.04	-.21 – -.06
RA							-.00	.01	-.03 – .03	.01	.03	-.05 – .07
CS							.01	.01	-.02 – .04	.01	.03	-.05 – .07
Group x Vision												
MCI x RA										-.02	.04	-.09 – .05
AD x RA										-.05	.04	-.14 – .04
MCI x CS										.03	.04	-.05 – .1
AD x CS										-.02	.04	-.11 – .06
Adjusted R_2		.05			.1			.09			.09	
AIC		-143.21			-151.57			-148.43			-142.4	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 6.13$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = .42$, $p = .66$)

Table 17

Pairwise Comparisons between Groups in Thickness of the Left Middle Occipital Lunatus Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.02	.02	1.97 – 2.06	
MCI	1.97	.02	1.94 – 2	
AD	1.89	.03	1.84 – 1.94	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.05	.03	1.59	.25
SCD – AD	.12	.04	3.46	.00
MCI – AD	.08	.03	2.63	.03

Note. Results are averaged over the levels of sex.

Table 18

Regression Models for the Volume of the Left Superior Occipital Gyrus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-63.03*	27.78	-117.81 – -8.25	-58.56*	28.48	-114.73 – -2.39	-49.48	29.62	-107.91 – 8.95	-51.57	25.05	-110.08 – 6.94
Sex	35.56	57.91	-78.65 – 149.76	45.93	60.55	-73.51 – 165.36	56.16	60.99	-64.14 – 176.47	38.68	61.58	-82.8 – 160.17
Education	48.88	27.84	-6.02 – 103.79	45.17	28.43	-10.9 – 101.24	47.36	28.45	-8.76 – 103.48	57.1*	28.54	.79 – 113.41
ICV	18.85	28.78	-37.92 – 75.52	20.7	28.99	36.48 – 77.87	22.87	29.01	-34.45 – 80.09	24.8	29.54	-33.48 – 83.08
Group (MCI)				-20.27	69.51	-157.37– 116.82	-19.88	69.59	-157.14 – 117.39	-37.07	76.22	-187.45 – 113.32
Group (AD)				-64.63	86.57	-235.38 – 106.11	-42.57	90.25	-220.58 – 135.44	5.03	95.74	-183.87 – 193.92
RA							28.63	32.32	-35.12 – 92.37	123.13	72.53	-19.96 – 266.22
CS							51.19	34.8	-17.44 – 119.82	129.10	72.4	-13.75 – 271.95
Group x Vision												
MCI x RA										-123.91	86.04	-293.66 – 45.84
AD x RA										-83.92	103.19	-287.5 – 119.67
MCI x CS										-134.53	85.78	-303.78 – 34.71
AD x CS										14.97	102.11	-186.49 – 216.44
Adjusted R_2		.02			.02			.02			.04	
AIC		2961.15			2964.55			2966.22			2968.63	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = .30$, $p = .74$) and Model 3 ($F(2,191) = 1.14$, $p = .32$) not better than Model 1.

Table 19

Pairwise Comparisons between Groups in Volume of the Left Superior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2322	57.0	2209 – 2434	
MCI	2302	38.9	2225 – 2378	
AD	2257	60.7	2138– 2377	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	20.3	69.5	.29	.95
SCD – AD	64.6	86.6	.75	.74
MCI – AD	44.4	72	.62	.81

Note. Results are averaged over the levels of sex.

Table 20

Regression Models for the Thickness of the Left Superior Occipital Gyrus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-.01	.01	-.04 – .01	-.01	.01	-.03 – .02	-.01	.01	-.04 – .01	-.01	.01	-.04 – .02
Sex	-.06*	.03	-.11 – -.01	-.05*	.03	-.1 – -.00	-.06*	.03	-.11 – -.00	-.07*	.03	-0.12 – -.01
Education	.03*	.01	.01 – .06	.03*	.01	.00 – .05	.03*	.01	.00 – .05	.03*	.01	.00 – .05
ICV	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02
Group (MCI)				-.03	.03	-.09 – .03	-.03	.03	-.09 – .03	-.03	.03	-.09 – .04
Group (AD)				-.06	.04	-.13 – .02	-.06	.04	-.14 – .02	-.08*	.04	-.17 – -.00
RA							-.01	.01	-.04 – .02	.02	.03	-.05 – .08
CS							-.01	.02	-.04 – .02	.00	.03	-.06 – .07
Group x Vision												
MCI x RA										-.06	.04	-.14 – .01
AD x RA										-.01	.05	-.1 – .08
MCI x CS										-.01	.04	-.08 – .07
AD x CS										-.04	.04	-.13 – .04
Adjusted R_2		.07			.07			.06			.08	
AIC		-132.18			-130.41			-127.56			-124.22	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 1.10$, $p = .34$) and Model 3 ($F(2,191) = .56$, $p = .57$) not better than Model 1.

Table 21

Pairwise Comparisons between Groups in Thickness of the Left Superior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.12	.02	2.07 – 2.17	
MCI	2.09	.02	2.06 – 2.12	
AD	2.06	.03	2.01 – 2.12	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.03	.03	.96	.60
SCD – AD	.06	.04	1.47	.31
MCI – AD	.03	.03	.84	.68

Note. Results are averaged over the levels of sex.

Table 22

Regression Models for the Volume of the Left Occipital Pole

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-10.67	31.05	-71.91 – 50.57	1.42	31.51	-60.74 – 63.57	8.89	29.62	-55.42 – 73.2	10.56	33.47	-55.47 – 76.59
Sex	-49.00	64.74	-176.67 –78.67	-10.00	67.01	-142.16 – 122.17	7.54	67.12	-124.85 – 139.94	-.44	69.49	-137.54 – 136.65
Education	47.38	31.12	-13.99 – 108.76	34.96	31.46	-27.08 – 97.01	37.74	31.31	-24.02 – 99.5	43.17	32.21	-20.38 – 106.72
ICV	96.82**	32.18	33.36 – 160.28	101.79**	32.08	38.52 – 165.06	105**	31.92	-42.03 – 167.97	102.4**	33.33	36.63 – 168.17
Group (MCI)				-117.90	76.92	-269.62– 33.81	-121.29	76.58	-272.34 – 29.77	-156.14	86.02	-325.85 – 13.57
Group (AD)				-201.96*	95.8	-390.31 – -13.01	-190.99	99.32	-386.89 – 4.9	-210.25	108.05	-423.42 – 2.92
RA							65.05	35.56	-5.10 – 135.2	74.07	81.85	-87.44 – 235.51
CS							66.07	38.29	-9.46 – 141.60	62.97	81.71	-98.24 – 224.18
Group x Vision												
MCI x RA										-17.13	97.09	-208.69 – 174.43
AD x RA										6.26	116.45	-223.49 – 236.01
MCI x CS										10.77	96.81	-180.23 – 201.77
AD x CS										3.88	115.24	-223.48 – 231.23
Adjusted R_2		.04			.05			.06			.03	
AIC		3005.75			3005.07			3004.52			3017	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 2.24$, $p = .10$) and Model 3 ($F(2,191) = 2.13$, $p = .12$) not better than Model 1.

Table 23

Pairwise Comparisons between Groups in Volume of the Left Occipital Pole

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2984	63.1	2859 – 3108	
MCI	2866	43.0	2781 – 2951	
AD	2782	67.2	2649– 2914	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	117.9	76.9	1.53	.28
SCD – AD	202.0	95.8	2.11	.01
MCI – AD	84.1	79.6	1.06	.54

Note. Results are averaged over the levels of sex.

Table 24

Regression Models for the Thickness of the Left Occipital Pole

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.00	.01	-.02 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03
Sex	-.06**	.02	-.11 – -.02	-.05	.02	-.09 – .00	-.04	.02	-.09 – .00	-.05	.02	-0.09 – .00
Education	.02*	.01	.00 – .04	.02	.01	-.01 – .04	.02	.01	-.01 – .04	.02	.01	-.00 – .04
ICV	.00	.01	-.02 – .03	.01	.01	-.02 – .03	.01	.01	-.02 – .03	.01	.01	-.02 – .03
Group (MCI)				-.06*	.03	-.11 – -.01	-.06*	.03	-.11 – -.01	-.07*	.03	-.13 – -.01
Group (AD)				-.09**	.03	-.16 – -.03	-.09*	.04	-.16 – -.02	-.12**	.04	-.19 – -.04
RA							.00	.01	-.02 – .03	.01	.03	-.05 – .06
CS							.01	.01	-.02 – .04	.01	.03	-.05 – .07
Group x Vision												
MCI x RA										-.01	.03	-.08 – .05
AD x RA										-.01	.04	-.09 – .07
MCI x CS										.01	.03	-.06 – .08
AD x CS										-.01	.04	-.09 – .07
Adjusted R_2		.04			.07			.07			.06	
AIC		-168.42			-172.65			-169.15			-160.73	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 3.98$, $p = .02$); Model 3 not better than Model 2 ($F(2, 191) = .24$, $p = .79$)

Table 25

Pairwise Comparisons between Groups in Thickness of the Left Occipital Pole

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.02	.02	1.97 – 2.06	
MCI	1.96	.02	1.93 – 1.99	
AD	1.93	.02	1.88 – 1.97	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.06	.03	2.20	.07
SCD – AD	.09	.03	2.76	.02
MCI – AD	.03	.03	1.19	.46

Note. Results are averaged over the levels of sex.

Table 26

Regression Models for the Volume of the Left Calcarine Sulcus

Variable	Model 1			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-3.29	40.90	-83.95 – 77.37	11.83	41.52	-70.06 – 93.72	5.37	43.41	-80.25 – 90.99	7.26	44.14	-55.47 – 76.59
Sex	115.08	85.27	-53.08 – 283.25	166.66	88.28	-7.46 – 340.79	162.91	89.37	-13.37 – 339.2	180.44	91.64	-137.54 – 136.65
Education	82.59*	40.99	1.75 – 163.43	66.45	41.45	-15.30 – 148.19	65.27	41.69	-16.96 – 147.49	56.7	42.48	-20.38 – 106.72
ICV	28.41	42.38	-55.18 – 112	34.62	42.27	-48.74 – 117.98	33.62	42.51	-50.22 – 117.47	38.26	43.96	36.63 – 168.17
Group (MCI)				-163.48	101.34	-363.36– 36.39	-165.2	101.97	-366.33 – 35.92	-118.64	113.44	-325.85 – 13.57
Group (AD)				-259.6*	126.21	-508.54 – -10.66	-278.09*	132.24	-538.92 – -17.26	-213.83	142.49	-423.42 – 2.92
RA							-4.26	47.35	-97.66 – 89.14	-37.22	107.94	-87.44 – 235.51
CS							-27.13	50.99	-127.7 – 73.44	-70.82	107.76	-98.24 – 224.18
Group x Vision												
MCI x RA										100.15	128.05	-208.69 – 174.43
AD x RA										-27.67	153.57	-223.49 – 236.01
MCI x CS										41.88	127.67	-180.23 – 201.77
AD x CS										35.36	151.97	-223.48 – 231.23
Adjusted R_2		.01			.02			.02			.00	
AIC		3115.94			3115.36			3119.04			3127.68	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 2.19$, $p = .11$) and Model 3 ($F(2,191) = .15$, $p = .86$) not better than Model 1.

Table 27

Pairwise Comparisons between Groups in Volume of the Left Calcarine Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	3058	83.1	2894 – 3222	
MCI	2894	56.7	2783 – 3006	
AD	2798	88.5	2623– 2973	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	163.5	101	1.61	.24
SCD – AD	259.6	126	2.06	.10
MCI – AD	96.1	105	.92	.63

Note. Results are averaged over the levels of sex.

Table 28

Regression Models for the Thickness of the Left Calcarine Sulcus

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-.00	.01	-.02 – .01	.00	.01	-.02 – .02	.00	.01	-.02 – .02	.00	.01	-.02 – .02
Sex	-.02	.02	-.05 – .02	-.00	.02	-.04 – .04	-.00	.02	-.04 – .04	-.00	.02	-.04 – .04
Education	.02*	.01	.00 – .04	.01	.01	-.00 – .03	.02	.01	-.00 – .03	.02	.01	-.00 – .04
ICV	-.00	.01	-.02 – .01	-.00	.01	-.02 – .02	-.00	.01	-.02 – .02	-.00	.01	-.02 – .02
Group (MCI)				-.05*	.02	-.09 – -.00	-.04	.02	-.09 – .00	-.05	.03	-.1 – .00
Group (AD)				-.07*	.03	-.12 – -.01	-.06*	.03	-.12 – -.00	-.06*	.03	-.13 – -.00
RA							-.00	.01	-.02 – .02	.01	.02	-.04 – .06
CS							.01	.01	-.02 – .03	.02	.02	-.03 – .07
Group x Vision												
MCI x RA										-.02	.03	-.07 – .04
AD x RA										-.03	.03	-.10 – .04
MCI x CS										-.02	.03	-.08 – .04
AD x CS										.00	.03	-.07 – .07
Adjusted R_2		.01			.03			.03			.00	
AIC		-244.76			-247.36			-243.91			-233.03	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 3.14$, $p < .05$); Model 3 not better than Model 2 ($F(2, 191) = .26$, $p = .77$)

Table 29

Pairwise Comparisons between Groups in Thickness of the Left Calcarine Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	1.86	.02	1.82 – 1.9	
MCI	1.81	.01	1.79 – 1.84	
AD	1.79	.02	1.75 – 1.83	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.05	.02	2.02	.11
SCD – AD	.07	.03	2.44	.04
MCI – AD	.02	.02	.99	.58

Note. Results are averaged over the levels of sex.

Table 30

Regression Models for the Volume of the Left Anterior Occipital Sulcus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.49	20.84	-40.61 – 41.58	4.48	21.35	-37.63 – 46.59	5.89	22.31	-38.12 – 49.9	6.18	22.74	-38.67 – 51.04
Sex	75.69	43.44	-9.99 – 161.37	84.91	45.4	-4.64 – 174.45	81.82	45.94	-8.78 – 172.43	71.93	47.21	-21.21 – 165.06
Education	19.91	20.88	-21.27 – 61.1	16.61	21.31	-25.43 – 58.64	16.45	21.43	-25.82 – 58.71	14.44	21.88	-28.73 – 57.61
ICV	17.39	21.59	-25.2 – 59.98	19.04	21.73	-23.83 – 61.91	18.65	21.85	-24.45 – 61.74	19.12	22.65	-25.56 – 63.8
Group (MCI)				-17.84	52.11	-120.63– 84.94	-15.88	52.41	-119.25 – 87.5	-12.17	58.43	-127.46 – 103.11
Group (AD)				-57.62	64.9	-185.63 – 70.39	-50.49	67.97	-184.55 – 83.57	-74.42	73.4	-219.23 – 70.39
RA							-16.84	24.34	-64.85 – 31.17	47.97	55.6	-61.73 – 157.66
CS							-4.32	26.21	-56.01 – 47.37	4.19	55.51	-105.33 – 113.7
Group x Vision												
MCI x RA										-98.29	65.96	-228.42 – 31.84
AD x RA										-77.16	79.11	-223.24 – 78.91
MCI x CS										-1.00	65.76	-130.74 – 128.75
AD x CS										-33.39	78.28	-187.83 – 121.06
Adjusted R_2		.01			.00			-.01			-.02	
AIC		2846.2			2849.34			2852.81			2682.33	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = .41$, $p = .66$) and Model 3 ($F(2,191) = .25$; $p = .78$) not better than Model 1.

Table 31

Pairwise Comparisons between Groups in Volume of the Left Anterior Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	973	42.7	889 – 1057	
MCI	955	29.2	898 – 1013	
AD	915	45.5	836 – 1005	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	17.8	52.1	.34	.94
SCD – AD	57.6	64.9	.89	.65
MCI – AD	39.8	53.9	.74	.74

Note. Results are averaged over the levels of sex.

Table 32

Regression Models for the Thickness of the Left Anterior Occipital Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-.00	.01	-.02 – .02	.01	.01	-.01 – .03	.01	.01	-.01 – .04	.02	.01	-.01 – .04
Sex	-.03	.02	-.07 – .02	-.00	.02	-.05 – .05	-.00	.02	-.05 – .04	-.00	.02	-.05 – .05
Education	.02	.01	.00 – .04	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03
ICV	-.01	.01	-.03 – .01	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02
Group (MCI)				-.05	.03	-.11– .00	-.05	.03	-.1 – .00	-.05	.03	-.11 – .01
Group (AD)				-.14***	.03	-.21 – -.08	-.13***	.04	-.2 – -.06	-.14***	.04	-.21 – -.06
RA							-.02	.01	-.04 – .01	-.03	.03	-.09 – .03
CS							.01	.01	-.02 – .03	-.04	.03	-.1 – .02
Group x Vision												
MCI x RA										.02	.03	-.04 – .09
AD x RA										.01	.04	-.17 – .09
MCI x CS										.07*	.03	.01 – .14
AD x CS										.03	.04	-.05 – .11
Adjusted R_2		.01			.03			.03			.00	
AIC		-244.76			-247.36			-243.91			-233.03	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 8.97$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = 1.50$, $p = .23$)

Table 33

Pairwise Comparisons between Groups in Thickness of the Left Anterior Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.22	.02	2.17 – 2.26	
MCI	2.16	.02	2.13 – 2.2	
AD	2.07	.02	2.03 – 2.12	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.05	.03	1.92	.14
SCD – AD	.14	.03	4.17	.00
MCI – AD	.09	.03	3.16	.01

Note. Results are averaged over the levels of sex.

Table 34

Regression Models for the Volume of the Left Parieto-Occipital Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-4.75	36.41	-76.56 – 67.06	24.88	35.88	-45.89 – 95.65	29.93	37.5	-44.03 – 103.9	32.34	38.15	-42.93 – 107.62
Sex	91.73	75.91	-57.98 – 241.44	162.37*	76.3	11.88 – 312.85	159.75*	77.2	7.47 – 312.03	146.59	79.22	-9.71 – 302.88
Education	63.51	36.49	-8.45 – 135.48	38.48	35.82	-32.16 – 109.13	38.81	36.01	-32.22 – 109.84	41.07	36.72	-31.37 – 113.52
ICV	100.24**	37.73	25.83 – 174.66	112.51**	36.53	40.47 – 184.55	112.42**	36.72	40 – 184.85	107.92**	38	32.94 – 182.9
Group (MCI)				-145.13	87.58	-317.87– 27.6	-141.53	88.08	-315.27 – 32.21	-173.78	98.06	-367.25 – 19.69
Group (AD)				-433.34***	109.08	-648.47 – -218.21	-414.49***	114.23	-639.8 – -189.17	-374.9**	123.17	-617.91 – -131.89
RA							-21.93	40.9	-102.61 – 58.75	68.77	93.31	-115.32 – 252.85
CS							6.65	44.04	-80.22 – 93.53	-53.24	93.15	-237.02 – 130.54
Group x Vision												
MCI x RA										-115.05	110.69	-333.43 – 103.22
AD x RA										-62.47	132.75	-324.38 – 199.45
MCI x CS										41.4	110.36	-176.34 – 259.13
AD x CS										149.41	131.37	-109.78 – 408.59
Adjusted R_2		.05			.11			.11			.09	
AIC		3069.43			3056.98			3060.49			3069.41	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 8.11$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = .23$, $p = .79$)

Table 35

Pairwise Comparisons between Groups in Volume of the Left Parieto-Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2934	71.8	2793 – 3076	
MCI	2789	49.0	2693 – 2886	
AD	2501	76.5	2350– 2652	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	145	87.6	1.66	.22
SCD – AD	433	109.1	3.97	.00
MCI – AD	288	90.7	3.18	.00

Note. Results are averaged over the levels of sex.

Table 36

Regression Models for the Thickness of the Left Parieto-Occipital Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-.01	.01	-.03 – .02	.00	.01	-.02 – .02	.00	.01	-.02 – .03	.00	.01	-.02 – .03
Sex	-.03	.02	-.07 – .02	-.02	.02	-.06 – .03	-.02	.02	-.06 – .03	-.02	.02	-.07 – .03
Education	.02	.01	-.00 – .04	.02	.01	-.01 – .04	.02	.01	-.01 – .04	.02	.01	-.00 – .04
ICV	-.01	.01	-.03 – .01	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02
Group (MCI)				-.00	.03	-.06 – .05	-.00	.03	-.06 – .05	-.02	.03	-.08 – .04
Group (AD)				-.09**	.03	-.15 – -.02	-.08*	.03	-.15 – -.01	-.09*	.04	-.16 – -.02
RA							-.01	.01	-.03 – .02	-.00	.03	-.06 – .05
CS							.00	.01	-.02 – .03	-.01	.03	-.07 – .04
Group x Vision												
MCI x RA										-.00	.03	-.07 – .07
AD x RA										-.02	.04	-.1 – .06
MCI x CS										.03	.03	-.04 – .09
AD x CS										.01	.04	-.06 – .09
Adjusted R_2		.02			.06			.05			.02	
AIC		-176.99			-182.99			-179.81			-167.29	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 4.77$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = .38$, $p = .68$)

Table 37

Pairwise Comparisons between Groups in Thickness of the Left Parieto-Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.14	.02	2.09 – 2.18	
MCI	2.13	.01	2.1– 2.16	
AD	2.05	.02	2 – 2.09	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.00	.03	.19	.98
SCD – AD	.09	.03	2.64	.02
MCI – AD	.08	.03	2.99	.01

Note. Results are averaged over the levels of sex.

Table 38

Regression Models for the Volume of the Right Inferior Occipital Gyrus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-10.93	36.43	-82.78 – 60.91	1.06	37.03	-71.98 – 74.10	13.82	38.36	-61.84 – 89.49	12.97	38.98	-63.94 – 89.88
Sex	115.51	75.95	-34.27 – 265.29	123.29*	78.74	-32.01 – 278.59	141.97	78.97	-13.8 – 297.75	127.29	80.93	-32.39 – 286.97
Education	92.3*	36.51	20.29 – 164.30	86.68*	36.97	13.77 – 159.19	90.21*	36.84	17.55 – 162.88	92.62*	37.51	18.6 – 166.63
ICV	66.48	37.75	-7.97 – 140.94	71.52	37.70	-2.83 – 145.87	75.25*	37.56	1.16 – 149.34	84.42*	38.83	7.82 – 161.02
Group (MCI)				61.14	90.38	-117.13– 239.41	59.95*	90.11	-117.78 – 237.68	88.5	100.19	-109.16 – 286.16
Group (AD)				-123.97	112.57	-345.99 – 98.05	-96.35	116.85	-326.84 – 134.14	-129.09	125.84	-377.37 – 119.19
RA							59.78	41.84	-22.76 – 142.31	145.68	95.33	-42.39 – 333.76
CS							83.23	45.05	-5.64 – 172.09	234.01*	95.17	46.25– 421.77
Group x Vision												
MCI x RA										-98.66	113.09	-321.78 – 124.45
AD x RA										-178.92	135.63	-446.51 – 88.67
MCI x CS										-158.43	112.75	-380.88 – 64.02
AD x CS										-262.05	134.22	-526.85 – 2.75
Adjusted R_2		.04			.05			.06			.05	
AIC		3069.64			3069.59			3069.57			3077.99	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 1.96$, $p = .14$) and Model 3 ($F(2,191) = 1.92$; $p = .15$) not better than Model 1.

Table 39

Pairwise Comparisons between Groups in Volume of the Right Inferior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2390	74.1	2244 – 2537	
MCI	2452	50.6	2352 – 2551	
AD	2266	78.9	2111 – 2422	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	90.4	90.4	-.68	.78
SCD – AD	124	112.6	1.1	.51
MCI – AD	158.1	93.6	1.98	.12

Note. Results are averaged over the levels of sex.

Table 40

Regression Models for the Thickness of the Right Inferior Occipital Gyrus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-.01	.01	-.04 – .02	-.01	.02	-.04 – .02	.00	.02	-.03 – .03	.00	.02	-.03 – .03
Sex	.01	.03	-.05 – .08	.02	.03	-.05 – .08	.02	.03	-.05 – .08	.02	.03	-.05 – .08
Education	.05***	.01	.02 – .08	.05**	.02	.02 – .08	.05**	.02	.02 – .08	.05**	.02	.02 – .08
ICV	-.02	.02	-.05 – .01	-.02	.02	-.05 – .01	-.02	.02	-.05 – .01	-.01	.02	-.05 – .02
Group (MCI)				.01	.04	-.06 – .09	.02	.04	-.06 – .09	.03	.04	-.05 – .12
Group (AD)				-.03	.05	-.12 – .06	-.01	.05	-.11 – .08	-.01	.05	-.11 – .09
RA							-.01	.02	-.04 – .02	-.01	.04	-.09 – .07
CS							.01	.02	-.02 – .05	.03	.04	-.05 – .1
Group x Vision												
MCI x RA										.01	.05	-.08 – .1
AD x RA										-.01	.06	-.13 – .1
MCI x CS										-.01	.05	-.10 – .09
AD x CS										-.03	.06	-.14 – .08
Adjusted R_2		.04			.04			.04			.01	
AIC		-53.21			-50.53			-48.2			-35.85	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = .62$, $p = .54$) and Model 3 ($F(2,191) = .78$; $p = .46$) not better than Model 1.

Table 41

Pairwise Comparisons between Groups in Thickness of the Right Inferior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.44	.03	2.38 – 2.5	
MCI	2.45	.02	2.41– 2.49	
AD	2.41	.03	2.35 – 2.47	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-.01	.04	-.38	.92
SCD – AD	.03	.05	.63	.8
MCI – AD	.04	.04	1.13	.5

Note. Results are averaged over the levels of sex.

Table 42

Regression Models for the Volume of the Right Cuneus

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-35	41.39	-116.63 – 46.33	-10.91	41.64	-93.03 – 71.22	-5.33	43.53	-91.19 – 80.54	-1.36	44.55	-89.25 – 86.53
Sex	97.39	86.29	-72.79 – 267.57	145.02	88.54	-29.61 – 319.65	143.33	89.62	-33.45 – 320.11	155.54	92.49	-26.95 – 338.02
Education	122.18**	41.48	40.37 – 203.99	103.95*	41.57	21.97 – 185.94	104.45*	41.81	21.99 – 186.9	97.78*	42.87	13.19 – 182.36
ICV	83.71	42.87	-.88 – 168.31	93.72*	42.39	10.12 – 177.33	93.81*	42.63	9.73 – 177.89	89.47*	44.37	1.93 – 177.01
Group (MCI)				-61.48	101.63	-261.94– 138.97	-57.99	102.26	-259.69 – 143.71	-52.35	114.19	-278.24 – 173.53
Group (AD)				-328.15*	126.58	-577.81 – -78.49	-308.29*	132.61	-569.86 – -46.72	-327.04*	143.81	-610.77 – -43.31
RA							-18.74	47.49	-112.4 – 74.93	-103.17	108.94	-318.11 – 111.76
CS							10.5	51.13	-90.35 – 111.35	-80.99	108.76	-295.56 – 133.59
Group x Vision												
MCI x RA										110.35	129.24	-144.62 – 365.33
AD x RA										110.62	155	-195.18 – 416.43
MCI x CS										141.84	128.85	-112.38 – 396.06
AD x CS										35.71	153.38	-266.9 – 338.33
Adjusted R_2		.05			.08			.07			.05	
AIC		3120.71			3116.52			3120.17			3131.38	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 3.90$, $p = .02$); Model 3 not better than Model 2 ($F(2, 191) = .16$, $p = .85$)

Table 43

Pairwise Comparisons between Groups in Volume of the Right Cuneus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	3161	83.3	2997 – 3326	
MCI	3100	56.9	2988 – 3212	
AD	2833	88.8	2658 – 3008	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	61.5	102	.61	.81
SCD – AD	328.2	127	2.59	.03
MCI – AD	266.7	105	2.54	.03

Note. Results are averaged over the levels of sex.

Table 44

Regression Models for the Thickness of the Right Cuneus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.01	.01	-.00 – .03	.02	.01	-.00 – .04	.02	.01	-.00 – .04	.02	.01	-.00 – .04
Sex	-.03	.02	-.07 – .01	-.02	.02	-.06 – .02	-.03	.02	-.07 – .01	-.02	.02	-.06 – .02
Education	.01	.01	-.01 – .03	.01	.01	.01– .02	.01	.01	-.01 – .02	.00	.01	-.02 – .02
ICV	-.00	.01	-.02 – .02	.00	.01	-.02 – .02	-.00	.01	-.02 – .02	-.00	.01	-.02 – .02
Group (MCI)				-.01	.02	-.06 – .03	-.01	.02	-.06 – .04	-.01	.03	-.06 – .04
Group (AD)				-.06	.03	-.11 – .00	-.06	.03	-.12 – .00	-.06	.03	-.12 – .01
RA							-.02	.01	-.04 – .00	-.05*	.02	-.1 – -.00
CS							-.02	.01	-.04 – .00	-.05	.02	-.1 – .00
Group x Vision												
MCI x RA										.04	.03	-.02 – .1
AD x RA										.04	.04	-.03 – .11
MCI x CS										.03	.03	-.02 – .09
AD x CS										.03	.03	-.04 – .1
Adjusted R_2		.01			.02			.03			.02	
AIC		-233.18			-233.49			-234.21			-224.35	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 2.09$, $p = .13$) and Model 3 ($F(2,191) = 2.24$; $p = .11$) not better than Model 1.

Table 45

Pairwise Comparisons between Groups in Thickness of the Right Cuneus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	1.9	.02	1.87 – 1.94	
MCI	1.89	.01	1.87 – 1.92	
AD	1.85	.02	1.81 – 1.89	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.01	.02	.5	.87
SCD – AD	.06	.03	1.9	.14
MCI – AD	.04	.02	1.8	.17

Note. Results are averaged over the levels of sex.

Table 46

Regression Models for the Volume of the Right Middle Occipital Gyrus

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-61.04	53.23	-166.02 – 43.94	-30.27	53.4	-135.6 – 75.06	-21.41	55.78	-131.44 – 88.63	-29.57	115.43	-139.25 – 80.12
Sex	219.12*	110.98	.25 – 438.00	260.96*	113.55	36.99 – 484.93	271.54*	114.85	45 – 498.08	250.08*	53.5	22.35 – 477.82
Education	92.56	53.35	-12.66 – 197.78	733.4	53.31	-31.75 – 178.54	75.6	53.57	-30.07 – 181.27	68.4	55.37	-37.16 – 173.96
ICV	114.35*	55.16	5.55 – 223.15	127.2*	54.36	19.98 – 234.42	129.41*	54.62	21.67 – 237.16	120.9*	142.88	11.65 – 230.14
Group (MCI)				30.81	130.35	-226.28– 287.9	30.96	131.04	-227.51 – 289.43	21.93	179.48	-259.97 – 303.83
Group (AD)				-372.13*	162.34	-692.32 – -51.93	-351.04*	169.94	-868.24 – -15.85	-321.65	143.81	-675.74 – 32.45
RA							30.6	60.85	-89.43 – 150.63	244.88	135.96	-23.35 – 513.11
CS							51.51	65.52	-77.73 – 180.75	-43.48	135.73	-311.27 – 224.3
Group x Vision												
MCI x RA										-379.85*	161.28	-698.05 – -61.64
AD x RA										-93.15	193.44	-474.79 – 288.49
MCI x CS										30.38	160.81	-286.88 – 347.65
AD x CS										344.92	191.42	-32.74 – 722.58
Adjusted R_2		.05			.08			.08			.1	
AIC		3221.36			3216.05			3219.37			3219.99	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 4.70$, $p = .01$); Model 3 not better than Model 2 ($F(2, 191) = .33$, $p = .72$)

Table 47

Pairwise Comparisons between Groups in Volume of the Right Middle Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	4567	106.9	4356 – 4778	
MCI	4598	72.9	4454 – 4742	
AD	4195	113.8	3970 – 4419	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-30.8	130	-.24	.97
SCD – AD	372.1	162	2.29	.06
MCI – AD	402.9	135	2.97	.01

Note. Results are averaged over the levels of sex.

Table 48

Regression Models for the Thickness of the Right Middle Occipital Gyrus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.01	.01	-.01 – .04	.02	.01	-.00 – .04	.02	.01	-.00 – .05	.02	.01	-.00 – .05
Sex	-.03	.03	-.08 – .02	-.01	.03	-.07 – .04	-.02	.03	-.07 – .04	-.02	.03	-.07 – .03
Education	.01	.01	-.01 – .03	.01	.01	.02 – .03	.01	.01	-.02 – .03	.01	.01	-.02 – .03
ICV	-.00	.01	-.03 – .02	.00	.01	-.02 – .03	.00	.01	-.02 – .03	.00	.01	-.02 – .03
Group (MCI)				-.02	.03	-.08 – .04	-.01	.03	-.07 – .04	-.01	.03	-.08 – .05
Group (AD)				-.08*	.04	-.15 – -.00	-.06	.04	-.14 – .01	-.07	.04	-.15 – .02
RA							-.02	.01	-.04 – .01	.01	.03	-.05 – .08
CS							.00	.02	-.03 – .03	.01	.03	-.06 – .07
Group x Vision												
MCI x RA										-.04	.04	-.12 – .03
AD x RA										-.04	.05	-.13 – .05
MCI x CS										-.01	.04	-.09 – .06
AD x CS										.02	.05	-.07 – .11
Adjusted R_2		-.00			.01			.01			-.02	
AIC		-133.09			-133.88			-131.76			-120.36	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 2.28$, $p = .10$) and Model 3 ($F(2,191) = .88$; $p = .42$) not better than Model 1.

Table 49

Pairwise Comparisons between Groups in Thickness of the Right Middle Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.48	.02	2.43 – 2.52	
MCI	2.46	.02	2.43 – 2.49	
AD	2.4	.03	2.35 – 2.45	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.02	.03	.57	.87
SCD – AD	.08	.04	2.02	.11
MCI – AD	.06	.03	1.88	.15

Note. Results are averaged over the levels of sex.

Table 50

Regression Models for the Volume of the Right Middle Lunatus Sulcus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-14.82	22.55	-59.3 – 29.66	-9.2	23.07	-54.71 – 36.3	-9.2	24.09	-56.72 – 38.32	-12.24	24.36	-60.29 – 35.82
Sex	126.57**	47.02	33.85 – 219.3	137.78**	49.06	41.02 – 234.55	142.99**	49.6	45.15 – 240.82	149.93**	50.57	50.16 – 249.71
Education	38.79	22.6	-5.78 – 83.37	34.52	23.03	-10.91 – 79.95	35.08	23.14	-10.55 – 80.71	34.68	23.44	-11.57 – 80.92
ICV	16.2	23.37	-29.89 – 62.29	18.53	23.49	-27.79 – 64.86	19.35	23.59	-27.18 – 65.88	29.96	24.26	-17.9 – 77.82
Group (MCI)				-14.95	56.32	-126.02 – 96.13	-17.06	56.59	-128.68 – 94.56	20.98	62.6	-102.52 – 144.49
Group (AD)				-76.76	70.14	-215.1 – 61.58	-80.85	73.39	-225.61 – 63.9	-32.82	78.63	-187.95 – 122.32
RA							23.68	26.28	-28.15 – 75.52	17.18	59.56	-100.33 – 134.7
CS							28.3	28.3	-42.13 – 69.49	56.47	59.46	-60.85 – 173.79
Group x Vision												
MCI x RA										26.81	70.66	-102.6 – 176.22
AD x RA										-58.88	84.75	-226.08 – 108.32
MCI x CS										-69.95	70.45	-208.65 – 69.35
AD x CS										1.03	83.86	-164.43 – 166.49
Adjusted R_2		.04			.03			.03			.03	
AIC		2877.83			2880.36			2883.5			2889.88	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = .71$, $p = .49$) and Model 3 ($F(2,191) = .41$; $p = .66$) not better than Model 1.

Table 51

Pairwise Comparisons between Groups in Volume of the Right Middle Lunatus Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	1199	46.2	1108 – 1290	
MCI	1184	31.5	1122 – 1247	
AD	1123	49.2	1026 – 1220	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	14.9	56.3	.27	.96
SCD – AD	76.8	70.1	1.10	.52
MCI – AD	61.8	58.3	1.06	.54

Note. Results are averaged over the levels of sex.

Table 52

Regression Models for the Thickness of the Right Middle Lunatus Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.02	.01	-.01 – .04	.03*	.01	.00 – .05	.03*	.01	.00 – .05	.03*	.01	.00 – .06
Sex	.01	.03	-.05 – .05	.03	.03	-.03 – .08	.02	.03	-.03 – .08	.02	.03	-.04 – .07
Education	.02	.01	-.01 – .04	.01	.01	-.02 – .03	.01	.01	-.02 – .03	.01	.01	-.02 – .03
ICV	-.02	.01	-.05 – .01	-.02	.01	-.04 – .01	-.02	.01	-.04 – .1	-.01	.01	-.04 – .02
Group (MCI)				-.03	.03	-.09 – .03	-.03	.03	-.09 – .03	-.02	.03	-.09 – .04
Group (AD)				-.13***	.04	-.2 – -.05	-.13**	.04	-.21 – -.05	-.13**	.04	-.22 – -.05
RA							-.02	.01	-.05 – .01	-.00	.03	-.07 – .06
CS							-.01	.02	-.04 – .02	.00	.03	-.06 – .07
Group x Vision												
MCI x RA										-.01	.04	-.08 – .07
AD x RA										-.06	.05	-.15 – .03
MCI x CS										-.00	.04	-.08 – .07
AD x CS										-.04	.05	-.13 – .05
Adjusted R_2		.01			.06			.06			.04	
AIC		-113.85			-122.78			-120.6			-110.14	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 6.31$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = .86$, $p = .43$)

Table 53

Pairwise Comparisons between Groups in Thickness of the Right Middle Lunatus Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.07	.03	2.02 – 2.12	
MCI	2.04	.02	2.01 – 2.07	
AD	1.94	.03	1.89 – 1.99	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.03	.03	.95	.61
SCD – AD	.13	.04	3.35	.00
MCI – AD	.10	.03	3.11	.01

Note. Results are averaged over the levels of sex.

Table 54

Regression Models for the Volume of the Right Superior Occipital Gyrus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-44.94	34.2	-112.38 – 22.5	-32.43	34.72	-100.9 – 36.04	-32.65	36.32	-104.3 – 39	-33.86	36.54	-105.94 – 38.23
Sex	67.36	71.29	-73.25 – 207.96	110.53	73.82	-35.06 – 256.13	111.71	74.78	-35.79 – 259.22	80.65	75.86	-69.02 – 230.32
Education	71.29*	34.27	3.7 – 138.88	57.83	34.66	-10.52 – 126.18	57.93	34.88	-10.88 – 126.73	67.58	35.16	-1.8 – 136.95
ICV	16.96	35.44	-52.94 – 86.65	22.09	35.34	-47.61 – 91.79	22.26	35.57	-47.9 – 92.42	24.56	36.39	-47.24 – 96.36
Group (MCI)				-138.19	84.74	-305.32 – 28.94	-138.78	85.32	-307.08 – 29.52	-171.3	93.9	-356.57 – 13.97
Group (AD)				-215.99*	105.53	-424.13 – -7.84	-217.66	110.65	-435.92 – .6	-200.01	117.95	-432.72 – 32.7
RA							5.82	39.62	-72.34 – 83.97	199.45*	89.35	23.17 – 375.73
CS							2.5	42.66	-81.65 – 86.66	91.72	89.2	-84.27 – 267.71
Group x Vision												
MCI x RA										-250.43 *	106	-459.55 – -41.31
AD x RA										-227.02	127.13	-477.84 – 23.79
MCI x CS										-144.54	105.68	-353.05 – 63.96
AD x CS										-25.26	125.8	-273.46 – 222.94
Adjusted R_2		.01			.03			.02			.03	
AIC		3044.34			3043.78			3047.76			3052.08	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 2.23$, $p = .11$) and Model 3 ($F(2,191) = .01$; $p = .98$) not better than Model 1.

Table 55

Pairwise Comparisons between Groups in Volume of the Right Superior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2834	69.5	2697 – 2971	
MCI	2696	47.4	2602 – 2789	
AD	2618	74.0	2472 – 2764	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	138.2	84.7	1.63	.23
SCD – AD	216	105.5	2.05	.10
MCI – AD	77.8	87.7	.89	.65

Note. Results are averaged over the levels of sex.

Table 56

Regression Models for the Thickness of the Right Superior Occipital Gyrus

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.01	.01	-.01 – .03	.01	.01	-.01 – .04	.01	.01	-.01 – .04	.01	.01	-.01 – .04
Sex	-.04	.02	-.09 – .00	-.03	.02	-.08 – .02	-.03	.02	-.08 – .02	-.03	.02	-.08 – .01
Education	.03**	.01	.01 – .05	.03*	.01	.00 – .05	.03*	.01	.00 – .05	.02*	.01	.00 – .05
ICV	-.01	.01	-.03 – .01	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02	-.01	.01	-.03 – .02
Group (MCI)				-.02	.03	-.08 – .03	-.02	.03	-.08 – .03	-.02	.03	-.08 – .04
Group (AD)				-.08*	.03	-.15 – -.02	-.08*	.04	-.15 – -.01	-.09*	.04	-.17 – -.02
RA							-.01	.01	-.04 – .01	.01	.03	-.04 – .07
CS							-.01	.01	-.03 – .02	.01	.03	-.04 – .07
Group x Vision												
MCI x RA										-.05	.03	-.12 – .02
AD x RA										-.03	.04	-.11 – .05
MCI x CS										-.03	.03	-.09 – .04
AD x CS										-.02	.04	-.1 – .06
Adjusted R_2		.05			.07			.07			.07	
AIC		-174.41			-177.1			-174.26			-167.15	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 3.26$, $p < .05$); Model 3 not better than Model 2 ($F(2, 191) = .55$, $p = .58$)

Table 57

Pairwise Comparisons between Groups in Thickness of the Right Superior Occipital Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.18	.02	2.13 – 2.22	
MCI	2.15	.02	2.12 – 2.18	
AD	2.09	.02	2.05 – 2.14	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.02	.03	.92	.63
SCD – AD	.08	.03	2.47	.04
MCI – AD	.06	.03	2.09	.10

Note. Results are averaged over the levels of sex

Table 58

Regression Models for the Volume of the Right Occipital Pole

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	1.39	49.98	-97.18 – 99.95	43.85	48.84	-52.49 – 140.19	66.31	50.54	-33.37 – 166	73.3	51.78	-28.87 – 175.46
Sex	66.36	104.19	-139.13 – 271.84	129.91	103.86	-74.94 – 334.76	153.61	104.05	-51.63 – 358.86	143.35	107.52	-68.77 – 355.48
Education	94.82	50.09	-3.96 – 193.6	67.11	48.76	-29.05 – 163.28	72.36	48.54	-23.38 – 168.09	81.15	49.84	-17.18 – 179.47
ICV	96.39	51.79	-5.76 – 198.53	114.1*	49.72	16.03 – 212.17	119.22*	49.49	21.61 – 216.84	114.64*	51.58	12.88 – 216.4
Group (MCI)				9.08	119.22	-226.06 – 244.22	10.72	118.72	-223.45– 244.89	-36.06	133.09	-298.64 – 226.52
Group (AD)				-527.96***	148.48	-820.82 – -235.10	-472.11**	153.96	-775.79 – -168.43	-472.81 **	167.17	-802.64 – -142.99
RA							63.43	55.13	-45.32 – 172.17	58.67	126.64	-191.18 – 308.51
CS							122.35*	59.36	5.27 – 239.44	123.62	126.43	-125.81 – 373.05
Group x Vision												
MCI x RA										34.95	150.23	-261.45 – 331.34
AD x RA										14.88	180.18	-340.61 – 370.36
MCI x CS										18	149.79	-277.52 – 313.51
AD x CS										-51.52	178.3	-403.29 – 300.26
Adjusted R_2		.02			.1			.11			.09	
AIC		3196.11			3180.35			3179.88			3191.59	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 9.88$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = 2.11$, $p = .12$)

Table 59

Pairwise Comparisons between Groups in Volume of the Right Occipital Pole

Group	Estimated Marginal Mean	SE	95% CI	
SCD	4759	97.8	4566 – 4952	
MCI	4768	66.7	4636 – 4900	
AD	4231	104.1	4026 – 4436	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-9.08	119	-.08	.97
SCD – AD	527.96	148	3.56	.00
MCI – AD	537.04	123	4.35	.00

Note. Results are averaged over the levels of sex.

Table 60

Regression Models for the Thickness of the Right Occipital Pole

Variable	Model 1			**Model 2***			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.01	.01	-.01 – .02	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03
Sex	-.04	.02	-.08 – .00	-.03	.02	-.07 – .01	-.03	.02	-.07 – .01	-.03	.02	-.07 – .02
Education	.02	.01	-.00 – .04	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03
ICV	-.00	.01	-.02 – .02	.00	.01	-.02 – .02	.00	.01	-.02 – .02	.00	.01	-.02 – .02
Group (MCI)				-.02	.02	-.06 – .03	-.01	.02	-.06 – .03	-.02	.03	-.08 – .03
Group (AD)				-.08*	.03	-.14 – -.02	-.07*	.03	-.13 – -.01	-.08*	.03	-.14 – -.01
RA							-.01	.01	-.03 – .01	-.01	.03	-.06 – .04
CS							.01	.01	-.02 – .03	-.01	.03	-.06 – .04
Group x Vision												
MCI x RA										-.00	.03	-.06 – .06
AD x RA										.00	.04	-.07 – .08
MCI x CS										.02	.03	-.05 – .08
AD x CS										.02	.04	-.05 – .09
Adjusted R_2		.02			.05			.05			.01	
AIC		-215.31			-219.27			-216.77			-203.78	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 3.78$, $p = .02$); Model 3 not better than Model 2 ($F(2, 191) = .70$, $p = .50$)

Table 61

Pairwise Comparisons between Groups in Thickness of the Right Occipital Pole

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2	.02	1.96 – 2.04	
MCI	1.99	.01	1.96 – 2.01	
AD	1.93	.02	1.88 – 1.97	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.02	.02	.68	.78
SCD – AD	.08	.03	2.59	.03
MCI – AD	.06	.03	2.46	.04

Note. Results are averaged over the levels of sex

Table 62

Regression Models for the Volume of the Right Calcarine Sulcus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-12.21	43.48	-97.95 – 73.54	1.79	44.36	-85.71 – 89.29	-11.29	46.2	-102.42 – 79.83	-14.62	46.79	-106.93 – 77.69
Sex	112.68	90.64	-66.08 – 291.44	147.61	94.33	-38.43 – 333.66	133.38	95.12	-54.23 – 320.99	147.73	97.14	-43.93 – 339.39
Education	67.17	43.57	-18.77 – 153.1	55	44.28	-32.34 – 142.35	51.9	44.37	-35.61 – 139.42	37.1	45.03	-51.74 – 125.94
ICV	33.06	45.05	-55.79 – 121.92	38.85	45.16	-50.22 – 127.92	35.8	45.24	-53.43 – 125.03	39.7	46.6	-52.24 – 131.64
Group (MCI)				-77.61	108.28	-291.17 – 135.96	-78.39	108.52	-292.44– 135.67	-10.83	120.25	-248.08 – 226.42
Group (AD)				-208.59	134.86	-474.57 – 57.39	-240.79	140.73	-518.38 – 36.81	-211.29	151.05	-509.29 – 86.71
RA							-38.89	50.4	-138.29 – 60.51	8.77	114.42	-216.97 – 234.51
CS							-72.39	54.26	-179.42 – 34.64	-74.22	114.23	-299.59 – 151.14
Group x Vision												
MCI x RA										-34.72	135.74	-302.52 – 233.07
AD x RA										-120.79	162.79	-441.97 – 200.4
MCI x CS										-22.34	135.33	-289.35 – 244.66
AD x CS										-24.32	161.1	-342.16 – 293.52
Adjusted R_2		.00			.01			.01			.00	
AIC		3140.38			3141.85			3143.95			3151	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = 1.22$, $p = .30$) and Model 3 ($F(2,191) = .91$; $p = .41$) not better than Model 1.

Table 63

Pairwise Comparisons between Groups in Volume of the Right Calcarine Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2976	88.8	2801 – 3152	
MCI	2899	60.6	2779 – 3018	
AD	2768	94.6	2581 – 2954	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	77.6	108	.72	.75
SCD – AD	208.6	135	1.55	.27
MCI – AD	131	112	1.17	.47

Note. Results are averaged over the levels of sex.

Table 64

Regression Models for the Thickness of the Right Calcarine Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.00	.01	-.02 – .02	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03
Sex	-.01	.02	-.06 – .03	.01	.02	-.04– .05	.00	.02	-.04 – .04	.00	.02	-.04 – .05
Education	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .02	.01	.01	-.01 – .03
ICV	-.00	.01	-.02 – .02	.00	.01	-.02 – .02	-.00	.01	-.02 – .02	.00	.01	-.02 – .02
Group (MCI)				-.06*	.02	-.11 – -.01	-.06*	.02	-.1 – -.01	-.06*	.03	-.12 – -.01
Group (AD)				-.11***	.03	-.17 – -.05	-.11***	.03	-.17 – -.05	-.12***	.03	-.19 – -.05
RA							-.02*	.01	-.05 – -.00	-.04	.03	-.09 – .01
CS							-.01	.01	-.04 – .01	-.02	.03	-.07 – .03
Group x Vision												
MCI x RA										.01	.03	-.05 – .07
AD x RA										.00	.04	-.07 – .07
MCI x CS										.01	.03	-.05 – .07
AD x CS										.04	.04	-.03 – .11
Adjusted R_2		-.01			.05			.06			.05	
AIC		-206.31			-216.27			-217.11			-208.15	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 6.99$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = 2.31$, $p = .10$)

Table 65

Pairwise Comparisons between Groups in Thickness of the Right Calcarine Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2	.02	1.96 – 2.04	
MCI	1.99	.01	1.96 – 2.01	
AD	1.93	.02	1.88 – 1.97	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.02	.02	.68	.78
SCD – AD	.08	.03	2.59	.03
MCI – AD	.06	.03	2.46	.04

Note. Results are averaged over the levels of sex

Table 66

Regression Models for the Volume of the Right Anterior Occipital Sulcus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-36.39 *	17.28	-70.47 – -2.3	-31.94	17.67	-66.79 – 2.91	-24.45	18.27	-60.48 – 11.59	-23.38	18.79	-60.44 – 13.69
Sex	33.78	36.03	-37.28 – 104.84	40.58	37.57	-33.53 – 114.69	49.94	37.62	-24.25 – 124.14	46.63	39.01	-30.34 – 123.59
Education	-10.2	17.32	-44.36 – 23.96	-13.13	17.64	-47.93 – 21.66	-11.23	17.55	-45.84 – 23.38	-11.58	18.08	-47.25 – 24.09
ICV	18.4	17.91	-16.92 – 53.72	20.25	17.99	-15.22 – 55.73	22.19	17.89	-13.1 – 57.48	23.23	18.71	-13.69 – 60.15
Group (MCI)				.16	43.13	-84.91 – 85.23	.11	42.92	-84.54 – 84.77	8.72	48.29	-86.55 – 103.99
Group (AD)				-55.66	53.72	-161.61 – 50.29	-38.18	55.66	-147.96 – 71.61	-38.86	60.65	-158.53 – 80.8
RA							27.79	19.93	-11.52 – 67.1	39.22	45.95	-51.43 – 129.86
CS							44.65*	21.46	2.32 – 86.97	57.52	45.87	-32.98 – 148.01
Group x Vision												
MCI x RA										-14.44	54.51	-121.98 – 93.09
AD x RA										-15.88	65.37	-144.85 – 113.1
MCI x CS										-6.3	54.34	-113.51 – 100.92
AD x CS										-35.77	64.69	-163.4 – 91.86
Adjusted R_2		.02			.02			.03			-.00	
AIC		2771.38			2773.66			2772.89			2786.04	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = .82$, $p = .44$) and Model 3 ($F(2,191) = 2.23$; $p = .11$) not better than Model 1.

Table 67

Pairwise Comparisons between Groups in Volume of the Right Anterior Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	1005	35.4	935 – 1075	
MCI	1005	24.1	958 – 1053	
AD	950	37.7	875 – 1024	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-.16	43.1	-.00	1.00
SCD – AD	55.66	53.7	1.04	.56
MCI – AD	55.82	44.6	1.25	.43

Note. Results are averaged over the levels of sex.

Table 68

Regression Models for the Thickness of the Right Anterior Occipital Sulcus

Variable	**Model 1**			Model 2			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.00	.01	-.02 – .03	.01	.01	-.02 – .03	.01	.01	-.02 – .03	.01	.01	-.01 – .04
Sex	-.00	.02	-.05 – .05	.01	.03	-.04 – .06	.01	.03	-.05 – .06	.01	.03	-.05 – .06
Education	.01	.01	-.02 – .03	.00	.01	-.02 – .03	.01	.01	-.02 – .03	.01	.01	-.02 – .03
ICV	-.01	.01	-.04 – .01	-.01	.01	-.04 – .01	-.01	.01	-.04 – .01	-.01	.01	-.03 – .02
Group (MCI)				-.03	.03	-.09 – .03	-.03	.03	-.08 – .03	-.03	.03	-.09 – .04
Group (AD)				-.05	.04	-.12 – .02	-.04	.04	-.11 – .04	-.05	.04	-.13 – .03
RA							-.01	.01	-.04 – .02	-.04	.03	-.1 – .03
CS							.00	.01	-.02 – .03	-.01	.03	-.07 – .05
Group x Vision												
MCI x RA										.03	.04	-.05 – .1
AD x RA										.03	.04	-.06 – .12
MCI x CS										.04	.04	-.04 – .11
AD x CS										-.00	.04	-.09 – .09
Adjusted R_2		-.01			-.01			-.02			-.03	
AIC		-142.72			-140.5			-137.75			-129.15	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 ($F(2,193) = .85$, $p = .43$) and Model 3 ($F(2,191) = .59$; $p = .55$) not better than Model 1.

Table 69

Pairwise Comparisons between Groups in Thickness of the Right Anterior Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.25	.02	2.21 – 2.3	
MCI	2.23	.02	2.19 – 2.26	
AD	2.21	.03	2.16 – 2.26	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.03	.03	.93	.62
SCD – AD	.05	.04	1.3	.4
MCI – AD	.02	.03	.66	.79

Note. Results are averaged over the levels of sex

Table 70

Regression Models for the Volume of the Right Parieto-Occipital Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	-38.14	36.84	-110.8 – 34.52	-10.49	36.52	-82.52 – 61.53	-1.88	38.14	-77.11 – 73.35	-3.35	38.91	-80.11 – 73.41
Sex	96.32	76.81	-55.17 – 247.8	165.34*	77.65	12.19 – 318.5	166.32*	78.52	11.44 – 321.21	146.37	80.78	-13 – 305.74
Education	69.78	36.93	-3.05 – 142.6	45.74	36.45	-26.16 – 117.64	46.89	36.63	-25.36 – 119.13	50.8	37.44	-23.07 – 124.67
ICV	80.75*	38.18	5.45 – 156.05	92.19*	37.17	18.87 – 165.51	92.88*	37.35	19.22 – 166.55	88.05*	38.75	11.59 – 164.5
Group (MCI)				-153.35	89.13	-329.15 – 22.46	-149.42	89.59	-326.13 – 27.3	-178.32	99.99	-375.6 – 18.96
Group (AD)				-412.09***	111.01	-631.04 – -193.13	-384.26**	116.19	-613.43 – -155.09	-399.68 **	125.6	-647.48 – -151.88
RA							-12.6	41.61	-94.67 – 69.46	106.2	95.14	-81.51 – 293.91
CS							25.63	44.8	-62.73 – 113.99	58.92	94.99	-128.48 – 246.32
Group x Vision												
MCI x RA										-186.25	112.87	-408.93 – 36.44
AD x RA										-84.88	135.37	-351.96 – 182.2
MCI x CS										-61.11	112.54	-283.14 – 160.92
AD x CS										1.53	133.96	-262.76 – 265.82
Adjusted R_2		.04			.09			.09			.07	
AIC		3074.17			3064.02			3067.28			3077.21	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 6.91$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = .35$, $p = .71$)

Table 71

Pairwise Comparisons between Groups in Volume of the Right Parieto-Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	3123	73.1	2979 – 3267	
MCI	2969	49.9	2871 – 3068	
AD	2711	77.8	2557 – 2864	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	153	89.1	1.72	.2
SCD – AD	412	111	3.71	.00
MCI – AD	259	92.3	2.8	.02

Note. Results are averaged over the levels of sex.

Table 72

Regression Models for the Thickness of the Right Parieto-Occipital Sulcus

Variable	Model 1			**Model 2****			Model 3			Model 4		
	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI	B	SE	95% CI
Age	.00	.01	-.02 – .02	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03
Sex	-.01	.02	-.06 – .03	.01	.02	-.03 – .05	.01	.02	-.04 – .05	.01	.02	-.04 – .05
Education	.02	.01	-.00 – .04	.01	.01	-.01 – .03	.01	.01	-.01 – .03	.01	.01	-.01 – .03
ICV	-.01	.01	-.03 – .01	-.01	.01	-.03 – .01	-.01	.01	-.03 – .01	-.00	.01	-.03 – .02
Group (MCI)				-.06*	.03	-.11 – -.01	-.06*	.03	-.11 – -.01	-.06*	.03	-.11 – -.00
Group (AD)				-.12***	.03	-.18 – -.06	-.11***	.03	-.18 – -.04	-.12**	.04	-.19 – -.05
RA							-.01	.01	-.03 – .02	-.00	.03	-.05 – .05
CS							.01	.01	-.02 – .03	.01	.03	-.04 – .06
Group x Vision												
MCI x RA										-.01	.03	-.07 – .05
AD x RA										-.02	.04	-.1 – .06
MCI x CS										-.00	.03	-.07 – .16
AD x CS										.01	.04	-.07 – .08
Adjusted R_2		.01			.07			.06			.04	
AIC		-189.68			-199.57			-196.35			-184.78	

Note. ** $p < .01$, * $p < .05$; RA = reading acuity, CS = contrast sensitivity; SE = standard error. Bolded model indicates best predictive model selected by ANOVA: Model 2 better than Model 1 ($F(2,193) = 6.72$, $p < .01$); Model 3 not better than Model 2 ($F(2, 191) = .36$, $p = .69$)

Table 73

Pairwise Comparisons between Groups in Thickness of the Right Parieto-Occipital Sulcus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.2	.02	2.16 – 2.24	
MCI	2.14	.01	2.11 – 2.17	
AD	2.08	.02	2.04 – 2.13	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.06	.03	2.45	.04
SCD – AD	.12	.03	3.71	.00
MCI – AD	.06	.03	2.1	.09

Note. Results are averaged over the levels of sex

Table 74

Pairwise Comparisons between Groups in Volume of the Left Precentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	5622	96.7	5431 – 5813	
MCI	5644	66	5514 – 5774	
AD	5405	103	5202 – 5608	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-22.4	118	-.19	.98
SCD – AD	216.6	147	1.47	.31
MCI – AD	239	122	1.96	.13

Note. Results are averaged over the levels of sex.

Table 75

Pairwise Comparisons between Groups in Thickness of the Left Precentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.65	.03	2.59 – 2.7	
MCI	2.65	.02	2.61 – 2.69	
AD	2.63	.03	2.58 – 2.69	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-.00	.03	-.13	.99
SCD – AD	.01	.04	.32	.95
MCI – AD	.02	.03	.51	.87

Note. Results are averaged over the levels of sex

Table 76

Pairwise Comparisons between Groups in Volume of the Left Postcentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	3749	85.9	3579 – 3918	
MCI	3776	58.6	3660 – 3892	
AD	3710	91.5	3530 – 3890	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-27.4	105	-.26	.96
SCD – AD	38.6	130	.3	.95
MCI – AD	66	108	.61	.82

Note. Results are averaged over the levels of sex.

Table 77

Pairwise Comparisons between Groups in Thickness of the Left Postcentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.11	.02	2.06 – 2.15	
MCI	2.14	.02	2.11 – 2.17	
AD	2.11	.02	2.06 – 2.15	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-.03	.03	-1.09	.52
SCD – AD	.00	.03	.01	.99
MCI – AD	.03	.03	1.07	.53

Note. Results are averaged over the levels of sex

Table 78

Pairwise Comparisons between Groups in Volume of the Right Precentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	5632	99.3	5435 – 5828	
MCI	5606	67.7	5472 – 5740	
AD	5407	105.7	5199 – 5616	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	25.9	121	.21	.97
SCD – AD	224.6	151	1.49	.3
MCI – AD	198.8	125	1.59	.25

Note. Results are averaged over the levels of sex.

Table 79

Pairwise Comparisons between Groups in Thickness of the Right Precentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.66	.03	2.6 – 2.72	
MCI	2.63	.02	2.6 – 2.67	
AD	2.63	.03	2.57 – 2.69	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.02	.04	.64	.8
SCD – AD	.03	.04	.68	.77
MCI – AD	.01	.04	.21	.98

Note. Results are averaged over the levels of sex.

Table 80

Pairwise Comparisons between Groups in Volume of the Right Postcentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	3444	74.3	3298 – 3591	
MCI	3470	50.7	3370 – 3570	
AD	3304	79.2	3148 – 3460	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	-26.1	90.6	-.29	.96
SCD – AD	140.2	112.9	1.24	.43
MCI – AD	166.4	93.8	1.77	.18

Note. Results are averaged over the levels of sex.

Table 81

Pairwise Comparisons between Groups in Thickness of the Right Postcentral Gyrus

Group	Estimated Marginal Mean	SE	95% CI	
SCD	2.15	.02	2.1 – 2.2	
MCI	2.13	.02	2.1 – 2.16	
AD	2.11	.03	2.06 – 2.16	
Group Contrast	Contrast Estimate (B)	SE	T	*p*-value
SCD – MCI	.02	.03	.65	.79
SCD – AD	.04	.04	1.24	.43
MCI – AD	.03	.03	.86	.67

Note. Results are averaged over the levels of sex.

1

Figures

Figure 1

Characterizing Visual Function based on Performance on Both Visual Measures

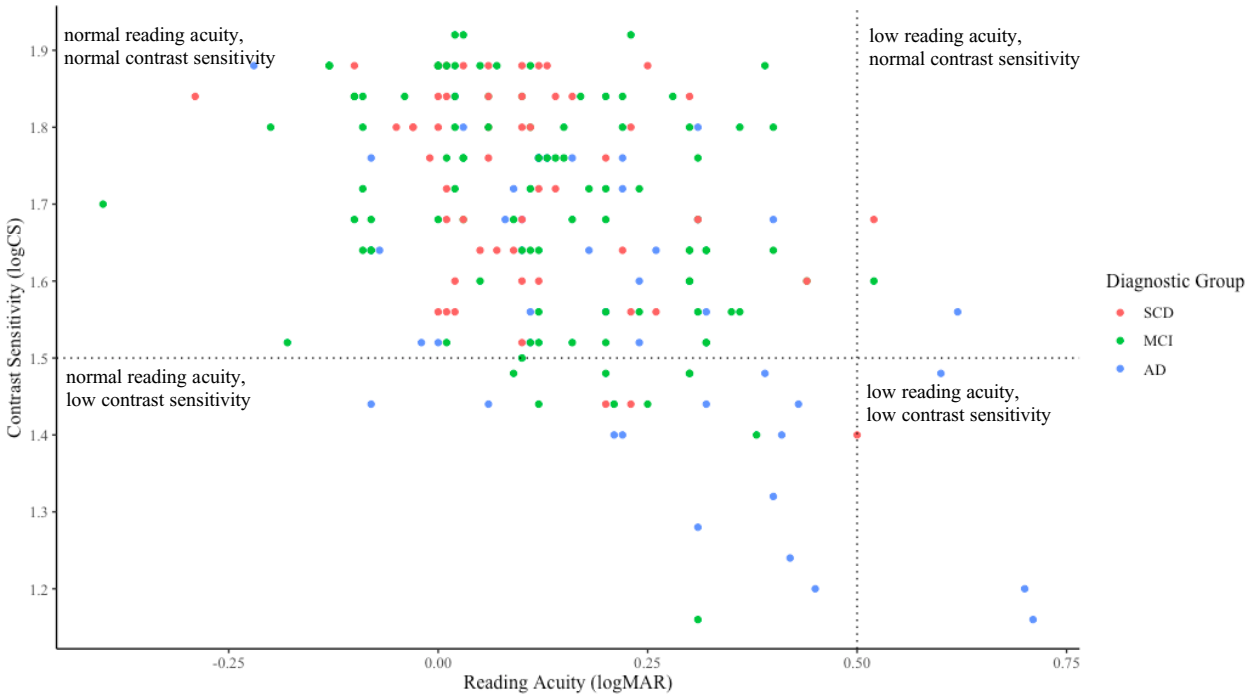
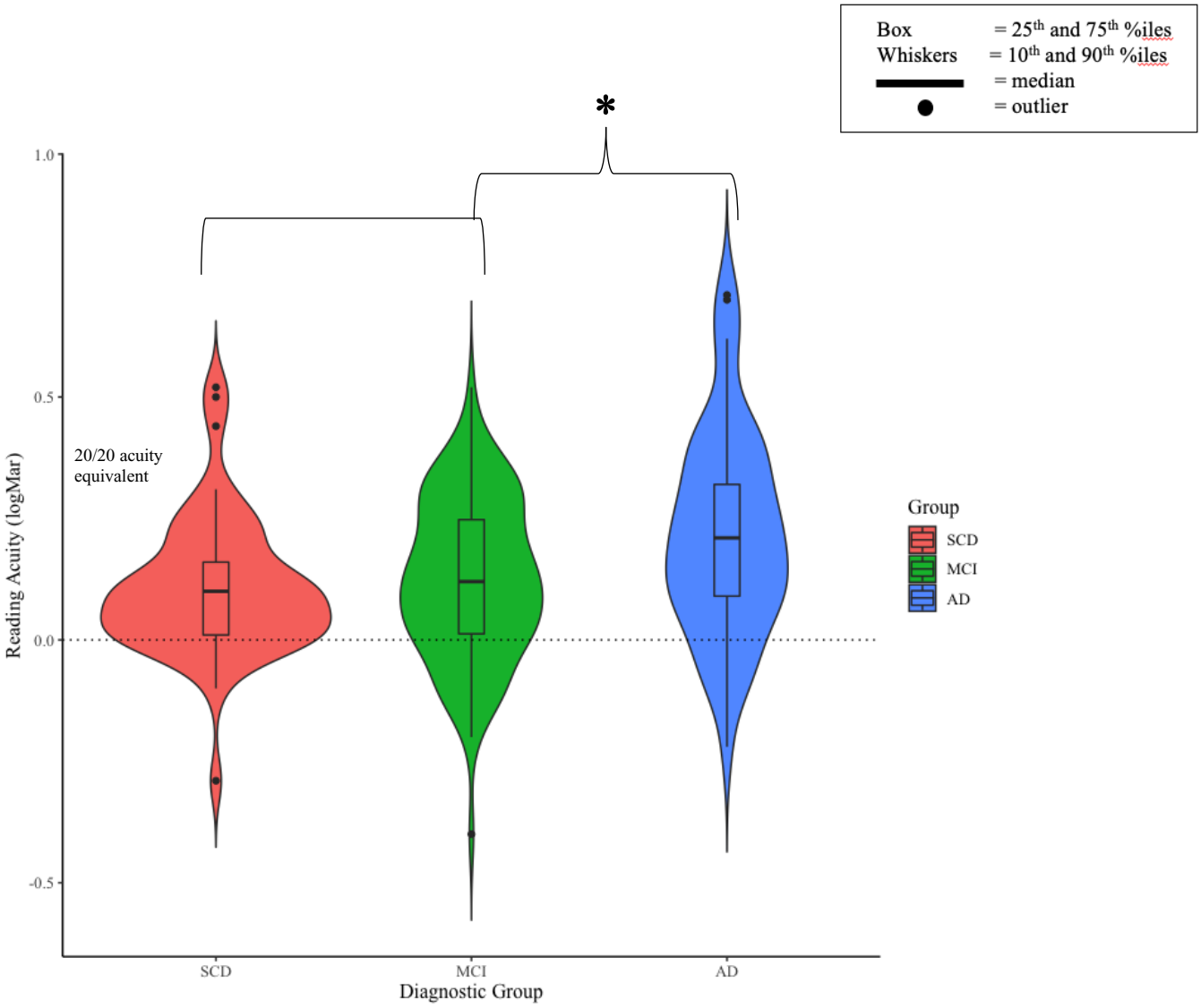


Figure 2

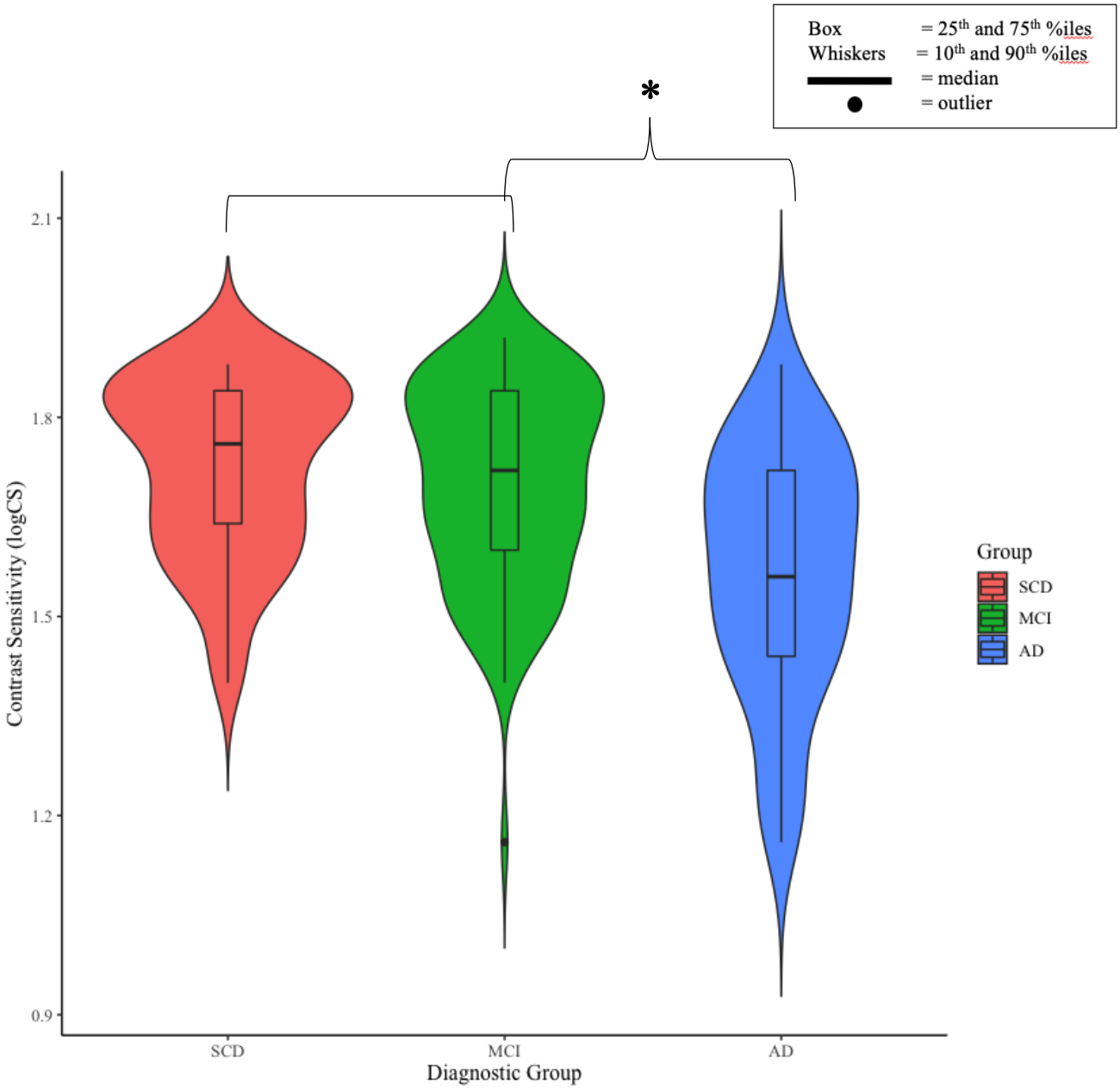
Performance on Reading Acuity across all Groups



Note. Reading acuity was measured using the MNRead Acuity Charts. * indicates a significant difference between groups ($p < .01$).

Figure 3

Performance on Contrast Sensitivity across all Groups



Note. Contrast sensitivity was measured using the MARS Contrast Sensitivity Test. * indicates a significant difference between groups ($p < .01$).