Subjective cognitive decline and related worry:

Examining biopsychosocial correlates in mid-age and older Canadians

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Abstract

Subjective cognitive decline (SCD), a self-reported decline in cognition in otherwise cognitively healthy people, has been acknowledged as a risk factor for Alzheimer's disease (AD). Research suggests that SCD may be a first symptomatic expression of preclinical AD, occurring before mild cognitive impairment (MCI). While there is a robust body of evidence highlighting health risk factors for SCD, less research has focused on psychosocial correlates. Using data from the Canadian Longitudinal Study on Aging (CLSA), a large national study with participants ages 45-85 years at baseline, this study sought to identify correlates of SCD and SCD-related worry.

The primary analysis, using a multivariate Poisson regression model, identified associations between biopsychosocial variables and SCD (analytic sample: n = 21,920). In a second analysis using an ordinal regression model, associations between biopsychosocial variables and SCD-related worry were identified (analytic sample: n = 12,694). Multiple risk and protective factors of cognitive decline were not associated with SCD within the sample (i.e., physical activity, hypertension, vision problems), nor were minority stress variables such as sexual orientation and race. Rather, psychosocial variables (i.e., depression, perceived social status, and personality traits) showed a more consistent association with SCD within the sample. Greater SCD-related worry, which has been suggested to increase the risk of future dementia, was associated with specific personality traits, depression, age, gender, and sexuality.

The results from this study confirm the association between multiple health variables and SCD but also emphasize the importance of considering psychological and social factors when conceptualizing SCD and its risk factors.

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List of Abbreviations

AD: Alzheimer's Disease

BMI: Body Mass Index

CCHS: Canadian Community Health Survey

CESD-10: Center for Epidemiologic Studies Short Depression Scale

CI: Confidence Interval

CIHR: Canadian Institutes of Health Research

CLSA: Canadian Longitudinal Study on Aging

FFM: Five Factor Model

HR: Hazard Ratio

LGBT: Lesbian, Gay, Bisexual, Transgender

MCI: Mild Cognitive Impairment

MCQ: Maintaining Contact Questionnaire

MICE: Multiple Imputation Using Chained Equations

MOS-SSS: Medical Outcomes Study Social Support Survey

OR: Odds Ratio

PASW: Physical Activity Scale for the Elderly

RAVLT: Rey Auditory Verbal Learning Test

REB: Research Ethics Board

RR: Relative Risk

SCD: Subjective Cognitive Decline

SGM: Sexual and Gender Minorities

SSA: Social Support Availability

TIPI: Ten-Item Personality Inventory

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Chapter 1: Background

Dementia is an overarching term used to describe a set of disorders affecting the brain including Alzheimer's disease (AD), vascular dementia, Lewy bodies dementia, frontotemporal dementia, and mixed dementia (Holmes & Amin, 2016). Dementia negatively impacts the ability to perform everyday activities through altering individuals' memory, thinking, orientation, comprehension, learning, language, and judgement (Buckley et al., 2015). In 2018, it was estimated that over 50 million individuals were living with dementia globally, and this number is predicted to increase to over 150 million by 2050 (Patterson, 2018). As there is currently no cure, focus has shifted towards prevention and improving quality of life for persons living with dementia (Reid & MacLullich, 2006).

Normal aging is associated with a decline in many cognitive domains including processing speed, working memory, recall, selective attention, and complex or novel problem solving (Harada et al., 2013). These declines are typically small and do not interfere with activities of daily living or quality of life (Harada et al., 2013). Carstensen's (2003) socioemotional selectivity theory proposes that as people age their motivation shifts from knowledge acquisition to emotional satisfaction. This shift has been found to impact various cognitive functions such as attention, memory, and facial recognition (Carstensen & Mikels, 2005). Given that such a large number of older adults complain of cognitive decline, the true value of assessing and diagnosing these complaints is not widely accepted in the literature (Balash et al., 2013).

Further, as some cognitive decline is part of normal aging, it can be difficult to distinguish between disease-related cognitive changes and those of normal aging (Murman, 2015). Dementia causes an acceleration of cognitive decline that impacts older adults' ability to

perform activities of daily living. Cognitive symptoms differ depending on the type of dementia and the stage of the illness. Decline in short-term memory is the most common complaint, but as the illness progresses, decline in long-term memory also occurs (Holmes & Amin, 2016). Although the symptoms of dementia typically progress slowly, the declines are more severe than those of normal cognitive aging. The typical progression of dementia begins with mild cognitive impairment (MCI), a mild, objectively-measured decline in cognition that may impact executive functioning but typically does not impact everyday activities (Reisberg et al., 2010). MCI has been identified as an intermediate stage between normal aging and dementia (Blackburn et al., 2014).

Subjective Cognitive Decline (SCD)

A review by Blackburn et al. (2014) suggests that using a measure of subjective cognitive decline (SCD) may allow for the identification of early stages of dementia years before a clinical diagnosis. The idea that subjective cognitive decline may be linked to future AD was first proposed by Reisberg (1986). When first introduced, SCD, described as stage two on the Functional Assessment Staging of Alzheimer's Disease, was believed to be common among older adults and in most cases did not lead to a further cognitive decline (Reisberg, 1986). Since this initial acknowledgement of SCD, much research has been done to better understand the link between SCD and dementia (Mitchell et al., 2014). Although considerable research has been done, results from studies on SCD are inconsistent regarding its predictive role of future dementia (Roberts et al., 2009).

SCD is defined as a self-perceived decline in cognition among otherwise cognitively healthy people (Si et al., 2020). Until recently, commonly accepted terminology surrounding SCD did not exist, with studies using various terminologies including subjective cognitive

impairment, subjective memory decline, subjective memory impairment, and subjective memory complaints (Jessen, Amariglio, et al., 2014). In 2014, the Subjective Cognitive Decline Initiative working group proposed a standardized definition of SCD. Despite memory complaints being the most common, declines are seen in more than just the memory domain, therefore 'cognition' has been identified as the most appropriate terminology. Additionally, decline refers to a change from a previous level of functioning, which reflects the temporal nature of SCD. Previously used terms such as impairment do not necessarily encompass the progressiveness of SCD (Jessen, Amariglio, et al., 2014).

A study by Amariglio and colleagues (2011) found that the type of subjective memory complaint predicted the odds of objective cognitive impairment. For example, *getting lost* was strongly associated with cognitive impairment in comparison to *forgetting things one second to the next*, which was found to be a part of normal aging. Additionally, researchers identified a positive correlation between the number of subjective memory complaints and cognitive impairment, with each additional complaint increasing the odds of impairment by 20 percent (Amariglio et al., 2011).

SCD as a Risk Factor for Dementia

SCD is now regarded by some researchers as a first symptomatic expression of preclinical dementia, an intermediate state between normal aging and dementia (Si et al., 2020). A study by Reisberg and colleagues (2010) found that the risk of developing MCI or dementia within seven years is 4.5 times greater for individuals with SCD compared to individuals without SCD (Hazard Ratio (HR) = 4.5, 95% CI = 1.9-10.3). Additionally, a study by van Harten and colleagues (2018) found that reporting any consistent SCD increased the risk of incident MCI by 2.17 times (HR = 2.17, 95% CI = 1.51-3.13). This study used two questionnaires, the Adapted

Blessed scale and the ECog, and one stand-alone question to measure SCD, taking into consideration consistency of the complaint as well as worry. To measure worry, the participants were asked the question "Are you concerned you have a memory or thinking problem?". After adjusting for confounding variables such as depressive symptoms, anxiety, and personality traits, the association between SCD and MCI risk remained.

Furthermore, Slot and colleagues (2019) found that the incidence rate of dementia for individuals with SCD was 17.7 per 1,000 person-years, compared to 14.2 for individuals without SCD. Recruitment for their study took place in both memory clinics and community-based cohorts, with individuals recruited from memory clinics having a significantly larger incidence of dementia. This study also identified the progression of SCD to non-AD dementias such as frontotemporal dementia and Lewy Bodies. These findings established the importance of considering non-memory characteristics when evaluating SCD, as other forms of dementia are not memory-specific (Slot et al., 2019). A meta-analysis of longitudinal studies concluded that SCD was associated with approximately two times the risk of developing AD (Pike et al., 2021).

SCD Criteria and Measures

To meet the criteria for SCD, an individual must be experiencing a decline in cognitive ability compared to a previous normal level of functioning, decline must not be related to an acute event, and the individual must test negative for MCI or dementia, as assessed with an objective measure (Molinuevo et al., 2017). Some characteristics have been categorized as SCD-plus criteria as they increase the likelihood of future objective cognitive decline (Jessen et al., 2020). SCD-plus criteria increase the likelihood of an underlying neurodegenerative disorder, such as AD (Studart & Nitrini, 2016). This criteria includes subjective decline in memory, onset of SCD in the last 5 years, age at onset of SCD 60+, concerns associated with SCD, feelings of

worse performance than others of the same age, and if available, informant reported cognitive decline, presence of APOE E4 genotype and biomarker evidence for AD (Jessen, Amariglio, et al., 2014).

Unlike objective measures of cognition, currently there is no single agreed upon approach to measure SCD, making it difficult to compare results across studies and fully understand SCD's prognostic value (Rabin et al., 2015). Buckley and colleagues (2015) recommend that large proportions of the community be screened for SCD, meaning assessments must be quick and reliable. Various self-reported questionnaires and scales have been developed to measure SCD (i.e., Everyday Cognition Scale, Memory Functioning Questionnaire, Subjective memory decline Scale) (Studart & Nitrini, 2016). These scales differ in length, cognitive domain of interest, and timeframes. While various methods of measurement exist (Hill et al., 2015), many population-based studies use a single question to determine SCD (Mitchell et al., 2014).

A single question measure of SCD, asking "Do you have memory complaints?", has been used in various studies over the years (Geerlings et al., 1999; Jessen, 2010; van Oijen et al., 2007). A study by Jungwirth and colleagues (2004) assessed SCD using the question "Do you have complaints about your memory in the last 2.5 years?". Possible answers included: *no*, *sometimes - but is no problem*, *yes - is a problem*, and *yes - is a serious problem*. They were then asked an additional four questions regarding changes in everyday memory (e.g., ''Do you have more trouble remembering things that have happened recently?') which were rated on a three-point scale (Jungwirth et al., 2004).

SCD-Related Worry

While it is unclear if SCD is indicative of future decline, there is increasing recognition of the potential importance of SCD-related worry in predicting future objective cognitive

decline. Research has found that individuals reporting SCD-related worry have almost double the risk of developing dementia, compared to individuals reporting SCD without worry (Jessen, 2010). Further research by Jessen and colleagues (2014) found that subjective memory impairment (also known as SCD) is only associated with an increased risk of dementia when it is accompanied by a concern, while people reporting SCD without worry are at no greater risk than controls. This finding suggests that SCD without concerns may be associated with normal age-related decline and is not an indicator of future objective decline (Jessen, Amariglio, et al., 2014). Based on these findings, worry or concern related to SCD has been included as one of the SCD-plus criterion, a feature thought to increase the likelihood of progression of SCD to AD (Jessen, Amariglio, et al., 2014).

When using a single question to measure SCD, Wagner and colleagues (2015) found that dementia risk increased with consistent subjective complaints and was even higher for people who also expressed worry about their complaints. In their study, the participants were asked: "Do you feel like your memory is becoming worse?" Possible responses included *no*, *yes,* and *yes that worries me*. The results of this study found that the risk of developing AD in participants with consistent SCD but without worries was almost double that of control participants without SCD (HR = 2.03, 95% CI = 1.30-3.15), with the risk increasing even more for participants with consistent SCD and with worries (HR = 3.72, 95% CI = 2.10-6.50). Another study by Chen and colleagues (2019) found that SCD participants with worry showed increased clinical characteristics such as depression and anxiety, in comparison to controls and SCD participants without worry, which may explain their higher risk of developing AD. Snitz and colleagues (2018) also found that reporting SCD with worry was associated with progression to MCI, whereas reporting SCD without worry was not.

A Biopsychosocial Framework for SCD

Biopsychosocial Frameworks

A biopsychosocial framework of dementia was first proposed in 2000 by Cohen-Mansfield. In his work on the heterogeneity of dementia, Cohen-Mansfield (2000) stated that the factors affecting cognition throughout the lifespan could be categorized into three domains: biologic/genetic/medical, psychosocial, and environmental. The framework acknowledges the genetic predisposition of dementia while still focusing on psychosocial variables such as education, stress, and social support (Cohen-Mansfield, 2000). In 2010, Spector and Orwell added 'fixed' versus 'tractable' psychosocial and biological factors to the biopsychosocial model of dementia. Additionally, they included the transition from normal aging, to MCI, to dementia, and eventually death (Spector & Orrell, 2010). Although some factors cannot be modified, Spector and Orrell (2010) discuss psychosocial and biological interventions that can decrease dependency of individuals living with dementia and delay institutionalization.

Recently, in their report of the Lancet Commission on dementia prevention, Livingston and colleagues (2020) identified potentially modifiable risk factors for dementia which include physical health factors (i.e., diabetes, hearing loss, hypertension) as well as psychosocial factors such as education, depression, social isolation, and physical activity. It is evident that interventions need to be implemented as soon as possible, especially those not able to cause harm, but which instead may lead to additional health benefits. Additionally, evidence shows that there is a need for holistic interventions which take into account an individual's medical, cognitive, psychological, and social needs (Livingston et al., 2020).

A biopsychosocial model of dementia indicates that cognition is not solely determined by biological and physical health factors, but that psychological and social factors also significantly

impact cognitive health and dementia risk (Spector & Orrell, 2010). While there is a robust body of research highlighting the role of biological and health risk factors of cognitive decline, less research has focused on psychosocial correlates. Potential psychosocial correlates of cognitive decline include, but are not limited to, depression, social support, caregiver status, and personality traits (Spector & Orrell, 2010).

Biological Factors

Abundant evidence links biological factors with higher risks of cognitive decline including age, genetic factors, sensory loss, obesity, smoking, physical inactivity, and diabetes (Qiu et al., 2009). Many of the known biological risk factors for cognitive decline, such as genetic determinants, are non-modifiable. Chronological age is the most commonly associated risk factor for dementia, with risk of dementia almost doubling every five years after age 65 (Qiu et al., 2009). Genetic determinants such as diagnosis of dementia in family members and/or the presence of the apolipoprotein E ε4 allele have also been found to increase risk of dementia (Liu et al., 2013). Additionally, sensory changes such as hearing loss have been found to be independently associated with accelerated cognitive decline, although in some cases hearing aids can be used to mitigate the negative impact on cognition (Lin et al., 2013).

While some biological risk factors, such as some of the ones described above, are not modifiable, many biological risk factors can be modified through interventions. For example, increased physical activity has been found to lower risk of cognitive decline by increasing blood flow to the brain, encouraging the formation of cognitive reserves, increasing brain volume, and reducing obesity (Mandolesi et al., 2018; Tan et al., 2017). Furthermore, obesity has been associated with late-life dementia (Albanese et al., 2017), whereas intentional weight loss in overweight (BMI 25-29.9) and obese (BMI ≥ 30) individuals has been found to improve

cognitive performance (Veronese et al., 2017). Similarly, elevated blood pressure during mid-life and persistent hypertension during late-life has also been associated with increased risks of dementia, with blood pressure modification showing cognitive benefits (McGrath et al., 2017). Other health behaviours are modifiable, such as smoking habits and avoiding excessive alcohol intake, which may delay the onset of dementia (Livingston et al., 2020).

Psychosocial Factors

Minority Stress. Forrester and colleagues (2019) proposed a framework to understand the role of minority stress in cognitive aging. Their framework emphasizes that experiencing minority stressors (i.e., racism, homophobia, stigma, discrimination, etc.) results in increased stress, which negatively impacts cognitive aging outcomes. In addition, the framework indicates that social factors experienced by individuals with minoritized identities, such as quality of education, socioeconomic status, and discrimination, are linked to behaviours such as drug and alcohol use, unhealthy diets and physical inactivity which may cause hypertension, diabetes mellitus, and heart disease. These factors, ultimately caused by minority stresses, increase the likelihood of MCI, AD, and vascular dementia (Forrester et al., 2019).

Further, minority stress has been acknowledged as a risk factor for cognitive decline for lesbian, gay, bisexual, and transgender (LGBT) individuals such that LGBT individuals may experience accelerated cognitive decline (Correro & Nielson, 2020). A study by Seelman (2019) found that in comparison to heterosexual women, older lesbian and bisexual women were more likely to report problems with cognitive health. Similar associations have been found when examining SCD, with LGBT racialized older adults being 2.5 times more likely to experience SCD compared to non-racialized LGBT older adults (OR = 2.5, 95% CI = 1.1-7.8) (Flatt et al., 2018). Consistent with the framework for minority cognitive aging, Stinchcombe and Hammond

(2021) found that racial minority status as well as lower perceived social standing were associated with lower memory and executive function in Canadians aged 45-85 years. Additionally, subjective social status has been found to be positively associated with older adults' mental and cognitive health, with both Black participants and females being more likely to report lower subjective social statuses (Zahodne et al., 2018).

Depression. A considerable amount of evidence shows that depression is associated with increased risk of cognitive decline (Nasisi, 2020). Along with cognitive decline, depression is one of the most prevalent health conditions experienced by older adults. Due to their similarities, symptoms of cognitive decline and depression are often seen at the same time in older adults (Korczyn & Halperin, 2009). Memory complaints have been found to be one of the main symptoms of older adults with depression (Reid & MacLullich, 2006), while many people experiencing cognitive decline also report symptoms of depression (Muliyala & Varghese, 2010). In consequence, research has struggled to understand the temporal relationship between cognitive decline and depression. Some evidence shows that depression increases the risk of cognitive decline (Geerlings et al., 2000; Köhler et al., 2010; Korczyn & Halperin, 2009), while other evidence finds that cognitive decline can cause depressive symptoms (Muliyala & Varghese, 2010; Schmand et al., 1997). Additionally, it is suggested that SCD is a result of experiencing depression, rather than experiencing objective cognitive decline (Reid & MacLullich, 2006; Zlatar et al., 2018). Given these lines of evidence, it is currently unclear whether depression is a predictive risk factor or an early outcome indicator of cognitive decline.

Some researchers suggest that depression is a harbinger of cognitive decline and future dementia (Köhler et al., 2010). In a prospective study, depression preceded cognitive impairment, and even increased the risk of future cognitive decline (Yaffe et al., 1999).

Additionally, it has been suggested that there is a dose-dependent relationship between depressive episodes and risk of MCI and dementia, with each depressive episode being associated with a 14% increase in risk for dementia (Dotson et al., 2010). A large study of over 4,000 older adults found that depression was in fact associated with cognitive decline. In the study, cognitive decline in individuals with four depressive symptoms was 20% more rapid than in those without depressive symptoms (Wilson et al., 2004). Even individuals with low levels of depressive symptoms have been found to have an increased risk of dementia (Korczyn & Halperin, 2009). Additionally, a study by Geerlings and colleagues (2000) found that depression may be an early indicator of AD in older adults with higher levels of education. These results can be understood as individuals with increased education tend to have greater cognitive reserves, therefore their depressive symptoms may be evident before symptoms of cognitive decline. In contrast, it is suggested that depression may be a psychological response to cognitive decline, especially in the early stages when the individual is aware of their decline in cognitive ability (Ganguli, 2009). Alternatively, self-awareness of cognitive decline may lead to feelings of depression, ultimately representing a reciprocal relationship between depression and decline in cognition (Schmand et al., 1997).

In contrast, a cross-sectional study of 590 older adults by Zlatar et al. (2018) found that SCD was not associated with objective cognitive decline but instead was associated with depression. As individuals experiencing depression may also have negative self-esteem, they may be more likely to negatively evaluate their cognition and therefore report SCD (Studer et al., 2014). Similarly, depression in some cases has been labeled “pseudodementia” such that an individual may present with dementia symptoms when, in reality, their depression symptoms are

temporarily impacting their ability to concentrate and retain new information (Spector & Orrell, 2010).

Personality Traits. Certain personality traits have also been associated with cognitive health and aging. The Five Factor Model (FFM) of personality is widely accepted as a theory of personality throughout psychology research (McCrae & John, 1992). The FFM of personality categorizes personality into five domains and provides common language to be used in the literature. The five personality traits are extraversion, conscientiousness, agreeableness, openness, and neuroticism. It is suggested that for older adults experiencing normal aging, SCD may be a reflection of specific personality traits and not an objective decline in cognition. The three personality traits most linked to cognition are conscientiousness (i.e., being organized, dependable and motivated), openness (i.e., being curious, creative and emotional), and neuroticism (i.e., easily angry, anxious, or depressed) (Kwantes et al., 2016; Luchetti et al., 2016). Therefore, along with depression, high levels of neuroticism as well as low levels of self-esteem, openness, and conscientiousness have been found to be correlated with complaints of SCD (Studer et al., 2014).

An association between low conscientiousness and increased subjective memory complaints was found by Pearman and Storandt (2004). Their study also found that neuroticism had a negative correlation with conscientiousness making it hard to determine which personality trait caused the memory complaints. Overall, the results of their study can be used to inform additional treatments outside of strictly memory skills, for example, treating low self-esteem and anxiety. The use of individually tailored interventions may also be helpful, as personality traits impact learning style (Pearman & Storandt, 2004). Identifying at-risk individuals based on personality traits also allows for earlier interventions (Luchetti et al., 2016).

Furthermore, a change in personality during older adulthood has been linked to MCI and dementia, especially as cognitive decline progresses. Ausén and colleagues (2010) identified progressive patterns of personality change that coincided with cognitive decline, such that increased personality changes were seen during the transition from normal aging, to SCD, to MCI. These changes related to the level of cognitive decline include increased proneness to stress, anxiety, and agitation, and lower extraverted behaviour. Evidence shows that individuals with high neuroticism and/or low conscientiousness are at a greater risk of developing dementia. Therefore, an increase in negative emotions such a neuroticism may occur earlier than an objective decline in cognition, meaning personality traits may be an early identifier of dementia risk (Ausén et al., 2010).

Education. It has been suggested that increased education is a protective factor against dementia, as education is positively associated with cognitive reserve (Ngandu et al., 2007). The cognitive reserve theory hypothesizes that individuals build up their cognitive abilities over the lifespan, which allows them to better tolerate age-related brain changes and pathology, and delays decline in cognitive function (Stern, 2012). It is suggested that a greater cognitive reserve can act as a protective factor against dementia in later life, as individuals with higher cognitive reserves have been found to cope with damage to their brain better than those with lower cognitive reserves (Steffener & Stern, 2012). As cognitive reserve is not fixed, education has been found to greatly increase cognitive reserve, along with occupation, physical activity, and social engagement (Valenzuela & Sachdev, 2006). Using education as a measure of cognitive reserve, individuals with higher education have been found to have a 47% decreased risk of dementia compared to individuals with lower education levels (Valenzuela & Sachdev, 2006).

The association between education and cognition becomes unclear when looking at

measures of SCD. Geerlings and colleagues (1999) found no association between SCD and level of education in relation to dementia risk. In contrast, van Oijen and colleagues (2007) found the association between SCD and risk of AD was actually higher in individuals with higher levels of education. Despite the evidence of education reducing an individual's risk of dementia, individuals with high levels of education who performed well on objective measures of cognition but complained of cognitive decline have been found to have a higher risk of AD compared to those with low levels of education (van Oijen et al., 2007). Similar findings have been reported, stating that SCD is predictive of dementia for individuals with high education levels but not those with low education levels (Chary et al., 2013). More recent literature has found that indicators of cognitive reserve (i.e., education, occupational complexity, and cognitive activities) attenuated the SCD associated risk of developing AD (Jia et al., 2021). The results of these studies support the importance of subjective measures of cognitive decline in specific populations, such as those with higher levels of education, or those with SCD and low cognitive reserve.

Social Support. Social support can be measured as both a structural objective measure, as well as a functional subjective measure. Structural social support includes relationship status, living arrangements, number of friends, participation in social events, etc. Functional social support is one's perception that they are loved, cared for and valued, and that their needs are being fulfilled (Sherbourne & Stewart, 1991). Aspects of social support have been linked to cognition; for example, decreased social participation, less frequent social contact, and feelings of loneliness have been found to increase the risk of dementia (Kuiper et al., 2015). Furthermore, evidence shows that increasing functional social support (i.e., one's perception that they are loved, cared for and valued, and that their needs are being fulfilled), and emotional support (i.e.,

having someone to talk to) may have a protective effect against cognitive decline, whereas increasing instrumental social support (i.e., the quantity of support) did not (Ellwardt et al., 2013; Sherbourne & Stewart, 1991). These results may be explained by the cognitive reserve theory in that more social interactions lead to greater brain adaptability and function (Evans et al., 2018). Similarly, a retrospective cohort study found that social contact has a protective effect against dementia, as social contact leads to greater cognitive reserves (Sommerlad et al., 2019). In contrast, social support responsibilities, such as caregiving, have been associated with cognitive health such that caregivers show lower cognitive test performance relative to non-caregivers (Corrêa et al., 2015).

Chapter 2: Rationale, Objectives, Hypotheses

Rationale

Cognitive decline negatively impacts an individual's overall wellbeing as well as the wellbeing of those in their care networks (Buckley et al., 2015). As a lack of consensus exists regarding SCD as a precursor to dementia, there is currently no recommended treatments for SCD (Cave et al., 2019; Si et al., 2020). With more research affirming SCD as a precursor for dementia, research can begin to focus on treating SCD earlier and possibly delaying the onset of MCI and dementia (Reisberg et al., 2008). Additionally, measures of SCD can be used to identify higher risk individuals for targeted interventions that promote cognitive functioning and functional well-being (Sánchez-Benavides et al., 2018).

Objectives

Based on existing literature describing risk and protective factors of dementia, this study aimed to identify associations between biopsychosocial variables and SCD and SCD-related worry in a sample of middle-aged and older Canadians.

Objective 1: To identify the biological, psychological, and social correlates of SCD in a large, national sample of middle-aged and older adults (aged 45-85).

Objective 2: To determine the associations between multiple biopsychosocial variables and the odds of reporting worry related to SCD in a large national sample of middle-aged and older adults (aged 45-85) who reported SCD.

Hypotheses

It was hypothesized that, in addition to commonly studied biological and health determinants of cognitive aging (e.g., poor sensory function, self-rated health), psychosocial variables (e.g., depression, personality traits, social support, etc.) would also emerge as correlates of SCD in the sample. Additionally, among those who report SCD, it was hypothesized that known risk and protective factors for dementia would be associated with participants' degree of worry about SCD. For example, given robust evidence linking mental health and cognition (Köhler et al., 2010), it was hypothesized that increased symptoms of depression would increase the risk of SCD. Based on evidence linking personality and cognition (e.g., Kwantes et al., 2016; Luchetti et al., 2016), it was hypothesized that emotional stability (i.e., low neuroticism), conscientiousness, and openness would be negatively associated with SCD. It is expected that individuals who experience minority stress or report low social support would be more likely to report SCD. Finally, among those who report SCD, it was hypothesized that a similar pattern of results would emerge when participants' degree of SCD-related concern was the outcome.

Chapter 3: Methodology

Data Source

Data reported here is from two waves of the comprehensive cohort of the Canadian Longitudinal Study on Aging (CLSA), a 20-year national study following more than 50,000

Canadians aged 45-85 at baseline. Recruitment began in 2010 with baseline data collection taking place between 2011 and 2015. Data are collected every three years for up to 20 years or until participant death, with the first follow-up taking place between 2015 and 2018 (Raina et al., 2019). Recruitment for the CLSA included using a subset of the Canadian Community Health Survey (CCHS) - Healthy Aging, provincial health care registration databases, and random digit dialing of landlines. To be eligible, participants must speak either English or French, and not have a cognitive impairment at baseline. Other exclusion criteria included individuals living in Canadian territories or certain remote areas, living on First Nations reserves or First Nations settlements, being a full-time member of the Canadian Armed Forces, and institutionalized populations. Informed consent was provided by all participants before participating in the study (Raina et al., 2019).

The CLSA consists of two cohorts, a comprehensive cohort (n = 30,097) and a tracking cohort (n = 21,241). As certain measures of interest to this study were only collected within the comprehensive cohort (e.g., personality traits), only data from the comprehensive cohort was analyzed in this study. The tracking cohort completed telephone interviews, whereas the comprehensive cohort underwent face-to-face in-home interviews, as well as in-depth data collection at data collection sites located in 11 cities across Canada. Data collected in the comprehensive cohort at baseline included questions regarding health and demographics as well as physical, psychological, and cognitive testing. To maintain participant retention, 18 months after each data collection, all participants were contacted by phone to complete a 30-minute Maintaining Contact Questionnaire (MCQ) (Raina et al., 2019).

Measures

Outcome variable

At first follow-up, participants were asked whether they had experienced **subjective cognitive decline** with the question, "Do you feel like your memory is becoming worse?" The possible response options were, *yes* and *no.* If participants responded *yes*, they were then asked, "Does this worry you?". This follow-up question gave a measure of **SCD-related worry** and had 5 possible answers including: *strongly agree, agree, undecided, disagree,* and *strongly disagree.* In the present study, responses were combined into three categories: *strongly agree / agree, undecided,* and *disagree / strongly disagree*. Many studies have used a single question to measure of SCD (Geerlings et al., 1999; van Oijen et al., 2007), as well as including a measure of worry within the responses (Jessen, 2010; Wagner et al., 2015).

Demographic, biological, and health variables

At baseline, **age** was recorded as a continuous variable. For purposes of this study, participants are referred to as men and women (**gender**). Participants were asked to report their total **household income** with possible responses falling into five categories: *Less than $20,000, $20,000-$49,999, $50,000-$99,999, $100,000-$149,999,* or *$150,000 or more.* At baseline, participants reported their highest level of **education**. Responses were collapsed into the following four categories: *less than secondary school education, secondary school graduate, some post-secondary, post-secondary graduate*. **Marital/partner status** was also asked with possible options including: *single, married/common law, widowed, divorced,* and *separated.* In this analysis, widowed, divorced, and separated were combined into one category. **Race/ethnicity** was self-reported and categorized as *White, Black,* and *other non-White.*

Participants were asked if they self-identify their **sexual orientation** as *heterosexual, homosexual,* or *bisexual*.

Self-reported general health was recorded by asking participants if, in general, they would say their health was *excellent, very good, good, fair,* or *poor.* **Hearing** and **vision** were both self-reported using the scale of *excellent, very good, good, fair,* or *poor.* **Body Mass Index (BMI)** (kg/m^2) was calculated using participants' weight and height. Participants were also asked to report health-professional diagnosed **hypertension** *(yes/no)*. **Alcohol use** in the past 12 months was measured using a categorical variable with responses combined into the categories: *regular drinker (at least once a month), occasional drinker,* and *did not drink in the last 12 months.* Participants were also asked if they had smoked at least 100 tobacco cigarettes in their life, and if so, their current frequency of smoking (i.e., daily, occasionally, not at all). Based on the participants' **smoking habits** they were categorized as *non-smokers* (≤ 100 cigarettes), *former smokers* (>100 cigarettes but does not currently smoke), or *current smokers* (>100 cigarettes and smokes occasionally or daily).

The Physical Activity Scale for the Elderly (PASE) (Washburn et al., 1993) was used to measure participants' **physical activity.** The PASE is a brief scale designed to assess physical activities such as walking, housework, yard work and caring for others, done over the past 7 days. The questionnaire asks both frequency of activities as well as duration. A measure of physical activity is calculated based on frequency of activity (hours/day over the past 7 days), multiplied by the activities PASE weight (determined by its intensity level). All scores are then summed, with possible scores ranging from 0 to 739, and higher scores indicating greater physical activity. PASE has high test-retest reliability ($r = 0.75$) and strong convergent validity (Washburn et al., 1993).

The Rey Auditory Verbal Learning Test (RAVLT) (*immediate* and *5-minute delayed* recall) was used to measure baseline **memory** (Rey, 1964). An abbreviated version of the RAVLT was administered in the CLSA, consisting of only trial 1 of the five RAVLT trials, and one delayed recall trail (Tuokko et al., 2017). The RAVLT test required participants to listen to a list of 15 words and immediately recall them within 90 seconds. After five minutes, during which participants completed the animal fluency task and the mental alternation test, they were asked to recall as many of the initial words as they could within 60 seconds. For each test, the participant received one point for each correct word that was recalled, creating two scores between 0 and 15. For this analysis, the immediate and delayed scores were combined to create a score between 0-30. The original RAVLT has been found to have good test–retest reliability (r = .51 - .86) (Lezak et al., 2004) and is widely used in neuropsychological testing (Butler et al., 1991).

Psychosocial variables

Depressive symptoms were measured at baseline using the Center for Epidemiologic Studies Short Depression Scale (CESD-10) (Andresen et al., 1994). The CESD-10 contains 10 questions assessing depressive symptoms over the past week. The following four response options are given for each question: *all of the time (5-7 days), occasionally (3-4 days)*, *some of the time (1-2 days)*, or *rarely or never (less than 1 day)*. Total scores ranged from 0 to 30, with a cut-off score of 10 or more indicating a positive screen for depression (Andresen et al., 1994). The CESD-10 has demonstrated good reliability and validity, as well as adequate but acceptable sensitivity and specificity in identifying depression (Björgvinsson et al., 2013; González et al., 2017). Additionally, the CESD-10 has been found to measure depressive constructs equivalently

across various populations regardless of age, level of education, or language used during administration (i.e., French or English) (O'Connell et al., 2018).

The Ten-Item Personality Inventory (TIPI) was used to measure **personality traits** at baseline (Gosling et al., 2003). This scale measures the Big-Five personality traits which include extraversion, agreeableness, conscientiousness, emotional stability (i.e., low neuroticism), and openness to experiences. Participants were asked questions regarding their personality with possible responses ranging from *strongly disagree* to *strongly agree* (1-7). For each personality trait, two items were averaged, with one being reversed scored, and higher scores indicating more of that trait. The TIPI has been described as having adequate convergent validity (mean r = 0.77) and test-retest reliability (mean r = 0.72) (Gosling et al., 2003).

Social Support Availability (SSA) was measured at baseline using the Medical Outcomes Study Social Support Survey (MOS-SSS) (Sherbourne & Stewart, 1991). This validated scale includes 19 items (such as, "Someone to help you if you were confined to bed?", "Someone to give you advice about a crisis?", "Someone who shows you love and affection?", etc.) with possible answers as follows: *none of the time* (1)*, a little of the time* (2)*, some of the time* (3)*, most of the time* (4)*,* and *all of the time* (5)*.* The MOS-SSS produces an overall score (range: 0-100) reflective of perceived social support, with higher scores indicating greater overall support. The MOS-SSS has been found to have high convergent validity (range r = 0.72 to r = 0.90) and discriminant validity, as well as high internal-consistency reliability (range r = 0.91 to r = 0.97) (Sherbourne & Stewart, 1991).

During the first MCQ participants were asked to report their perceived **social standing** in their community, using the MacArthur Scale of Subjective Social Status (Adler et al., 2000). Participants were asked to think of a ladder with 10 rungs, with the bottom rung (1) representing

people with the lowest social standing in their community, and the top rung (10) representing people with the highest social standing in their community. They were then asked to place themselves on this ladder (range: 1-10). The MacArthur Scale of Subjective Social Status has been found to have moderate test-retest reliability in the community (k = 0.58, ICC= 0.64) with reliability being better among adults 55 years and older (Giatti et al., 2012).

Caregiving status was also assessed by asking a series of questions regarding various caregiving roles, which resulted in participants being classified as a *caregiver* or a *non-caregiver*. Caregivers are defined as individuals who provided assistance (excluding financial assistance) in the past 12 months to another person (e.g., friends, family) due to a health condition or limitation.

Statistical Analyses

All data analyses were conducted using Stata/SE 15.1, College Station, TX: StataCorp LLC. Differences in baseline characteristics between participants who reported SCD at first follow-up and those who did not are reported in Table 1. For categorical variables, number of participants (*n*) and percentages (*%*) are presented, whereas for continuous measures, means (*M*) and standard deviations (*SD*) are presented. Also presented in Table 1 are tests of group differences using t-tests for continuous variables and Pearson's chi-squared tests for categorical variables.

Analysis 1: Subjective Cognitive Decline

The primary analysis consisted of a Poisson regression model treating SCD (i.e., dichotomous variable) as the outcome and biological and psychosocial variables from baseline as explanatory variables. The vce(robust) option was applied to obtain Huber-White robust estimates of the standard errors. In cases where the outcome is common (i.e., > 10%) logistic

models may overstate the relative risk (RR) (McNutt et al., 2003). Thus, a robust Poisson model was used, as it is the preferred choice for estimating RRs for binary response variables (W. Chen et al., 2018). The comprehensive cohort sample size at first follow-up included n = 27,765 before removal of missing data. Only participants with data available for all variables were included in this analysis. The proportion of missing data in the outcome variable, SCD, was 0.75% (n = 209). For explanatory variables, the proportion of missing data ranged from 0.03% to 6.21%, with the highest missingness appearing in household income (6.21%). After removing missing data through listwise deletion, the final sample size was n = 21,920. First, the crude relationship between baseline memory and SCD was examined. Next, variables were entered into the model simultaneously, producing a multivariable model. Relative risks and corresponding 95% confidence intervals (CI) are reported in Table 2. Alpha (α) was set to 0.05.

Analysis 2: SCD-Related Worry

In a secondary analysis of participants who reported SCD, the amount of worry related to their SCD was examined (n = 12,707). Again, only participants with data available for all variables were included in this analysis. Using an ordinal logistic regression model, the relationships between potential biopsychosocial correlates and the level of SCD-related worry (outcome) were explored. Variables were entered into the model simultaneously. After the removal of participants who did not respond to the question regarding SCD-related worry (n = 13) the analytic sample for the secondary analysis was n = 12,694. Odds ratios (OR) and corresponding CIs are reported in Table 3. Alpha (α) was set to 0.05.

Sensitivity Analysis: Multiple Imputation

Following the main analyses, multiple imputation was conducted to account for missing data. Multiple imputation is a statistical technique for handling missing data by producing

multiple estimates of missing values using a regression-based procedure (White et al., 2011). Data were considered missing at random. Multiple imputation using chained equations (MICE) was conducted with $m = 5$ imputed datasets. MICE has been found to be the preferred method for data consisting of a mixture of continuous and categorical variables because each variable is imputed using its own imputation model (Van Buuren et al., 2006). All variables included in the two primary analyses were included in the imputation process. Missingness by variable can be seen in Table 4.

Exploratory Analysis: Age Interactions

Given the possibility that some of the associations observed in the main analyses may depend on age, an additional exploratory block of interactions was entered to determine if the associations were consistent across ages. The following interactions were simultaneously entered as a block into both analysis 1 and analysis 2: age × income, age × depression, and age × sexual orientation.

Ethics and Data Access

Ethical review of the CLSA protocol was conducted by the Ethical, Legal, and Social Issues Committee, falling under the jurisdiction of the Canadian Institutes of Health Research (CIHR), and research ethics board approval (REB) was then acquired from each research site. Written, informed consent was obtained from all participants before data collection. To ensure

confidentiality, identifying information was removed, and participants' data were identified by a number code rather than by name.

The current study falls under the broader CLSA project #190238. The analyses presented here have been cleared by the Brock University REB (19-008 – STINCHCOMBE), and the University of Ottawa REB (H-07-21-7271).

Chapter 4: Results

Participant Characteristics

Participant characteristics are presented in Table 1. More than half of the sample (58.0%) reported subjective cognitive decline at follow-up. Statistically significant differences ($p < 0.05$) were found for all variables except for education, sexual orientation, hypertension, and caregiving status. Of those who reported SCD, 49.1% were men and 50.9% were women. Participants who reported SCD were also older (mean age 62.4 compared to mean age 61.3). Furthermore, participants who reported SCD tended to have lower self-rated general health, and lower levels of physical activity, and were more likely to have hearing and vision problems, as well as a positive screen for depression, in comparison to individuals who did not report SCD.

Analysis 1: Subjective Cognitive Decline

Results from the Poisson regression model treating SCD as the outcome variable are presented in Table 2. In the crude analysis, baseline memory was negatively associated with SCD at follow-up, with each additional recalled word being associated with a small reduction in the risk of SCD (RR = 0.99, CI: 0.99-1.00). No relationships were found between SCD and most health and lifestyle variables, including hypertension, vision problems, physical activity, alcohol intake, and current smoker status. Statistically significant results include an association between age and SCD (RR = 1.00, CI: 1.00-1.01), such that increasing age was associated with a greater

risk of SCD after controlling for covariates, though the RR was 1.00. In terms of marital/partner status, participants currently in a relationship (married/common-law) (RR = 1.10, CI: 1.05-1.15) or with a history of a married/common-law relationship (widowed/divorced/separated) (RR = 1.08, CI: 1.02-1.13) were at greater risk of SCD when compared to those who were single. There was also a small significant negative association between BMI and SCD (RR = 0.99, CI: 0.99-0.99) such that with each increase in BMI score, the risk of SCD decreased.

In comparison to the lowest income bracket, individuals with higher income reported a greater risk of SCD. A similar relationship was found between education and SCD; post-secondary school graduates were at greater risk of SCD when compared to those with less than a secondary school education. Women were also at greater risk of SCD when compared to men. No statistically significant associations were found between SCD and sexual orientation, race, and social support availability. A negative relationship between perceived social standing and SCD was identified such that as one's perceived social standing increased, they had a reduced risk of SCD.

Self-reported hearing problems were associated with an increased risk of SCD (RR = 1.09, CI: 1.06-1.12). Additionally, self-rated general health had a negative association with SCD, with those who reported greater general health having a reduced risk of SCD. No associations were found between caregiving status or social support availability and SCD. A positive screen for depression significantly related to SCD (RR = 1.13, CI: 1.10-1.16). All personality traits (i.e., extraversion, agreeableness, conscientiousness, emotional stability, and openness) were negatively associated with SCD, with conscientiousness having the largest association (RR = 0.95, CI: 0.94-0.96). For example, more conscientious individuals were at lower risk of SCD.

Analysis 2: SCD-Related Worry

Results from the ordinal logistical regression model treating SCD-related worry as the outcome are presented in Table 3. When compared to men, women had an increased odds of reporting greater SCD-related worry (OR = 1.33, CI: 1.23-1.44). Interestingly, among individuals who reported experiencing SCD, those who were older had a small decreased odds of reporting SCD-related worry within the sample (OR = 0.99, CI: 0.98-0.99). Higher baseline memory was associated with a small, reduced odds of SCD-related worry (OR = 0.98, CI: 0.97-0.99). Higher BMI was also associated with reduced SCD-related worry (OR = 0.99, CI: 0.98-1.00). Participants with higher levels of education had an increased odds of reporting SCD-related worry, though the results from the secondary school graduate / some post-secondary school category were not statistically significant. Further, no relationship was found between SCD-related worry and being married/common-law, though participants who were widowed/divorced/separated had increased odds of reporting SCD-related worry compared to single participants. No relationship was found between income and SCD-related worry.

Caregivers had increased odds of reporting SCD-related worry (OR = 1.11, CI: 1.04-1.19). A positive screen for depression was also associated with increased SCD-related worry (OR = 1.49, CI: 1.34-1.66). No relationship was found between agreeableness or openness and SCD-related worry. Extraversion, conscientiousness, and emotional stability were associated with reduced odds of SCD-related worry. Within the personality traits, emotional stability showed the strongest association, with individuals who scored higher on emotional stability having reduced odds of reporting SCD-related worry (OR = 0.86, CI: 0.84-0.89).

In terms of minority stress variables, bisexual participants had an increased likelihood of SCD-related worry (OR = 1.90, CI: 1.09-3.31) compared to heterosexual participants. No

association was found between SCD-related worry and homosexuality within the sample. Similarly, no relationships were found between race, perceived social standing, or social support availability and SCD-related worry.

Sensitivity Analysis: Multiple Imputation

Imputed results for analyses 1 and 2 are reported in Table 5 and 6 respectively. Results from the MICE models were largely similar to those of the initial analyses. Since the MICE results significantly overlapped with the initial analyses results (i.e., no associations changed in direction, or in notable magnitude), the results from the initial listwise deletion analyses are presented in the results section and interpreted in the discussion section.

Exploratory Analysis: Age Interactions

Three age-related interactions were tested within both analysis 1 and analysis 2: age × sexual orientation, age × income, and age × depression. None of the interactions tested reached statistical significance in either model, therefore the initial models excluding the interactions were retained and interpreted in the discussion. A summary of the age interaction results can be seen in Tables 7 and 8.

Chapter 5: Discussion

Subjective Cognitive Decline (SCD)

A robust body of evidence exists highlighting biological and health risk factors for SCD, whereas less research to date has focused on psychosocial correlates of SCD and SCD-related worry. This study sought to identify prospective biopsychosocial correlates of SCD and SCD-related worry in a sample of mid-life and older adults (aged 45-85).

Objectively assessed memory was prospectively negatively associated with SCD at first follow-up in the CLSA, suggesting that SCD may be indicative of memory deterioration across

time, as measured by standardized neuropsychological tests. While there are inconsistent findings in the literature in regards to the relationship between SCD and cognitive functioning (Reid & MacLullich, 2006; Zullo et al., 2021), the findings of this study demonstrate a link between lower memory scores and memory concerns three years later.

While there was a clear association between objective memory and SCD within the sample, many of the commonly studied risk factors for cognitive aging and dementia were not associated with SCD risk or ran contrary to the expected direction of the associations. For example, factors that have been found to have a negative association with cognitive decline, such as income and education (Forrester et al., 2019), were found to be positively associated with SCD within the sample. Although contrary to most community-based studies, a few studies have reported similar findings regarding education and SCD. For example, in a longitudinal study Comijs and colleagues (2002) found that individuals who reported SCD but did not show an objective cognitive decline tended to have a higher levels of education. They suggested that individuals with higher education may express memory complaints due to overall decline in well-being and a greater sensitivity to cognitive changes (Comijs et al., 2002). Similarly, van Oijen and colleagues (2007) suggested that individuals with high levels of education may be better able to detect even subtle declines in cognitive abilities, and would thus be more likely to report SCD compared to people with lower educational levels. Furthermore, physical activity, a known protective factor against cognitive decline (Tan et al., 2017), and other health-related risk factors such as hypertension, alcohol intake, and smoking were not associated with SCD in the multivariable model.

Our results show that psychosocial factors were more consistently associated with subsequent SCD, compared to biological and health factors. Specifically, a positive screen for

depression was associated with an increased risk of SCD. This aligns with previous research findings that depression accelerates changes in the brain that lead to decline in cognitive abilities and may be an early indicator of impairment (Korczyn & Halperin, 2009). On the other hand, as depression was associated with SCD in the sample while holding baseline memory constant, it is possible that SCD may also be indicative of individuals' mental health in addition to their cognitive health. Similar findings stating that SCD may be a reflection of depression rather than objective cognitive decline have been reported (Studer et al., 2014; Zlatar et al., 2018). Other research has suggested that negative affect and the associated lower level of self-esteem which results from mood disorders, such as depression, may increase the likelihood that individuals will negatively evaluate their cognitive abilities, or even result in poorer scores on tests of cognition (Pearman & Storandt, 2004). Other studies with similar results have concluded that SCD without objective cognitive decline or impairment may be reflecting psycho-affective or health problems instead of an underlying cognitive impairment (Comijs et al., 2002).

In the sample, as individuals' perceptions of their social standing increased, their risk of SCD decreased. This aligns with previous research that has found associations between lower social standing and poorer cognition (Stinchcombe & Hammond, 2021; Zahodne et al., 2018). This association may be explained by the impact of social stress on brain health, outlined in Forrester and colleagues' (2019) framework for minority stress, as well as an increase in stress-related biological factors which can impact cognition, showing both a direct and indirect relationship between perceived social standing and cognitive health (Euteneuer, 2014). Surprisingly, no associations were observed between SCD and the minority stress variables of sexual orientation and race. In a recent paper, Flatt and colleagues (2021) found that the prevalence of SCD in sexual and gender minorities (SGM) in the United States was higher

compared to non-SGM adults, although this relationship was largely attenuated after accounting for depression. Similar findings have also been reported and may be explained by the minority stress model not applying to SCD, a subjective measure, after adjusting for other biopsychosocial variables (Brown & Patterson, 2020). The inclusiveness of the model (i.e., the inclusion of numerous biopsychosocial variables) may have led to attenuated relationships between the analyzed minority stress factors and SCD.

Interestingly, all five personality traits were associated with a reduced risk of SCD, with conscientiousness and emotional stability having the strongest negative associations. These results are in line with previous research that found that subjective memory complaints were associated with low conscientiousness and high neuroticism (the opposite of emotional stability) (Luchetti et al., 2016; Steinberg et al., 2013; Studer et al., 2014). Conscientious individuals have been found to have better cognitive function and show less decline over time (Luchetti et al., 2016). Luchetti and colleagues (2016) even noted that the effect of conscientiousness on cognition was larger than other clinical and lifestyle risk factors, such as smoking and physical inactivity. Neuroticism has also consistently been associated with cognitive complaints in the literature (Koller et al., 2019). Work by Graham and colleagues (2021) found that neuroticism is negatively associated with cognitive resilience stating that individuals with low neuroticism had better cognitive abilities than expected given the level of pathology. Further, progressive personality shifts during cognitive decline have been identified, such that an increase in negative emotions may be seen during the transition from normal aging to SCD, and SCD to MCI. Therefore, an increase in personality traits associated with negative emotions (e.g., neuroticism) may occur earlier than an objective decline in cognition, meaning personality traits may be an early identifier of dementia risk (Ausén et al., 2010). Rather than being related to common risk

factors for dementia, SCD may instead be associated with psychosocial factors such as depression, perceived social status, and personality traits (Zullo et al., 2021).

SCD-Related Worry

Some research has questioned the role of SCD in predicting future progress to MCI and dementia, because the majority of individuals reporting SCD do not progress to cognitive decline (Balash et al., 2013; Jessen et al., 2020). However, evidence shows that those who report worry associated with SCD are at a higher risk of future dementia (Jessen, 2010; Wolfsgruber et al., 2016). Despite these findings, there is a lack of research identifying individuals who are more likely to report SCD-related worry. The second analysis sought to understand the characteristics of individuals who reported higher worry related to their SCD. Results show that higher SCD-related worry was associated with being younger, a woman, bisexual, and having a positive screen for depression. Interestingly, no association was found between lesbian/gay identities and SCD-related worry; however, bisexual participants reported higher SCD-related worry in comparison to heterosexual participants. Other work has shown greater health disparities among bisexual people in comparison to people who identify as heterosexual, lesbian, and gay, attributable to bisexual-specific stigma, lack of visibility of bisexual identities, and lack of bisexual affirmative care and support (Ross et al., 2018). Taken alongside the results related to sexual orientation and SCD, additional research is clearly needed to determine the relationship between minority stress and SCD/SCD-related worry. For example, it may be worthwhile to tease apart the role of minority stress and other forms of stressors as they contribute to SCD and SCD-related worry as minority stress may be unique and have a differential impact when compared to general life stress.

Furthermore, certain personality traits (i.e., extraversion, conscientiousness, emotional stability) reduced the odds of reporting SCD-related worry. Emotional stability had the largest negative association with SCD-related worry. This may be due to the characteristics of this personality trait (i.e., less negative feelings, calm). These results are similar to previous studies which have found an association between high neuroticism (the inverse counterpart to emotional stability) and greater SCD and SCD-related worry (Comijs et al., 2002). Identifying and minimizing worry associated with SCD may be an important factor to reduce the risk of future cognitive decline.

Exploratory Analysis: Age Interactions

None of the age-related interactions that were tested were statistically significant. Chronological age is an important determinant of SCD, but it is known there is a myriad of factors that also predict risk of cognitive decline. For example, brain age, a measure that differs from chronological age, may be a better indicator of brain aging and risk for cognitive decline (Elliott et al., 2021). Brain age differs from chronological age as genetic, environmental, and lifestyle factors impact the rate of brain aging. As the sample in the study ranged from 45-85 years of age, it is possible that as the sample continues to age, some interactions may become detectable.

Strengths

Our study had multiple strengths including the large population-based sample size from locations across Canada. Given that SCD is still an under-researched area, even small effect sizes may be of interest as they may generate new hypotheses and advance the understanding of SCD. Additionally, the breadth and depth of the dataset allowed for a thorough examination of potential correlates of SCD whereas existing studies are commonly limited to only a few

explanatory variables. However, it is important to note that other confounding factors not included in this study may contribute to SCD (e.g., medication use, illness, and anxiety/stress). The inclusion of multiple psychosocial and minority stress variables provided novel results as these topics are understudied, yet very important, within the concept of SCD. The prospective nature of this study is also a strength as it was possible to determine associations between baseline characteristics and SCD three years later. Due to the longitudinal nature of the CLSA, future research may be able to identify potentially causal relationships between biopsychosocial variables, SCD, and objective cognitive decline.

Limitations

This study is not without its limitations. Most prominent is the brief measure of SCD and SCD-related worry using a simple two-question approach. Although similar measures are commonly used (Geerlings et al., 1999; van Oijen et al., 2007) and have the advantage of ease of use in large epidemiological samples such as the CLSA, many in-depth scales exist which may be able to better differentiate between individuals with and without SCD (Jessen et al., 2020). Further, due to cell sizes, it was not possible to explore the intersectional/multiplicative effects of multiple social locations on cognition (e.g., race, gender, and sexual orientation). With respect to minority stress, it may be useful for future research to examine participants' self-reported minority stress experiences and not just their minoritized identities as they relate to cognition. Additionally, many measures within the study are self-reported (i.e., income, physical activity, vision, and hearing problems). The use of self-reported data introduces the possibility of discrepancies between participants' reported and actual behaviours; for example, participants may over-report their physical activity level.

At baseline, the CLSA was comprised of a large portion of younger healthy individuals, for whom SCD may not yet be predictive of cognitive impairment (Jessen et al., 2020). Instead, the relatively young age of the sample may explain the reported associations, or lack thereof, between psychosocial factors and SCD. Future longitudinal research should focus on the trajectory of individuals reporting SCD in terms of future cognitive decline and dementia risk, also considering the psychosocial correlates presented here.

Conclusion

This study builds on existing literature describing biological, health behaviour, and psychosocial correlates of SCD and SCD-related worry. Many known risk and protective factors of cognitive decline were not associated with SCD within the sample. Rather, psychosocial variables (i.e., depression, perceived social status, and personality traits) showed a more consistent association with SCD in the sample. Greater SCD-related worry, which has been found to increase the risk of later dementia, was associated with specific personality traits, depression, age, gender, and sexuality. The results from this study support the potential importance of psychosocial factors in identifying individuals with SCD and, in addition to confirming previous work, highlights the contribution of personality traits and perceived social standing to cognitive complaints. Psychosocial variables, in addition to health variables, may warrant attention as part of standard cognitive screening.

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Table 1

Baseline characteristics of the study population between persons with and without subjective cognitive decline (SCD)

Variable	Total (*n*=21,920)	No SCD (*n*=9,213)	SCD (*n*=12,707)	*p*
Baseline Memory	10.2 (3.7)	10.3 (3.6)	10.1 (3.7)	<0.001
Age	61.9 (9.9)	61.3 (9.6)	62.4 (10.0)	<0.001
Income				0.005
$<20,000	940 (4.3%)	445 (4.8%)	495 (3.9%)	
$20,000-49,999	4,427 (20.2%)	1,857 (20.2%)	2,570 (20.2%)	
$50,000-99,999	7,871 (35.9%)	3,230 (35.1%)	4,641 (36.5%)	
$100,000-149,999	4,555 (20.8%)	1,943 (21.1%)	2,612 (20.6%)	
$150,000+	4,127 (18.8%)	1,738 (18.9%)	2,389 (18.8%)	
Education				0.26
< Secondary school grad	956 (4.4%)	424 (4.6%)	532 (4.2%)	
Sec. school grad / Some Post-Secondary	3,471 (15.8%)	1,473 (16.0%)	1,998 (15.7%)	
Post-Secondary grad	17,493 (79.8%)	7,316 (79.4%)	10,177 (80.1%)	
Marital Status				<0.001
Single	1,807 (8.2%)	844 (9.2%)	963 (7.6%)	
Married/Common-law	15,748 (71.8%)	6,550 (71.1%)	9,198 (72.4%)	
Widowed/Divorced/Separated	4,365 (19.9%)	1,819 (19.7%)	2,546 (20.0%)	
Gender				<0.001
Man	11,013 (50.2%)	4,769 (51.8%)	6,244 (49.1%)	
Woman	10,907 (49.8%)	4,444 (48.2%)	6,463 (50.9%)	
Race				0.018
White	20,871 (95.2%)	8,754 (95.0%)	12,117 (95.4%)	
Black	131 (0.6%)	71 (0.8%)	60 (0.5%)	
Other non-White	918 (4.2%)	388 (4.2%)	530 (4.2%)	
Sexual Orientation				0.61
Heterosexual	21,412 (97.7%)	9,007 (97.8%)	12,405 (97.6%)	

Homosexual	405 (1.8%)	161 (1.7%)	244 (1.9%)	
Bisexual	103 (0.5%)	45 (0.5%)	58 (0.5%)	
Smoking Status				<0.001
Never	10,358 (47.3%)	4,536 (49.2%)	5,822 (45.8%)	
Former	9,847 (44.9%)	3,910 (42.4%)	5,937 (46.7%)	
Current	1,715 (7.8%)	767 (8.3%)	948 (7.5%)	
Self-Rated General Health				<0.001
Poor/Fair	1,686 (7.7%)	575 (6.2%)	1,111 (8.7%)	
Good	6,295 (28.7%)	2,472 (26.8%)	3,823 (30.1%)	
Very good	9,288 (42.4%)	3,906 (42.4%)	5,382 (42.4%)	
Excellent	4,651 (21.2%)	2,260 (24.5%)	2,391 (18.8%)	
Hypertension				0.18
No	14,113 (64.4%)	5,979 (64.9%)	8,134 (64.0%)	
Yes	7,807 (35.6%)	3,234 (35.1%)	4,573 (36.0%)	
Alcohol Intake				0.013
Never	2,265 (10.3%)	968 (10.5%)	1,297 (10.2%)	
Infrequent	6,213 (28.3%)	2,679 (29.1%)	3,534 (27.8%)	
Regular	7,385 (33.7%)	3,123 (33.9%)	4,262 (33.5%)	
Frequent	6,057 (27.6%)	2,443 (26.5%)	3,614 (28.4%)	
Body Mass Index (BMI)	28.0 (5.4)	28.3 (5.4)	27.9 (5.3)	<0.001
Physical Activity (PASE)	145.8 (73.8)	150.4 (76.0)	142.5 (72.0)	<0.001
Vision Problems				<0.001
No	20,434 (93.2%)	8,686 (94.3%)	11,748 (92.5%)	
Yes	1,486 (6.8%)	527 (5.7%)	959 (7.5%)	
Hearing Problems				<0.001
No	19,552 (89.2%)	8,428 (91.5%)	11,124 (87.5%)	
Yes	2,368 (10.8%)	785 (8.5%)	1,583 (12.5%)	
Caregiving Status				0.098
No	12,041 (54.9%)	5,121 (55.6%)	6,920 (54.5%)	
Yes	9,879 (45.1%)	4,092 (44.4%)	5,787 (45.5%)	
Depression Screen				<0.001

Negative	18,795 (85.7%)	8,255 (89.6%)	10,540 (82.9%)	
Positive	3,125 (14.3%)	958 (10.4%)	2,167 (17.1%)	
Perceived Social Standing	6.3 (1.8)	6.4 (1.8)	6.2 (1.8)	<0.001
Social Support Availability	82.1 (16.7)	82.9 (16.5)	81.5 (16.8)	<0.001
Personality Traits				
Extraversion	4.4 (1.8)	4.5 (1.8)	4.3 (1.8)	<0.001
Agreeableness	5.9 (1.1)	6.0 (1.1)	5.8 (1.1)	<0.001
Conscientiousness	6.2 (1.1)	6.3 (1.0)	6.1 (1.1)	<0.001
Emotional Stability	5.8 (1.4)	6.0 (1.3)	5.7 (1.4)	<0.001
Openness	5.5 (1.4)	5.6 (1.3)	5.4 (1.4)	<0.001

Table 2

Poisson regression model of the relationships between explanatory variables and subjective cognitive decline within the CLSA (n=21,920)

Variable	*RR*	*p*	CI (lower)	CI (upper)
Baseline Memory	0.995**	0.003	0.991	0.998
Age	1.005***	<0.001	1.003	1.006
Income				
$20,000-49,999	1.131***	<0.001	1.059	1.207
$50,000-99,999	1.195***	<0.001	1.118	1.277
$100,000-149,999	1.208***	<0.001	1.125	1.297
$150,000+	1.265***	<0.001	1.176	1.361
Education				
Secondary school grad / Some Post-Secondary	1.064	0.053	0.999	1.133
Post-Secondary grad	1.099**	0.002	1.036	1.167
Marital Status				
Married/Common-law	1.097***	<0.001	1.045	1.151
Widowed/Divorced/Separated	1.075**	0.005	1.022	1.130
Gender				
Woman	1.087***	<0.001	1.060	1.115
Race				
Black	0.842	0.062	0.702	1.008
Other non-White	0.997	0.926	0.943	1.055
Sexual Orientation				
Homosexual	1.082	0.053	0.999	1.172
Bisexual	0.969	0.712	0.820	1.145
Smoking Status				
Former	1.058***	<0.001	1.033	1.083
Current	0.971	0.211	0.927	1.017
Self-Rated General Health				
Good	0.953*	0.019	0.915	0.992
Very good	0.925***	<0.001	0.888	0.965
Excellent	0.835***	<0.001	0.795	0.877
Hypertension				
Yes	0.990	0.450	0.966	1.016
Alcohol intake				
Infrequent	1.013	0.551	0.972	1.055
Regular	1.04	0.058	0.999	1.084
Frequent	1.048*	0.027	1.005	1.093
Body Mass Index (BMI)	0.992***	<0.001	0.989	0.994
Physical Activity (PASE)	1	0.069	1.000	1.000
Vision Problems				

Yes	1.039	0.061	0.998	1.081
Hearing Problems				
Yes	1.101***	<0.001	1.067	1.137
Caregiving Status				
Yes	1.021	0.069	0.998	1.044
Depression Screen				
Positive	1.129***	<0.001	1.096	1.164
Perceived Social Standing	0.993*	0.026	0.986	0.999
Social Support Availability	1.000	0.493	0.999	1.000
Personality Traits				
Extraversion	0.988***	<0.001	0.982	0.995
Agreeableness	0.977***	<0.001	0.967	0.987
Conscientiousness	0.949***	<0.001	0.940	0.958
Emotional Stability	0.975***	<0.001	0.967	0.983
Openness	0.979***	<0.001	0.971	0.987

***p<0.001, ** p<0.01, * p<0.05

Table 3

Ordinal logistic regression model of the relationships between explanatory variables and subjective cognitive decline (SCD)-related worry within the CLSA (n=12,694)

Variable	*OR*	*p*	CI (lower)	CI (upper)
Baseline Memory	0.981***	<0.001	0.970	0.991
Age	0.987***	<0.001	0.982	0.991
Income				
$20,000-49,999	1.045	0.665	0.856	1.277
$50,000-99,999	1.178	0.114	0.962	1.443
$100,000-149,999	1.130	0.268	0.910	1.404
$150,000+	1.199	0.110	0.960	1.499
Education				
Sec. school grad / Some Post-Secondary	1.160	0.134	0.955	1.408
Post-Secondary grad	1.255*	0.015	1.045	1.506
Marital Status				
Married/Common-law	1.092	0.241	0.943	1.264
Widowed/Divorced/Separated	1.167*	0.048	1.002	1.359
Gender				
Woman	1.328***	<0.001	1.227	1.437
Race				
Black	0.877	0.604	0.533	1.442
Other non-white	0.921	0.357	0.773	1.097
Sexual Orientation				
Homosexual	1.204	0.154	0.933	1.553
Bisexual	1.901*	0.023	1.093	3.308
Smoking Status				
Former	1.057	0.138	0.982	1.138
Current	0.770***	<0.001	0.670	0.887
Self-Rated General Health				
Good	0.956	0.528	0.833	1.098
Very good	0.800**	0.002	0.695	0.921
Excellent	0.681***	<0.001	0.581	0.797
Hypertension				
Yes	0.897**	0.006	0.830	0.969
Alcohol intake				
Infrequent	1.119	0.081	0.986	1.270
Regular	1.137*	0.045	1.003	1.290
Frequent	1.122	0.081	0.986	1.278
Body Mass Index (BMI)	0.989**	0.002	0.982	0.996

Physical Activity (PASE)	1.000	0.271	1.000	1.001
Vision Problems				
Yes	1.099	0.170	0.960	1.257
Hearing Problems				
Yes	1.037	0.502	0.932	1.155
Caregiving Status				
Yes	1.114**	0.002	1.039	1.194
Depression Screen				
Positive	1.491***	<0.001	1.343	1.656
Perceived Social Standing	0.985	0.144	0.964	1.005
Social Support Availability	0.998	0.105	0.996	1.000
Personality Traits				
Extraversion	0.967**	0.001	0.948	0.987
Agreeableness	1.001	0.962	0.969	1.034
Conscientiousness	0.945***	<0.001	0.915	0.975
Emotional Stability	0.863***	<0.001	0.839	0.888
Openness	1.010	0.447	0.984	1.037

***p<0.001, ** p<0.01, * p<0.05

Table 4

Missing data

Variable	*Missing Data (n)*	*Missing (%)*
SCD	209	0.75
SCD-Related Worry	233	0.84
Baseline Memory	1,168	4.21
Age	0	0.00
Income	1,724	6.21
Education	43	0.15
Marital Status	8	0.03
Gender	0	0.00
Race	25	0.09
Sexual Orientation	38	0.14
Smoking Status	76	0.27
Self-Rated General Health	19	0.07
Hypertension	148	0.53
Alcohol intake	639	2.30
Body Mass Index (BMI)	111	0.39
Physical Activity (PASE)	662	2.3
Vision Problems	14	0.05
Hearing Problems	23	0.08
Caregiving Status	20	0.07
Depression Screen	94	0.44
Perceived Social Standing	1,069	3.85
Social Support Availability	506	1.8
Personality Traits		
Extraversion	704	2.5
Agreeableness	630	2.3
Conscientiousness	683	2.5
Emotional Stability	572	2.1
Openness	827	3.0

Table 5

Imputed results: Poisson regression model of the relationships between explanatory variables and subjective cognitive decline within the CLSA (n=27,745)

Variable	*RR*	*p*	CI (lower)	CI (upper)
Baseline Memory	0.995*	0.037	0.990	1.000
Age	1.005***	<0.001	1.003	1.006
Income				
$20,000-49,999	1.108*	0.013	1.022	1.202
$50,000-99,999	1.178***	<0.001	1.084	1.281
$100,000-149,999	1.194***	<0.001	1.089	1.308
$150,000+	1.246***	<0.001	1.131	1.373
Education				
Secondary school grad / Some Post-Secondary	1.072	0.100	0.987	1.164
Post-Secondary grad	1.109**	0.009	1.027	1.198
Marital Status				
Married/Common-law	1.108**	0.002	1.039	1.182
Widowed/Divorced/Separated	1.084*	0.018	1.014	1.159
Gender				
Woman	1.082***	<0.001	1.044	1.159
Race				
Black	0.839	0.106	0.678	1.038
Other non-White	0.987	0.728	0.915	1.064
Sexual Orientation				
Homosexual	1.079	0.206	0.959	1.213
Bisexual	0.912	0.458	0.716	1.162
Smoking Status				
Former	1.061**	0.001	1.026	1.097
Current	0.966	0.287	0.908	1.029
Self-Rated General Health				
Good	0.952	0.103	0.897	1.010
Very good	0.919**	0.007	0.865	0.977
Excellent	0.828***	<0.001	0.772	0.888
Hypertension				
Yes	0.988	0.516	0.954	1.024
Alcohol intake				
Infrequent	1.010	0.725	0.955	1.068
Regular	1.051	0.080	0.994	1.111
Frequent	1.061*	0.043	1.002	1.124
Body Mass Index (BMI)	0.991***	<0.001	0.988	0.994
Physical Activity (PASE)	1.000	0.218	1.000	1.000

Vision Problems				
Yes	1.046	0.133	0.987	1.108
Hearing Problems				
Yes	1.096***	<0.001	1.045	1.149
Caregiving Status				
Yes	1.032	0.052	1.000	1.065
Depression Screen				
Positive	1.131***	<0.001	1.081	1.184
Perceived Social Standing	0.992	0.070	0.982	1.000
Social Support Availability	1.000	0.629	0.999	1.000
Personality Traits				
Extraversion	0.988*	0.010	0.978	0.997
Agreeableness	0.978**	0.003	0.964	0.993
Conscientiousness	0.954***	<0.001	0.941	0.967
Emotional Stability	0.973***	<0.001	0.961	0.986
Openness	0.980**	0.001	0.969	0.992

***p<0.001, ** p<0.01, * p<0.05

Table 6

Imputed results: Ordinal logistic regression model of the relationships between explanatory variables and subjective cognitive decline (SCD)-related worry within the CLSA (n=15,836)

Variable	*OR*	*p*	CI (lower)	CI (upper)
Baseline Memory	0.983***	<0.001	0.973	0.992
Age	0.986***	<0.001	0.982	0.990
Income				
$20,000-49,999	0.956	0.609	0.805	1.136
$50,000-99,999	1.040	0.675	0.866	1.248
$100,000-149,999	1.027	0.795	0.837	1.261
$150,000+	1.097	0.380	0.891	1.349
Education				
Sec. school grad / Some Post-Secondary	1.161	0.075	0.985	1.370
Post-Secondary grad	1.233**	0.008	1.056	1.440
Marital Status				
Married/Common-law	1.121	0.085	0.985	1.276
Widowed/Divorced/Separated	1.166*	0.024	1.021	1.332
Gender				
Woman	1.347***	<0.001	1.254	1.445
Race				
Black	0.917	0.603	0.603	1.396
Other non-white	0.916	0.254	0.788	1.065
Sexual Orientation				
Homosexual	1.221	0.094	0.967	1.542
Bisexual	1.857*	0.017	1.116	3.090
Smoking Status				
Former	1.046	0.184	0.979	1.118
Current	0.766***	<0.001	0.676	0.868
Self-Rated General Health				
Good	0.925	0.206	0.820	1.044
Very good	0.785***	<0.001	0.694	0.888
Excellent	0.667***	<0.001	0.580	0.767
Hypertension				
Yes	0.901**	0.003	0.840	0.966
Alcohol intake				
Infrequent	1.153*	0.011	1.033	1.288
Regular	1.178**	0.004	1.054	1.317
Frequent	1.168*	0.008	1.041	1.310
Body Mass Index (BMI)	0.990**	0.002	0.984	0.996
Physical Activity (PASE)	1.000	0.267	1.000	1.001

Vision Problems				
Yes	1.137*	0.032	1.011	1.278
Hearing Problems				
Yes	1.064	0.201	0.967	1.171
Caregiving Status				
Yes	1.115**	0.001	1.047	1.186
Depression Screen				
Positive	1.444***	<0.001	1.318	1.582
Perceived Social Standing	0.989	0.234	0.971	1.007
Social Support Availability	0.997*	0.021	0.995	1.000
Personality Traits				
Extraversion	0.963***	<0.001	0.945	0.981
Agreeableness	1.000	0.959	0.971	1.029
Conscientiousness	0.947***	<0.001	0.920	0.974
Emotional Stability	0.861***	<0.001	0.839	0.883
Openness	1.001	0.479	0.985	1.033

***p<0.001, ** p<0.01, * p<0.05

Table 7

Summary table of exploratory age-related interactions in SCD model

	RR	***p***	**CI (lower)**	**CI (upper)**
Sexual Orientation*Age				
Homosexual	1.004	0.383	0.995	1.013
Bisexual	0.985	0.143	0.966	1.005
Income*Age				
$20,000-49,999	1.002	0.583	0.995	1.008
$50,000-99,999	1.002	0.454	0.996	1.008
$100,000-149,000	1.002	0.520	0.996	1.009
$150,000+	0.998	0.565	0.991	1.005
Depression*Age	0.999	0.310	0.996	1.001

Table 8

Summary table of exploratory age-related interactions in SCD-related worry model

	RR	***p***	**CI (lower)**	**CI (upper)**
Sexual Orientation*Age				
Homosexual	1.021	0.134	0.994	1.049
Bisexual	1.022	0.419	0.969	1.078
Income*Age				
$20,000-49,999	0.984	0.086	0.967	1.002
$50,000-99,999	0.997	0.747	0.980	1.015
$100,000-149,000	0.994	0.509	0.976	1.012
$150,000+	1.000	0.831	0.983	1.021
Depression*Age	0.995	0.239	0.986	1.004