Cognitive Change in Individuals with Posttraumatic Stress Disorder

by

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Abstract

Posttraumatic stress disorder (PTSD) is a prevalent psychiatric condition in Canada, with a lifetime prevalence of 9.2% among Canadian civilians and 12.7% among Canadian veterans. While there exists a substantial body of research delving into the cognitive abilities of younger adults affected by PTSD, less is known about the cognitive profile of middle-aged and older adults with symptoms of PTSD. Often built on cross-sectional designs with relatively small sample sizes, and frequently utilizing group analysis, these studies might have restricted capacity to unveil distinct cognitive profiles within people exhibiting symptoms of PTSD symptoms.

In addition, recent research indicates that people with PTSD face an elevated risk of developing dementia, with subtle cognitive deficits potentially serving as precursors to cognitive decline leading to dementia. Nonetheless, specific lifestyle elements, such as education, physical activity, social support, and mental engagement, have demonstrated their potential to alleviate cognitive decline in various conditions. These factors, termed cognitive reserve factors, remain scarcely investigated in relation to their influence on cognition among individuals with PTSD.

The dissertation focuses on three main goals: 1) measuring cognitive changes related to PTSD in a diverse sample of middle-aged and older adults, including veterans; 2) assessing cognitive decline over time between those with and without symptoms of PTSD; 3) investigating if certain lifestyle factors can serve as cognitive reserve mechanisms to reduce cognitive decline over time.

Using baseline data from the Canadian Longitudinal Study on Aging, Study 1 examined neuropsychological performance in a large group of middle-aged to older adults with PTSD symptoms. The study assessed impairment rates (performance scores 1.5 or more standard deviations below the mean) and also explored if a cognitive reserve factor (social support) could

mitigate cognitive decline in both the PTSD and comparison groups, laying the groundwork for Study 2.

Study 2 aimed to assess the three-year longitudinal neuropsychological performance of middle-aged to older adults with PTSD symptoms. Expanding on Study 1, it investigated more cognitive reserve factors like physical activity, cognitive stimulation, education, social participation, and social support. The goal was to determine if these factors could improve neurocognitive test performance and if benefits were similar for the PTSD and comparison groups.

Given the unique health and well-being characteristics among Canadian veterans, especially their vulnerability to PTSD, Study 3 aimed to explore the cognitive differences between veterans and non-veterans with PTSD. Combining Study 1 and Study 2 objectives, it assessed the longitudinal neuropsychological performance of veterans with PTSD over three years. The study also assessed if a larger subset of veterans experienced clinically significant decline compared to civilians with PTSD.

The results indicated that a subset of people within the PTSD group initially showed low performance on tasks involving executive functioning. These individuals also showed significant decline in executive functioning tasks during the FU1 assessment. Intriguingly, veterans' cognitive profiles within the PTSD group remained similar to non-veterans over three years after accounting for TBI. Regarding cognitive reserve, the findings of both Study 1 and Study 2 imply that cognitive reserve factors might have a stronger impact on modifying cognitive processes in individuals without PTSD compared to those with PTSD.

General Introduction

Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is a persistent and often debilitating condition that occurs as a direct consequence of being exposed to a traumatic event. Individuals exhibiting symptoms of PTSD can experience significant functional impairments, leading to an estimated increase of $838 CAD per person in annual healthcare costs compared to those without such symptoms (Lamoureux-Lamarche et al., 2016). According to the Diagnostic and Statistical Manual, Fifth Edition- Text Revision (DSM-5-TR; American Psychiatric Association, 2022), the traumatic event can be directly experienced, witnessed, learned about, or individuals can be repeatedly exposed to details of actual or threatened death, serious injury or sexual violence. Following the traumatic event, individuals diagnosed with PTSD experience symptoms from the following four symptom clusters: intrusion (e.g., involuntary memories of the traumatic event, nightmares, flashbacks), avoidance (e.g., avoidance of people, places, memories of traumatic event), negative cognition and/or mood (e.g., unable to remember aspect of traumatic event, persistent negative mood, diminished interest), and marked alterations in arousal (e.g., hypervigilance, angry outbursts, difficulty with concentration). For a diagnosis of PTSD, the aforementioned symptoms need to persist for a duration that exceeds one month after the event, and lead to significant distress or functional impairment. The symptoms outlined above may manifest alongside dissociative symptoms, leading to a dissociative subtype of PTSD. These dissociative symptoms encompass depersonalization, where individuals feel detached from their own bodies, and derealization, where external events may seem unreal or unfamiliar (American Psychiatric Association, 2022). The specifier of delayed onset PTSD can be applied when the

full diagnostic criteria are not met until at least six months have elapsed since the traumatic event (American Psychiatric Association, 2022).

Exposure to traumatic events seems to be relatively common among Canadians (76.1%), although, only a small percentage of individuals go on to develop PTSD as a result (Van Ameringen et al., 2008). Although most of the research on PTSD has focused on the United States, a study by Van Ameringen et al. (2008) sheds light on the prevalence rates in Canada. The participants of this study comprised a nationally representative sample of 2991 individuals living in Canada during July and August 2002, all aged 18 years and older. According to their findings, the lifetime prevalence rate of PTSD in Canada was 9.2%, while the current rate stood at 2.4%. Rates were comparable with previous studies examining the prevalence of PTSD in the general Canadian population (Stein et al., 1997).

Numerous studies have examined the risk factors related to the onset of PTSD, which include factors occurring before the traumatic event (pre-trauma), during the event itself (peritraumatic), and after the event (post-trauma). Consistent evidence has shown that pre-trauma risk factors include being a female, having low I.Q. (intelligence quotient), having a previous psychiatric disorder, having a family history of psychiatric problems, experiencing childhood abuse, or encountering trauma at a young age (Breslau et al., 1995; Sareen, 2014; Stein et al., 1997; Van Ameringen et al., 2008). Trauma factors such as perceived fear of death, assaultive trauma, severity of trauma, and physical injury also increase the risk for the development of PTSD (Sareen, 2014). There is growing evidence regarding post-trauma factors, suggesting low social support, financial stress, pain severity, traumatic brain injury (TBI), and peritraumatic dissociation following the trauma can play a significant role in the development of this disorder (Breslau et al., 1995; Sareen, 2014; Van Ameringen et al., 2008).

Posttraumatic Stress Disorder in Older Adults

In Canada, the aging population is steadily increasing. As of 2016, approximately one in eight Canadians were aged 65 years or older. This trend is expected to accelerate, with projections indicating that by 2031, one out of every four Canadians will surpass the age of 65 (Statistics Canada, 2016). While there is a significant body of research on PTSD in the adult population, there is a notable dearth of literature addressing PTSD in older adults (Cook & O'Donnell, 2005). Older adults are often more susceptible to chronic physical conditions, mental health conditions, cognitive deterioration, and the erosion of social connections. Additionally, they may encounter other stressors associated with aging, which have the potential to contribute to diverse manifestations of PTSD during altered stages of life (Lapp et al., 2011). Therefore, it is essential that PTSD in older adults is approached from a developmental perspective. In other words, PTSD must be considered in the context of the typical biological, psychological, and social changes that occur alongside the aging process (Lapp et al., 2011). Studies have shown that older adults who experience PTSD face considerable challenges, including significant impairment in their daily lives, decreased life satisfaction, inadequate perceived care, reporting feeling older, and increased health issues (Kubzansky et al., 2007; Solomon et al., 2009; Spitzer et al., 2008; van Zelst et al., 2006).

Nevertheless, studies have also indicated that older adults generally exhibit lower rates of PTSD compared to younger or middle-aged adults (Böttche et al., 2012; Kessler et al., 2005; Reynolds et al., 2016). In a study conducted by Reynolds et al. (2016) in the United States, they found that the prevalence of current PTSD was 2.6% for older adults compared to 5.2% for middle-aged adults. However, it is important to approach these findings cautiously. There are concerns that these rates may be artificially deflated due to potential under-reporting or because

older individuals may perceive or express their PTSD symptoms as somatic rather than psychological (Lapp et al., 2011; van Zelst et al., 2006).

PTSD in older adults presents itself in diverse ways, encompassing multiple potential trajectories. These trajectories, proposed by Busuttil (2004), include various forms of manifestation. Firstly, there is "de novo PTSD," which arises from a traumatic event experienced in late life. Secondly, chronic PTSD emerges when the trauma occurs earlier in life, leading to enduring PTSD symptoms that may fluctuate in intensity over time. Thirdly, delayed onset PTSD can occur, where after a prolonged period of minimal or controlled symptoms, full PTSD appears in later years. However, the notion of delayed onset PTSD is not without controversy. Some argue that what may appear as delayed onset is actually due to under-reporting, delayed recognition, subclinical PTSD exacerbation, or misdiagnosis (Hiskey et al., 2008). Additionally, the cognitive status of older adults plays a significant role as a risk factor when it comes to the occurrence or recurrence of PTSD in later life (Achterberg & Southwick, 2001; Cook et al., 2003; Johnston, 2000; Mittal et al., 2001). It has been observed that certain individuals who have successfully managed or experienced an absence of PTSD symptoms for decades develop PTSD in old age when they also start to experience symptoms related to cognitive decline or face neurological disorders (Mittal et al., 2001). These findings suggest that cognitive decline could disrupt previously employed strategies or defense mechanisms used to cope with traumatic memories (Achterberg & Southwick, 2001).

Posttraumatic Stress Disorder in Veterans

Current estimates suggest that there are approximately 461,240 living veterans who served in the Canadian Armed Forces (Statistics Canada, 2022). The occurrence of mental health disorders among veterans is significantly higher, up to three times more prevalent, when

compared to the general population (VanTil et al., 2016). PTSD is a major contributor to disability among veterans. Studies have shown that around 12.7% of Canadian veterans have been diagnosed with PTSD, making it the third most common service-related disability (Thompson et al., 2016; Veterans Affaire Canada, 2017). Additionally, nearly half (42.5%) of Canadian veterans seeking assistance through the New Veterans Charter have been diagnosed with PTSD (Thompson et al., 2011). However, variations in the prevalence of PTSD within veteran communities have been documented, taking into account factors such as the era of service, branch of service, country of service, and deployment status (Forbes et al., 2019; Spiro et al., 2016).

Veterans possess various characteristics that can impact the development and nature of PTSD symptoms. Along with the risk of war-related trauma exposure, recruits are disproportionately chosen from underprivileged environments and are therefore at increased risk of experiencing adverse childhood experiences. In addition, as military personnel advance in their careers, it is inevitable that they will encounter a higher probability of experiencing multiple traumatic events, increasing their risk of PTSD (Forbes et al., 2019). A recent study conducted by Gauvin et al. (2022) investigated the factors associated with positive PTSD screening among Canadian veterans within the context of the Canadian Longitudinal Study on Aging. The study aimed to identify any differences between various veteran sub-groups and non-veterans who screened positive for PTSD. The study revealed that Canadian Regular Force Veterans were more likely to screen positive for PTSD compared to Reserve Force Veterans and non-veterans. The authors also discovered that younger age, depression, anxiety, comorbidities, and retirement were associated with an increased likelihood of screening positive for PTSD. The study also indicated a negative association between advanced age and screening positive for

PTSD (Gauvin et al., 2022). This pattern, as previously stated, is not necessarily limited to veterans and could be attributed to survivor bias. It implies that individuals who reach old age and participate in research are less prone to developing PTSD or encountering severe symptoms. In addition, the proximity of the trauma to the study's timeframe may impact the recollection and reporting of PTSD. This aspect holds particular importance as military-related trauma among older veterans may have transpired several years or even decades before the study (Gauvin et al., 2022; Konnert & Wong, 2015).

Neurocognitive functioning in PTSD

Although PTSD is commonly discussed in terms of emotional dysregulation, it is also associated with cognitive deficits. Memory abnormalities, such as intrusive memories as well as attention deficits in the form of impaired concentration and hypervigilance, play a central role in the clinical manifestation of PTSD (Dolan et al., 2012). In the last two decades, a substantial amount of research has provided evidence for structural, functional, and neurocognitive changes associated with PTSD (Brown & Morey, 2012; Douglas Bremner et al., 2008; Patel et al., 2012; Pitman et al., 2012; Scott et al., 2015)

Neurocognitive performance encompasses various domains. In the context of PTSD research, the domains that are the most commonly investigated include attention (e.g., orienting to stimuli and sustaining focus), working memory (e.g., manipulating and updating information in the moment), processing speed (e.g., rate at which an individual can perceive, process, and respond to incoming information), executive functioning (e.g., constellation of higher order cognitive processes including inhibition and set-shifting), as well as learning and memory (e.g., capacity to acquire novel information, preserve it in memory, and subsequently retrieve it after a period of time; Jacob et al., 2019).

Cross-sectional Studies

Numerous cross-sectional studies have shown that individuals with PTSD experience difficulties in multiple of the aforementioned cognitive areas, including attention, working memory, processing speed, executive function, and learning and memory (Aupperle et al., 2012.; Brewin et al., 2007; Jak et al., 2018; Johnsen & Asbjørnsen, 2008; Polak et al., 2012; Scott et al., 2015). A meta-analysis involving 60 studies conducted by Scott et al. (2015) examined the cognitive functioning of individuals with PTSD. The results revealed that individuals with PTSD consistently performed at lower levels in all domains compared to those without PTSD (Scott et al., 2015). The effect sizes, indicating the magnitude of the differences, ranged from small to medium (Cohen's d = -0.29 to -0.62). The most substantial differences were observed in the areas of verbal learning (d = -0.62), speed of information processing (d = -0.59), and attention/working memory (d = -0.50).

It is important to note that while there are differences in cognitive performance between individuals with and without PTSD, these differences typically do not reach the level of clinically significant impairment as defined as scores that are 1.5 or 2 standard deviations below the average scores of the general population (Gilbertson et al., 2001; Nijdam et al., 2013; Samuelson, 2011; Samuelson et al., 2016; Scott et al., 2015; Vasterling et al., 1998).

Nonetheless, other studies have yielded contradicting results questioning the presence or magnitude of cognitive impairments associated with PTSD (Crowell et al., 2002; Elsesser & Sartory, 2007; Gurvits et al., 1996; Neylan et al., 2004; Pederson et al., 2004; Twamley et al., 2004).

Neurocognitive Functioning of Older Adults with PTSD. While there is a better understanding of how PTSD affects cognition in younger adults, the research on PTSD in older adults is limited (Cook & O'Donnell, 2005). Considering the anticipated behavioural, physical, hormonal, cognitive, and cerebral changes associated with aging, it is crucial to contextualize the cognitive alterations associated with PTSD in older adults (Lapp et al., 2011). There are noticeable similarities in symptoms between late-life cognitive disorders and PTSD, such as hypervigilance, anxiety, and difficulties with concentration. Older adults tend to exhibit greater variability in cognitive test performance compared to younger adults (Christensen, 2001), making it challenging to distinguish between normal cognitive aging and PTSD without age-corrected norms or statistical adjustments for age (Hannay & Lezak, 2004). Early research has suggested that PTSD, along with its associated cognitive profile and biological features, is not static over the lifespan (Lapp et al., 2011). A meta-analysis conducted by Schuitevoerder et al. (2013) aimed to investigate the cognitive performance of older adults with PTSD. The results revealed that compared to their counterparts without PTSD, older adults with PTSD exhibited worse performance in various cognitive areas, including processing speed, attention, working memory, learning, language, visuospatial abilities, and executive functioning, with the largest effect size found in the domain of learning (Schuitevoerder et al., 2013). Due to the scarcity of studies in this area, there was a limited number of distinct samples used, which contributed to the overlap in participants included across multiple studies. In addition, most studies included in the meta-analysis have a cross-sectional design, thereby restricting the ability to draw conclusions about how the trajectory of PTSD and the fluctuation of symptoms affect cognitive functioning (Schuitevoerder et al., 2013).

Neurocognition of Veterans with PTSD. The military environment inherently influences various factors associated with cognitive aging (Brown et al., 2014). Military service and training are linked to both protective factors, such as higher education, stimulating work environments, physical and mental activity, access to healthcare, and social camaraderie, as well as potential detrimental effects on cognition due to service-related accidents, operational stress injuries, substance use, and exposure to hazardous conditions (Padula et al., 2016; VanTil et al., 2018; Yaffe et al., 2014). Moreover, recruits are often selected from underprivileged backgrounds, and early-life disadvantages may have enduring consequences for cognitive outcomes (Forbes et al., 2019).

Multiple investigations have examined the cognitive abilities of veterans in comparison to non-veterans. Wilmoth et al. (2011) examined subjective memory measurements and found that male veterans had lower odds of memory-related disability compared to non-veterans based on cross-sectional data. Building upon these findings, Brown et al. (2014) investigated the cognitive trajectory of men using longitudinal data and discovered that veterans initially outperformed non-veterans on a cognitive test at an average age of 75. However, as veterans aged, their cognitive scores declined more rapidly than those of non-veterans. Similarly, Padula et al. (2016) examined the longitudinal cognitive trajectories of women veterans and found comparable baseline cognitive scores between veterans and non-veterans, but veterans exhibited greater cognitive decline over time. However, no studies to date have directly compared the cognitive profiles of veterans with PTSD to those of non-veterans with PTSD. Longitudinal studies are needed to better comprehend the long-term effects of PTSD on cognition as veterans age.

Longitudinal Studies

Despite the strong association between PTSD and lower cognitive function observed in cross-sectional studies, there is a paucity of longitudinal studies examining the trajectory of cognitive change as individuals age. Within the limited body of research, conflicting findings have surfaced regarding the rate of decline in neuropsychological measures and the specific cognitive domains that are affected among the aging population with PTSD (Roberts et al., 2022; Samuelson et al., 2009; Schuitevoerder et al., 2013; Vasterling et al., 2018; Yehuda et al., 2006). One such longitudinal study observed a discrepancy in memory performance between two tests of verbal memory, the California Verbal Learning Test (CVLT) and the paired-associated learning test, following an improvement in PTSD symptoms (Yehuda et al., 2006). The study found that in the PTSD group, performance on the CVLT showed improvement over time and was positively correlated with symptom improvement, indicating that group differences were no longer discernible during the follow-up period. However, despite this improvement, the PTSD group still displayed a decline in paired-associated learning, which did not exhibit any correlation with the severity of symptoms.

Conversely, a study conducted by Samuelson et al. (2009) investigated the longitudinal changes in memory functioning among Vietnam veterans over two-time points. Their findings showed that in comparison to veterans without PTSD, those with PTSD exhibited a great decline in delayed facial recognition (i.e., visual memory), although this decline was extremely subtle. In addition, both groups did not differ regarding rates of decline in domains of verbal memory and working memory, as previously suggested by Yehuda et al. (2006).

A study conducted by Vasterling et al. (2018) revealed that the increasing severity of PTSD was linked to impaired verbal recall, visual recall, visual reproduction, and reaction time.

These effects were observed both before and after Iraq War deployment, as well as during an average follow-up period of 7.6 years. Furthermore, the study also identified a clear association between TBI and adverse outcomes in PTSD symptoms, which persisted throughout the post-deployment phase and long-term follow-up. Similarly, a recent study investigated the association between PTSD and accelerated cognitive decline in 12,270 middle-aged women (Roberts et al., 2022), and found that an increased number of PTSD symptoms was linked to a more pronounced decline in cognitive function over time. When compared to women who did not experience any PTSD symptoms, women with the highest level of symptoms demonstrated a greater decline in learning, working memory, psychomotor speed and attention, after adjusting for demographic characteristics. The largest cognitive differences were observed in the domain of learning and memory (Roberts et al., 2022). These findings suggest a possible differentiation between cognitive functions associated with aging and trauma exposure versus those related to the severity of PTSD symptoms. In future studies, it would be valuable to explore the relationship between PTSD and cognitive decline over an extended duration, particularly through longitudinal research that includes comparison groups. Such studies would help control for cohort effects and account for the common fluctuating symptom course observed in individuals with PTSD (Roberts et al., 2022; Schuitevoerder et al., 2013).

The evidence suggesting that older adults with PTSD experience greater decline in certain cognitive domains compared to those without PTSD has led researchers to propose an interaction between PTSD and aging, potentially resulting in accelerated age-related cognitive decline (Lapp et al., 2011; Yehuda et al., 2006). Over the past decade, numerous studies have explored the relationship between PTSD and the development of dementia (Desmarais et al., 2020; Qureshi et al., 2010; Yaffe et al., 2010). A recent meta-analysis has revealed that

individuals diagnosed with PTSD have a 1.61-1.99 times higher risk of developing dementia compared to those without a PTSD diagnosis (Günak et al., 2020).

Conceptualization of neurocognitive disfunction in PTSD

Understanding the impact of PTSD on neurocognition is enhanced by exploring neurobiological processes, which predominantly categorize PTSD as a fear-based disorder. The processes of fear learning and memory are facilitated by a brain network that revolves around the prefrontal cortex (PFC), hippocampus, and amygdala (Harnett et al., 2020). Extensive research on the neurobiology of PTSD has employed various techniques such as functional magnetic resonance imaging (fMRI), structural magnetic resonance imaging (MIR), and positron emission tomography (PET), and has found that individuals with PTSD tend to exhibit hyperactivation in limbic regions, particularly the amygdala, and insula, while showing hypoactivation in certain prefrontal regions (i.e., anterior cingulate cortex, encompassing both its rostral and dorsal portions, as well as the ventromedial prefrontal contex) (Aupperle et al., 2012.; Francati et al., 2007; Liberzon & Sripada, 2007; Shin & Liberzon, 2009).

In recent years, significant efforts have been made to consolidate diverse research findings on PTSD into a unified biological model of PTSD. It has been proposed that individuals with PTSD experience heightened activation of the amygdala (i.e., responsible for processing emotions, particularly in relation to fear) in response to highly arousing threatening stimuli. This leads to increased output of neurotransmitters (dopamine, noradrenaline, and serotonin) to the prefrontal cortex, which provides inadequate "top-down" regulation of amygdala activity and amplifies fear learning (Harnett et al., 2020; Kunimatsu et al., 2019; Pitman et al., 2012). Research incorporating cognitive functioning models suggests that when the prefrontal cortex is offline, working memory is disrupted, impacting downstream neurocognitive processes reliant on

the prefrontal cortex's integrity, such as memory encoding and retrieval. Multiple studies have hypothesized that individuals with PTSD may allocate excessive neurobiological resources to affective processing and associated regulation networks (amygdala and medial prefrontal cortex) while insufficiently allocating resources to cognitive control networks (dorsolateral prefrontal cortex; Aupperle et al., 2012; Jacob et al., 2019; Scott et al., 2015). This imbalance may lead to compromised neurocognitive integrity, specifically affecting information processing speed and executive functioning (Aupperle et al., 2012; Jacob et al., 2019; Scott et al., 2015).

Complexities of Cognitive Performance in PTSD

Investigating the neurocognitive alterations related to PTSD in humans is a complex endeavour due to the intricate interplay between the characteristics of traumatic experiences, psychosocial factors and the complex interaction between the human brain, emotions, and neurocognitive processes (Jacob et al., 2019). Numerous factors need to be taken into account when conducting research on the cognitive performance of individuals with PTSD. First and foremost, it has become apparent to researchers that there is a bidirectional link between PTSD and neurocognitive functioning (Jacob et al., 2019; Vasterling & Brailey, 2005). Evidence suggests that lower neurocognitive function prior to trauma, particularly in attention, executive function, and memory, can act as a risk factor for PTSD development. However, other studies have confirmed that premorbid I.Q. alone does not appear to entirely explain posttraumatic neurocognitive impairments (Aupperle et al., 2012). Differences in the nature, frequency, length, and intensity of traumatic experiences, as well as the age at which they occurred, and the severity of PTSD, can influence performance on neuropsychological measures. Additionally, certain elements related to the trauma, like malnutrition during the Holocaust, can have an impact on both psychological and physical well-being, further increasing the impact on cognition

(Schuitevoerder et al., 2013; Yehuda et al., 2006). The presence of additional psychiatric disorders, substance abuse issues, and neurological conditions, such as TBI, has been shown to introduce variability in neurocognitive findings (Danckwerts & Leathem, 2003; Horner & Hamner, 2002; Isaac et al., 2006). It is noteworthy that a large proportion of studies investigating neurocognitive functioning in PTSD have focused on combat veterans, who exhibit a higher incidence of head injuries. Many military personnel who have experienced a TBI exhibit cognitive symptoms, including challenges in executive functioning and disinhibition, reduced processing speed, as well as compromised attention and concentration (Dolan et al., 2012; Rice et al., 2020).

Numerous studies have highlighted that cognitive impairments observed in individuals with PTSD can be significantly impacted by the presence of psychiatric comorbidities (Barrett et al., 1996; Gil et al., 1990). PTSD commonly coexists with various disorders, most notably major depressive disorder (MDD), as well as alcohol and substance abuse (Creamer et al., 2001; Perkonigg et al., 2000). Major depressive disorder is linked to mild impairments in cognitive domains that are also impacted in individuals with PTSD (Lee et al., 2012; Snyder, 2013). The presence of high levels of alcohol and substance use among individuals with PTSD can have an impact on cognitive outcomes. Extensive research suggests that chronic alcohol and substance use can have adverse effects on memory, attention, processing speed, visuospatial abilities, set-shifting, and abstraction and conceptualization, even after months or years of abstinence (Hanson et al., 2011; Le Berre et al., 2017). The factors mentioned above, while not consistently addressed in research, can present challenges to cognitive assessment in individuals with PTSD. These factors have the potential to blur the cognitive interpretation of the impact of PTSD and, therefore, should be meticulously taken into account.

Cognitive Reserve

Some studies have hypothesized that cognitive reserve may account for diverse cognitive trajectories in older adults with PTSD (Brown et al., 2014). The burgeoning interest in the cognitive reserve model arises from its intriguing proposition that the brain's networks possess remarkable flexibility and adaptability, enabling the brain to preserve cognitive function, notwithstanding the presence of damage or disease. Studies have revealed that certain individuals with augmented cognitive reserve further facilitate the development of alternative neural networks, delaying the onset of functional impairments typically linked to dementia neuropathology (Nelson et al., 2021; Stern, 2012). The assessment of cognitive reserve conventionally relies on proxies that aim to rely on lifestyle factors or experiences purported to impact this reserve (Stern et al., 2019). These proxies encompass various variables, such as educational attainment, social support, and engagement in cognitively demanding activities. Although these proxy measures serve to moderate the relationship between brain changes and functional impairments, they do not directly measure cognitive reserve, nor do they elucidate the underlying neural mechanisms that contribute to cognitive reserve (Stern et al., 2019). Nonetheless, a substantial body of evidence has consistently demonstrated that individuals exhibiting elevated levels of cognitive reserve proxies experience less severe functional impairments even in the presence of more advanced Alzheimer's type pathology, as opposed to those with lower levels of cognitive reserve proxies (Bennett et al., 2003; Ewers et al., 2013; Stern et al., 1999).

Education, physical exercise, and cognitively stimulating activities have received the strongest support through the literature as factors that reduce the risk of dementia. Roe et al. (2007) conducted a large study involving 2400 participants over the age of 65 and found that an

additional year of education was associated with a 13-18% reduction in the likelihood of receiving a diagnosis of dementia with the neuropathology of Alzheimer's disease (AD). This finding signifies that participants had the pathological condition indicative of AD, although their symptoms did not cross the clinical threshold (i.e., no cognitive impairment). Similarly, research has suggested that aerobic exercise reduces the risk of being diagnosed with dementia (Hamer & Chida, 2009; Kishimoto et al., 2016; Llamas-Velasco et al., 2015; Luck et al., 2014). However, the role of cognitive activity as a cognitive reserve factor is less clear. Some data suggest that physical activity is essential and cognitive activity adds further benefits (Hughes et al., 2015).

Social connectedness is also posited as a cognitive reserve factor; however, the evidence for this factor is less clear, and there are conflicting findings (Evans et al., 2019; Fratiglioni et al., 2004; Kuiper et al., 2016). One hypothesis that could account for this discrepancy is that social connectedness is broad and can encompass different components, including structural aspects (e.g., social network, living situation) and functional aspects (e.g., the individual's perception or experience of the social interaction as being helpful) (Evans et al., 2019). Social cognition theories have supported the idea that functional aspects of social support accentuate interaction with others, which is mentally stimulating because it demands mental flexibility to accept individual differences and acknowledge the perspectives of others through empathy and compassion in order to form reciprocal bonds (Windsor et al., 2020).

Most of the research surrounding cognitive reserve has focused on cognitive decline and dementia; however, this mechanism has been shown to be effective in the prevention or amelioration of cognitive impairment due to other conditions (e.g., multiple sclerosis, Parkinson's, HIV, and traumatic brain injuries; Stern & Barulli, 2019).To our knowledge, only one study has examined the impact of cognitive reserve in individuals who have PTSD. A study

conducted by Seil and colleagues (2019) examined whether self-reported confusion or memory loss was impacted by differing levels of cognitive reserve in those with and without PTSD following the terrorist attacks of September 11th, 2001 (Seil et al., 2019). The researchers subdivided the PTSD and control groups into four subgroups according to the level of cognitive reserve indicators they possessed (high, medium-high, medium-low, and low). The cognitive reserve factors included education, marital status, employment, social support, social integration, and physical activity. Overall, confusion/memory loss was higher in participants with PTSD (17%) than in participants who did not have PTSD (6%). For both groups (PTSD+ and PTSD-), they found that participants categorized in the group with high cognitive reserve were less likely to report confusion or memory loss; however, the association was weaker in the group with PTSD. These indicators were grouped together with education, employment, and physical activity in order to examine the impact of the global cognitive reserve. Furthermore, subjective self-report questionnaires were used to measure the impacts of these indicators rather than objective neuropsychological tests. Therefore, it is difficult to decipher the true impact of cognitive reserve factors along with the magnitude of their effects on participants with PTSD.

Recent research suggests that individuals diagnosed with PTSD manifest a heightened proclivity for the development of dementia relative to their counterparts without PTSD (Günak et al., 2020). Given the current dearth of disease-modifying interventions and medications, recognizing and mitigating alterable factors that contribute to dementia holds significant importance within the realm of public health initiatives (Anderson, 2019). There is a need for more studies investigating cognitive reserve in individuals with PTSD to determine if they could slow the decline of cognitive deficits.

Clinical implications

Spanning across varying age categories encompassing both younger and older adults, cognitive deficits are among one of the most important indicators for prolonged disability (Green et al., 2000; Heaton & Pendleton, 1981; Schuitevoerder et al., 2013; Twamley et al., 2002). In addition, a decrease in cognitive function has been linked to an elevated likelihood of being hospitalized, a heightened sedentary lifestyle, earlier onset of frailty, and earlier mortality (Chodosh et al., 2004; Maasakkers et al., 2021; Rajan et al., 2014; Roberts et al., 2022; Robertson et al., 2013; Yaffe et al., 2016). The neurocognitive alteration associated with PTSD has elicited substantial scholarly interest, owing to their ramifications for day-to-day functioning, their capacity to contribute to the advancement of neurobiological frameworks underpinning our comprehension of PTSD, and their potential to indirectly influence the course of the disease via their impact on coping mechanisms and treatment response (Jacob et al., 2019; Kalechstein et al., 2003; Machamer et al., 2005; Papero et al., 1992). Drawing upon an extensive body of research spanning numerous years, Jacob, Dodge and Vasterling (2019) have proposed the existence of a feedback loop between PTSD and neurocognitive integrity. For some individuals, the cycle begins with trauma exposure or shortly thereafter. Certain neurocognitive abilities act as safeguards, aiding in trauma processing, controlled retrieval of traumatic memories, and emotional response regulation to trauma cues. However, for those developing PTSD symptoms, the disorder might erode neurocognitive integrity, escalating symptom persistence or exacerbation by impeding cognitive control mechanisms and recovery (Jacob et al., 2019). Conversely, the treatment literature has provided evidence for the improvement of neurocognitive performance concurrent with the amelioration of PTSD symptoms (Fani et al., 2009; Jacob et al., 2019; Vermetten et al., 2003; Walter et al., 2010; Yehuda et al., 2006). This

observation holds the promise of interrupting the feedback loop, thus contributing to the recovery from PTSD symptoms facilitated by the reengagement of cognitive coping mechanisms (Jacob et al., 2019).

The Current Research

While a significant body of research has delved into the cognitive abilities of younger adults with PTSD, the same cannot be said for middle-aged and older adults. These age groups, distinct from their younger counterparts, manifest an elevated susceptibility to persistent physical afflictions, a gradual wane in social connections, and pivotal life transitions – each of which could independently exert its influence on cognition. Consequently, the adoption of a developmental perspective becomes imperative when investigating the cognitive ramifications of PTSD. More longitudinal studies are needed to assess whether cognitive changes associated with PTSD are exacerbated with age and lead to further decline. In addition, there exists very limited research exploring cognitive reserve factors that could aid in mitigating cognitive change associated with PTSD as individuals age. The focus of this research is thus to begin to quantify the magnitude of cognitive change associated with PTSD in diverse samples (within the CLSA) of middle-aged and older adults, including veterans, and explore if any lifestyle elements can act as cognitive reserve factors by mitigating cognitive decline.

Study 1: Social Support, Neurocognition, and Posttraumatic Stress Disorder: Findings from the Canadian Longitudinal Study on Aging

Utilizing baseline data from the Canadian Longitudinal Study on Aging, Study 1 sought to evaluate the neuropsychological performance in a large sample of middle to older-aged adults with symptoms of PTSD. Specifically, the study investigated the prevalence of impairment, defined as performance scores falling 1.5 or more standard deviations below the population

mean. This aspect has been notably underexplored in existing literature (Schinka et al., 2010; Schuitevoerder et al., 2013; Strauss et al., 2006). Multiple research studies have underscored the pivotal significance of social support in reducing the risk of PTSD development (Brewin et al., 2000; Ozer et al., 2003). Consequently, there is a growing interest in investigating factors that can improve or mitigate deficits, because better neurocognitive functioning has been shown to be associated with lower PTSD severity and improved functioning (Jacob et al., 2019). As a second objective, Study 1 aimed to bridge a gap in PTSD research by examining the impact of social support as a cognitive reserve factor in participants with PTSD using objective neuropsychological tests.

Study 2: Cognitive Change and Cognitive Reserve in Posttraumatic Stress Disorder: Findings From the Canadian Longitudinal Study on Aging

Drawing upon data from the first follow-up wave from the Canadian Longitudinal Study on Aging, Study 2 aimed to quantitatively assess longitudinal neuropsychological performance in middle to older-aged adults exhibiting symptoms of PTSD. Given the rising population of older adults in Canada (Statistics Canada, 2016), the issue of cognitive impairment among older adults has gained heightened prominence in public health discourse. When assessing cognitive functioning in older adults, it becomes imperative to account for the complex interplay between various health conditions, each potentially linked to cognitive decline and the natural aging process itself. The intricate relationship between PTSD and the unfolding course of cognitive deterioration with advancing age remains a poorly understood aspect of PTSD literature. Therefore, building upon study 1, a second research objective was to determine if additional lifestyle factors such as cognitive stimulation, education, physical activity, and social

participation could also act as cognitive reserve factors by mitigating cognitive decline in those who experience symptoms of PTSD.

Study 3: Cognitive Changes in Veterans and Civilians with Posttraumatic Stress Disorder: Findings from the Canadian Longitudinal Study on Aging.

As Canada's aging demographic continues to expand, a parallel trend is observed in the population of veterans. In accordance with a study conducted in 2017, projections suggest that by 2026, approximately 33% of the veteran cohort will have surpassed the age of 70 (VanTil et al., 2018). Past research has demonstrated that Canadian veterans exhibit distinct health and well-being attributes in comparison to the broader population (VanTil et al., 2018). Notably, mental health conditions, particularly PTSD, present with heightened prevalence, increased severity, and clinical diversity within the veteran community (Gauvin et al., 2022; Gaylord et al., 2009; Lehavot et al., 2018; O'Toole & Catts, 2017). To date, findings have yielded varied outcomes regarding the impact of trauma type on the extent of the effect size pertaining to cognitive performance in individuals experiencing symptoms of PTSD (Schuitevoerder et al., 2013; Scott et al., 2007). Study 3 aimed to integrate the research objective of the preceding two studies, this time focusing on discerning the differences in neuropsychological functioning between veterans and non-veterans with symptoms of PTSD.

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Study 1: Social support, neurocognition, and posttraumatic stress disorder: Findings from the Canadian Longitudinal Study on Aging[1]

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Abstract

Objective: Most research investigating neurocognitive changes in participants with PTSD has focused on young adults. Numerous studies have recognized the crucial role of social support in diminishing the likelihood of developing PTSD. The current study evaluates the cognitive performance of middle-aged and older adults with symptoms of PTSD, and examines if perceived social support can act as a cognitive reserve factor. ***Method:*** The study was conducted using data from the Canadian Longitudinal Study on Aging, a nationwide study on health and aging. The current study included 1,096 participants in the PTSD group and 22,158 participants in the comparison group, all between the ages of 45 and 85. Participants completed the MOS (Medical Outcomes Study) Social Support Survey as well as neuropsychological tests in the domains of executive functioning, declarative memory, and prospective memory. ***Results:*** The PTSD group had worse performance in the domains of executive functioning and prospective memory than the comparison group. Furthermore, when examining global cognitive impairments (impairment was defined as scoring 1.5 or more standard deviations below age and education adjusted comparison group), the PTSD group demonstrated greater impairment rates than the comparison group on two or more tests. Moderation analyses revealed that greater social support was associated with better executive functioning for the comparison group, although this was not found to be true for the PTSD group. ***Conclusion:*** The PTSD group experienced greater cognitive deficits compared to the comparison group. Higher levels of perceived social support were associated with better performance on neurocognitive measures for the comparison group. However, social support did not appear to moderate this relationship for the PTSD group.

Keywords: posttraumatic stress disorder; neurocognition; social support; cognitive reserve; CLSA

Introduction

Posttraumatic stress disorder (PTSD) is classified as a trauma-and-stress-related disorder (American Psychiatric Association, 2013) with an estimated lifetime prevalence of 6–7% (Alegría et al., 2013; Goldstein et al., 2016). PTSD is often discussed in terms of emotional dysfunction encompassing four main symptom clusters: intrusion, avoidance, negative cognition/mood, and arousal (American Psychiatric Association, 2013). However, over the last two decades, numerous studies have highlighted the role that cognitive functioning plays in the development, maintenance, and exacerbation of PTSD symptoms (Jak et al., 2016). Furthermore, cognition has significant implications on the quality of life of individuals with PTSD, as it is predictive of obtaining and maintaining employment, job advancements, maintaining relationships, wealth, and health (Diamond & Ling, 2016). A better understanding of the neuropsychological profile of individuals with PTSD may help target interventions to improve the long-term outcomes of individuals with this disorder.

Neurocognitive Functioning in PTSD

Numerous studies have demonstrated cognitive, structural, and functional alterations associated with PTSD (Bremner et al., 2008; Brown & Morey, 2012; Patel et al., 2012). With respect to neurocognition, a large body of research has provided robust evidence of deficits across multiple cognitive domains in participants with PTSD, including attention, working memory, episodic memory, processing speed, executive function, learning, and memory (Aupperle et al., 2012; Brewin et al., 2007; Jak et al., 2016; Johnsen & Asbjørnsen, 2008; Scott et al., 2015). A recent meta-analysis of 60 studies examined multiple cognitive domains across four types of index traumas (military trauma, interpersonal trauma, state persecution/terror, and mixed/unknown trauma) and found that PTSD was associated with lower performance across all

domains (Scott et al., 2015). Effect sizes were small to medium (Cohen's $d = -0.29$ to -0.62). The largest effect sizes were in the domains of verbal learning ($d = -.62$), speed of information processing ($d = -.59$), and attention/working memory ($d = -.50$). No significant differences were found between the four trauma types in the magnitude of effect sizes.

It is important to note that there appears to be a bidirectional link between PTSD and neurocognitive functioning (Jacob et al., 2019). Research has shown that lower pre-traumatic neurocognitive function, especially in the areas of attention, executive function and memory, may serve as a risk factor for the development of PTSD. However, there are also indications that pre- traumatic neurocognitive function does not fully account for posttraumatic neurocognitive deficits (Aupperle et al., 2012).

Less research has investigated cognitive functioning in older adults than in younger adults with PTSD (Cook et al., 2017). Nonetheless, in a meta-analysis conducted by Schuitevoerder et al. (2013) including 11 studies, older adults with PTSD exhibited worse performance than trauma-exposed older adults without PTSD in all cognitive domains tested, which included global cognitive functioning, premorbid intelligence, processing speed, attention and working memory, learning, language, visuospatial abilities, executive functioning, and fine motor skills. Researchers have found that deficits in cognitive domains associated with PTSD closely resemble normal cognitive decline in aging (Schuitevoerder et al., 2013). Therefore, parsing which cognitive deficits are associated with the development of PTSD rather than normal cognitive aging has proven to be difficult (Cook et al., 2017). Furthermore, there is interest in investigating factors that improve or mitigate the decline, as studies have shown that better neurocognitive function is associated with lower PTSD severity and improved functioning (Jak et al., 2016).

Cognitive Reserve, Social Support and PTSD

When comparing individuals with a similar degree of brain pathology (e.g., atrophy), some individuals will experience a greater clinical manifestation of symptoms (e.g., cognitive or functional deficits) than others (Stern, 2009). Cognitive reserve theory proposes that people with greater cognitive reserve are better able to preserve cognitive performance by recruiting differential brain networks or using alternative cognitive strategies when confronted with pathology or increased demand (Stern, 2002). Protective lifestyle factors, including physical exercise, education, occupational intricacy, social support and cognitively demanding activities have been recognized as cognitive reserve factors (Opdebeeck et al., 2016; Stern, 2009).

Numerous studies have recognized the crucial role of social support as a risk-resilience factor associated with PTSD. Social support is among one of the most important protective factors against the development of PTSD and its absence has been shown to be a factor that increases risk (Brewin et al., 2000; Ozer et al., 2003). Yet, little research exists exploring the impact of social support on cognition in participants with PTSD. To our knowledge, only one study has examined the impact of social support on cognition in participants with PTSD. Seil et al. (2019) examined whether self-reported confusion or memory loss was impacted by differing levels or cognitive reserve in those with and without PTSD following the terrorist attacks of September 11th, 2001. The researchers subdivided the PTSD and control groups into four subgroups according to their level of cognitive reserve indicators (high, medium-high, medium-low, low). The cognitive reserve factors included: education, marital status, employment, social support, social integration, and physical activity. Overall, confusion/memory loss was higher in participants with PTSD (17%) than in participants who did not have PTSD (6%). For both groups (PTSD+ and PTSD-), participants categorized as having high cognitive reserve were less

likely to report confusion or memory loss; however, the association was weaker in the group with PTSD. The study included three indicators of cognitive reserve that could be classified under social support/connectivity (marital status, social support, and social integration). These indicators were grouped together with education, employment, and physical activity in order to examine the impact of global cognitive reserve. Furthermore, subjective self-report questionnaires were used to measure the impacts of these indicators rather than objective neuropsychological tests. Therefore, it is difficult to decipher the true impact of social support as a cognitive reserve factors along with the magnitude of its effects on participants with PTSD.

The aim of the current study is to evaluate neuropsychological performance in a large sample of middle-aged and older adults with symptoms of PTSD. Furthermore, we will compare impairment rates on neuropsychological measures between the PTSD and comparison groups. Finally, we will assess if perceived social support is associated with better performance in each group.

Method

Data Source and Procedures

The data are taken from the Comprehensive Cohort of the Canadian Longitudinal Study on Aging (CLSA). The present study used the baseline data, including demographic, clinical, and cognitive data collected through 90-minute home interviews and/or assessments that were conducted at one of the 11 data collection sites across Canada. For more detailed information on procedure and sampling in the CLSA, please refer to Raina et al. (2019). Ethics approval was obtained for the CLSA protocol by the Canadian Institutes of Health Research (CIHR) and approval was acquired from each individual research site prior to data collection. Furthermore,

the current study was also approved by the Bruyère Research Institute and the University of Ottawa ethics boards.

Participants

The baseline Comprehensive Cohort was comprised of a stratified random sample of approximately 30,000 Canadians between the ages of 45 and 85 who were fluent in English and/or French. Participants were excluded from the current study if they were diagnosed with a neurological disorder (e.g., Alzheimer's, Parkinson's, multiple sclerosis). Participants were divided into two groups based on their score on the Primary Care PTSD Screen (PC-PTSD). Participants who earned a score of three or higher on the PC-PTSD were categorized in the PTSD group, whereas participants who earned a score of two or lower on the PC-PTSD were categorized in the comparison group. Previous research has supported that using a study-specific comparison group as the reference group produces better normative criteria than using published normative references group (Clapp et al., 2018). The CLSA sample sizes are larger than any previous study utilizing the neuropsychological tests described below (Bleecker et al., 1988; Kempler et al., 1998; Morrow, 2013). For a detailed comparison of published norms and CLSA norms on neuropsychological tests please consult Tuokko et al. (2017).

Measures

Demographic Data and Lifestyle Factors

Demographic information pertaining to age, education, sex, alcohol consumption, sleep time, and depression were obtained through in-person structured interviews. Alcohol frequency was assessed by asking participants how frequently they drank alcohol in the past 12 months. Their answers varied from never to almost every day. Sleep time was measured by asking participants how many hours of actual sleep they got a night, on average, during the past month. Depression

was assessed using the Center for Epidemiologic Studies Short Depression Scale (CES-D10). The scores range from 0 to 30 (α = 0.79), with a score higher than 10 indicating depression (Andresen et al., 1994).

Posttraumatic Stress Disorder

PTSD symptoms were evaluated with the PC-PTSD (Prins et al., 2003). The PC-PTSD is a quick self-report screening tool for PTSD that comprises four questions focusing on the detection of the main symptom clusters: reexperiencing, numbing, avoidance, and hyperarousal. The total score ranges from 0 to 4 (α = 0.64), with a higher score indicating greater PTSD symptomatology. A score of 3 or greater is indicative of clinically significant PTSD symptomatology, with a sensitivity rate of 0.78 and a specificity rate of 0.87. It shows good test-retest reliability (r = .83) and predictive validity against the Clinician-Administered PTSD Scale (r = .83; Prins et al., 2003). Other studies have also found the PC-PTSD to have good discriminatory strength (C-statistics = .82; Ouimette et al., 2008).

Social Support

Social Support was assessed with the Medical Outcomes Study (MOS) Social Support Survey (Sherbourne & Stewart, 1991). The scale comprises 19 items that are answered on a five-point Likert scale, with items summed within each of four social support subscales: (1) emotional/information support (α = 0.93; i.e., empathetic understanding, support of expression of feelings, and expression of positive affection, advice, guidance, and information) (2) tangible support (α = 0.87; i.e., cognitive or physical assistance) (3) positive social interaction (α = 0.88; i.e., availability to join in leisurely activities) (4) affectionate support (α = 0.86; i.e., expression of love and affection). A higher score is indicative of greater social support. The scale has previously demonstrated excellent internal consistency with overall and subscale Cronbach

alphas ranging from 0.91 to 0.97, test-retest reliability (ICC = 0.78 after one year) and good convergent validity (ranging from 0.72–0.87; Sherbourne & Stewart, 1991).

Neurocognitive Measures

Executive Functioning. The Controlled Oral Word Association Test (COWAT; Spreen & Benton, 1977) is a measure of verbal fluency that uses the three letters *F, A*,and *S*. Participants are asked to name as many words as they can beginning with each of the given letters in a time frame of 1 minute, receiving 1 point for every word. A separate trial is done for each letter, and the 3 trials are compiled to form a global score. The Animal Fluency Test (AFT; Rosen, 1980) is a measure of verbal fluency in which participants are instructed to list as many animals as they can in a time frame of 1 minute, receiving 1 point for every word. For both tests of verbal fluency, a higher score was indicative of better performance.

The Victoria Stroop Test (Stroop; Regard, 1981), is a test that measures inhibition, mental speed, and mental control. The test comprises three trials: 1) participants read a list of words printed in different ink colors (Word trial), 2) participants are asked to name the ink color of the dots (Dot Trial), 3) participants name the color of the ink in which the color of the words are printed and not the color that is written (Color-Word Trial). Scoring is based on the time it takes to complete the 100 items in each trial. From these data, an interference score was calculated and consisted of dividing the time on the Color- Word Trial by the time of the Dot Trial, to account for the influence of cognitive slowing (Strauss et al., 2006). A shorter interference time is indicative of better performance. Errors were not analyzed in the present study.

The Mental Alternation Test (MAT; Teng, 1994) is a set-shifting task. Participants are asked to count aloud, alternating between numbers and letters in ascending order (i.e., 1-A, 2-B, 3-C, etc.) as quickly as possible in a time frame of 30 seconds. The total score is deter

mined by the number of correct alternations consisting of each correct number-letter sequence. The score can range from 0–52, with higher scores indicating better executive functioning.

Prospective Memory. The Miami Prospective Memory Test (MPMT; Hernandez Cardenache et al., 2014), is a task that evaluates prospective memory functioning. The MPMT consists of 2 trials where the participants are asked to select a $5 bill from several other denomi nations and hand it to the examiner, and take a $10 bill and keep it. In the first trial, an event-based trial, the participant is instructed to conduct the task with the bills after hearing a timer ring after 15 minutes. In the second trial, a time-based trial, a clock is placed on the wall behind the examiner in the participant's view, and it is set to 08:00. The participants are instructed to conduct the task with the bills at 08:15. The MPMT trials are score from 0–3 according to the intention to perform the task, if they performed it correctly, and if they needed a reminder. Reminders are provided after 4 minutes without response during the time-based trials or during the event-based trial if the participant has not initiated a response within 60 seconds of the timer. A higher score is indicative of better performance.

Declarative Memory. The Rey Auditory Verbal Learning Test (RAVLT; Rey, 1964) is a two-part test, including an immediate recall score and a delayed recall score, designed to assess verbal learning and retention. Fifteen nouns are read to the participants (one word per second), after which participants asked to recall as many of the words as they can, in any order (immediate recall). In the CLSA administration, participants are asked again after 5 minutes to recall as many of the words as they can (delayed recall). The number of correctly recalled words constitutes the score, for a maximum of 15 points for each trial. A higher score is indicative of better performance. The RAVLT can also be used as an embedded performance validity test, which is designed to assess credibility of test performance and recognize potential response bias,

low effort, or malingering (Pliskin et al., 2021). A raw cutoff of ≤ 4 for the immediate trial may indicate non-credible performance (Binder et al., 2003; Suhr & Gunstad, 2000), and for the delayed trial, a raw score of ≤ 2 may be used (Boone et al., 2005). These raw score cutoffs allow for specificity of ≥ 90% in the standard RAVLT administration.

Statistical Analyses

Statistical analyses were performed using SPSS version 26 (Armonk, NY, USA: IBM Corp.). All continuous variables were normally distributed as checked with Q-Q plots and skew statistics, except for the Stroop time, which were positively skewed. They were normalized with the use of logarithmic transformation. An F-Test confirmed that there was no unequal variance between both groups (i.e., comparison group and PTSD group).

Group differences on continuous demographic and clinical data were analyzed with univariate analysis of variance (ANOVA). Categorical data were analyzed with chi-square tests, and ordinal data were examined with Mann-Whitney U. A multivariate analysis of covariances (MANCOVA) was conducted to identify group differences on each neuropsychological test, while controlling for age, education, sex, depression levels, sleep time, alcohol frequency, and testing language.

Additionally, bivariate correlations analyses were performed between the neuropsychological test scores and social support variables, separately for the PTSD group and the comparison group. This analysis was done to examine the degree of association between each neuropsychological test score and social support.

Moderation analyses were used to examined whether the association between PTSD group membership (independent variable) and cognitive functioning (dependent variable) would differ as a function of perceived social support (moderator variable). The same covariates used in

the MANCOVA were entered in the moderation analyses (age, education, sex, depression levels, sleep time, alcohol frequency, and testing language). Moderation analyses were performed using Model 1 of Hayes's PROCESS macro (v. 3.1; Hayes, 2017) for SPSS (IBM, v. 22). Bootstrap resampling (5,000 samples) was used to estimate 95% confidence intervals. This analysis was done for each raw neuropsychological test score.

Neuropsychological impairment was determined by calculating z-scores using the mean and standard deviation of the comparison group's data. Using standard conventions (Schinka et al., 2010; Strauss et al., 2006), impairment was defined as a score 1.5 or more standard deviations below age- and education-adjusted comparison group means (Bedard & Taler, 2021; Bedard et al., 2018). All of the data used in the calculation of z-scores were first adjusted by age and education. First, unstandardized predictors were acquired through linear regression, separately for each neuropsychological measure, with age and education included as covariates. These values then served as adjusted scores to obtain the control group mean and standard deviations upon which impairment was indexed. Moreover, an index of global impairment was calculated by first summing dichotomized impairment rates across tests, and was categorized as having scored impaired on two or more tests. Bonferroni corrected chi-square tests were used to assess group differences across impairment rates. Binary logistic regressions were then conducted on the dichotomized global impairment metric, by including the social support subscale variables as predictors; this was done separately for the comparison group and for the PTSD group. For all analyses, significance was established at $p < .05$ unless explicitly noted in the result section.

Results

Demographic and Clinical Characteristics

Demographic and clinical characteristics of the sample are displayed in Table 1. The present study included 1096 participants who screened positive for PTSD, and 22,158 comparison participants. Relative to the comparison group, the PTSD group had a larger proportion of females relative to males ($p < .01$, OR = 1.43, 95% CI = 1.32–1.55), were younger ($p < .01$, $d = 0.30$), reported less formal education ($p < .01$, $d = 0.11$), less sleep ($p < .01$, $d = 0.19$), greater depressive symptoms ($p < .01$, $d = 0.95$), and consumed alcohol less frequently ($p < .01$, $d = 0.10$). The PTSD group also reported perceiving less social support overall ($p < .01$, $d = 0.45$), including in the subscales of affectionate support ($d = 0.40$), positive social interaction ($d = 0.45$), emotional support ($d = 0.37$), and tangible support ($d = 0.40$), all ps $< .01$. The PTSD group did not differ from the comparison group with respect to veteran status ($p = .17$). Regarding testing language, a larger proportion of the comparison group were assessed in English (relative to French) as compared to those in the PTSD group ($p < .01$, $d = 0.16$).

Table 1
Participant Demographic and Clinical Characteristics

	Comparison Group (*n* = 22158)	PTSD+ (*n* = 1096)
Age, mean (SD)	62.2 (9.9)	59.4 (9.0)
Sex		
Female (%)	50.3	65.2
Male (%)	49.7	34.8
Education		
< High school (%)	4.6	8.4
High school (%)	9.1	9.3
Some college (%)	17.5	23.3
College diploma (%)	21.3	24.9
University degree (%)	24.6	20.2
Graduate degree (%)	22.9	14.0
Marital status		
Married (%)	71.4	55.2
Widowed (%)	7.9	9.2
Divorced (%)	9.8	17.9
Separated (%)	2.6	5.4
Single (%)	8.4	12.3
Veteran status (%)	9.1	7.8
Depression, mean (SD)	4.9 (4.3)	10.1 (6.6)
Sleep hours, mean (SD)	6.8 (1.2)	6.6 (1.5)
Alcohol Frequency		
Never (%)	10.6	13.7
< once a month (%)	11.7	17.9
About once a month (%)	6.5	8.5
2-3 times a month (%)	10.4	10.2
Once a week (%)	11.6	11.2
2-3 times a week (%)	21.9	18.5
4-5 times a week (%)	10.8	8.6
Almost everyday (%)	16.5	11.5
Social Support		
Total scale score	81.5 (12.6)	75.0 (15.7)
Tangible subscale	17.0 (3.3)	15.5 (4.1)
Affection subscale	13.5 (2.3)	12.4 (3.0)
Positive interaction	13.0 (2.2)	11.9 (2.8)
subscale	33.9 (5.9)	31.5 (7.0)
Emotional subscale		
Testing Language		
French (%)/English (%)	80.6/19.4	73.5/26.5

Note. PTSD+ = screened positively for posttraumatic stress disorder.

Group Differences on Neuropsychological Measures

Central tendency figures for the measures of cognitive functioning are presented in Table 2. Chi-square analyses investigating for possible non-credible performance did not reveal significant differences on RAVLT immediate $\chi 2$ (1) = 0.01, p = .92, or RAVLT delayed, $\chi 2$ (1) = 0.05, p = .83. Scoring beyond cutoffs on both the RAVLT immediate and delayed, more indicative of non-credible performance, did not reveal group differences between the comparison group (11.9%), and the PTSD group (13.0%), $\chi 2$ (1) = 1.13, p = .29.

The MANCOVA revealed omnibus level significant differences, F(8, 23,230) = 4,35, p < .01, ηp2 = .001. Effect size was measured using partial-eta squared (ηp2). Values of 0.01 are considered a small effect, 0.06 represents a medium effect, and 0.14 or larger indicates a large effect (Cohen, 1988). Inspection of the follow- up between-subjects univariate tests revealed that the PTSD group performed worse than the comparison group on the MAT (F(1, 23,237) = 23.11, p < .01, ηp2 = .02), MPMT (F(1, 23,237) = 6.88, p = .01, ηp2 = .01), and higher on Stroop time (F(1,23,237) = 8.85, p = .02, ηp2 = .01). No group differences emerged on the RAVLT immediate (p = .29), delayed (p = .25), COWAT (p = .20), or the AFT *(*p = .23). Results remained unchanged when additionally controlling for probable non-credible performance (two-test invalidity), or when those who exhibited probable non-credible performance were removed from analyses.

Table 2
Raw Neuropsychological Test Scores and Impairment Rates

	Comparison Group (n = 22158)			PTSD+ (n = 1096)				Effect Size
Test	*M*	*SD*	*%*	*M*	*SD*	*%*	*p-value*	η_p^2
Executive functioning								
COWAT	39.81	12.65		38.66	12.54		.20	0.00
AFT	20.04	5.63		19.58	5.48		.23	0.00
Stroop	2.14	0.71		2.20	0.78		.02	0.01
MAT	27.07	8.54		25.01	8.93		.01	0.02
Impairment rates (%)								
COWAT			8.7			10.7	.02	
AFT			8.9			10.9	.02	
Stroop			4.7			5.8	.12	
MAT			8.5			8.0	.65	
Prospective Memory								
MPMT	17.23	1.67		17.06	1.76		.01	0.01
Impairment rates (%)								
MPMT			5.9			9.2	.01	
Declarative Memory								
RAVLT immediate	5.96	1.88		5.96	1.87		.29	0.00
RAVLT delayed	4.16	2.15		4.21	2.14		.24	0.00
Impairment rates (%)								
RAVLT immediate			8.8			8.5	.64	
RAVLT delayed			9.0			8.4	.47	
Global Impairment			10.4			15.6	.01	
Non-credible RAVLT								
Immediate ≤ 4			21.6			21.7	.92	
Delayed ≤ 2			21.1			21.4	.83	

Note. PTSD+ = screened positively for posttraumatic stress disorder; COWAT = Controlled Oral Word Association Test; AFT = Animal Fluency Test; MAT = Mental Alternating Test; MPMT = Miami Prospective Memory Test ; RAVLT = Rey Auditory Verbal Learning Test. Means and standard deviations presented reflect raw unadjusted scores; p-values and partial eta squared (η_p^2) reflect values from the MANCOVA, controlling for age, education, sex, depression levels, sleep time, alcohol frequency, and testing language; p-values for impairment rates reflect values from Bonferroni corrected chi-square tests that were used to assess group differences across impairment rates.

Correlational Analyses

Bivariate relationships were run separately for the comparison group and the PTSD group. A correlation coefficient of 0.1 is considered a small association, 0.3 represents a moderate correlation, and 0.5 or larger represents a strong correlation (Cohen, 1988). As shown in Table 3, below the diagonal, the comparison group demonstrated small positive correlations between each of the neuropsychological test scores and social support (*ps* < .007), with the exception of the Stroop time, which was found to have small negative correlations with social support (*ps* < .007). However, as can be seen above the diagonal in Table 3, the PTSD group only demonstrated a small positive correlations between the RAVLT Immediate score and social support and a small negative correlation between Stroop time and social support (*ps* < .007). No other correlation was found between social support and neuropsychological test scores for the PTSD group.

Table 3

Intercorrelations for Study Variables Disaggregated by Group Membership

Variable	1	2	3	4	5	6	7	8
1. MAT	-	0.18*	0.26*	0.24*	-0.19*	0.37*	0.35*	0.08
2. MPMT	0.17*	-	0.17*	0.18*	-0.13*	0.14*	0.24*	0.06
3. RAVLT Immediate	0.25*	0.18*	-	0.71*	-0.16*	0.29*	0.35*	0.08*
4. RAVLT Delayed	0.21*	0.20*	0.70*	-	-0.19*	0.25*	0.34*	0.09
5. Stroop	-0.16*	-0.10*	-0.12*	-0.13*	-	-0.18*	-0.13*	-0.08*
6. COWAT	0.39*	0.12*	0.30*	0.25*	-0.13*	-	0.44*	0.03
7. AFT	0.35*	0.19*	0.34*	0.32*	-0.15*	0.43*	-	0.08
8. Social Support	0.10*	0.09*	0.11*	0.09*	-0.03*	0.09*	0.10*	-

Note. MAT = Mental Alternation Test; MPMT = Miami Prospective Memory Test; RAVLT = Rey Auditory Verbal Learning Test; COWAT = Controlled Oral Word Association Test; AFT = Animal Fluency Test. The results for the participants that screened positively for posttraumatic stress disorder (n= 1096) are shown above the diagonal. The results for the comparison group (n=22,158) are shown below the diagonal.

* $p < .007$, to account for multiple comparisons (Curtin & Schulz, 1998).

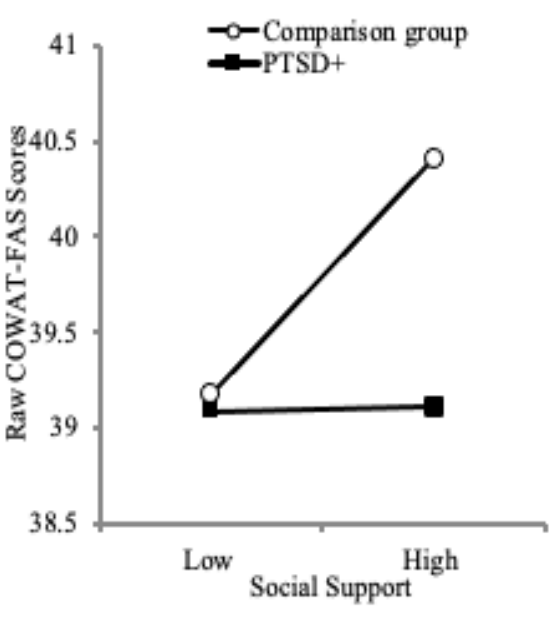
Moderation Analyses

The interaction between group and social support was found to moderate COWAT scores, $\Delta R2 = 0.12$, $b = -0.05$, $t = -2.10$, $p = .04$ (see, Figure 1(A)). Simple slope analyses indicated that although increased social support was associated with higher scores on the COWAT for the comparison group ($b = 0.05$, $p < .01$), this was not the case for participants in the PTSD group ($b = 0.00$, $p = .99$). Social support also moderated the group by Stroop time relationship, $\Delta R2 = 0.07$, $b = -0.003$, $t = -2.44$, $p = .01$ (see, Figure 1(B)). Whereas the comparison group displayed better Stroop time with more perceived social support ($b = -0.025$, $p = .04$), for participants in the PTSD group, higher social support was linked with worse Stroop time ($b = 0.001$, $p = .02$). Social support was not found to moderate the relation between group and the other neuropsychological test scores, including on the RAVLT and MPMT ($p > .05$).

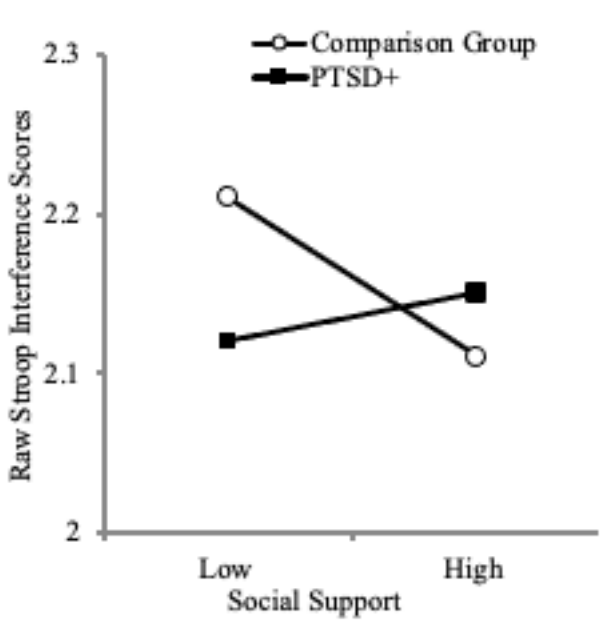
Figure 1

Social support moderating the relation between group and executive functioning

A)



B)



Note. With regards to the relation between group and social support, panel **A)** shows the relationship for the Controlled Oral Word Association Test (COWAT-FAS) and Panel **B)** displays the relationship for Stroop interference scores (high interference score is associated with worse performance). PTSD+ = screened positively for posttraumatic stress disorder.

Neuropsychological Impairment

Rates of neuropsychological impairment across measures are presented in Table 2. Participants who screened positive for PTSD were more likely to be impaired on the AFT, $\chi 2$ (1) = 5.46, p = .02, OR = 1.26, 95% CI = 1.04–1.53, the COWAT, $\chi 2$ (1) = 5.15, p = .02, OR = 1.25, 95% CI = 1.03–1.53, MPMT, $\chi 2$ (1) = 13.90, p < .01, OR = 1.56, 95% CI = 1.23–1.98. The PTSD group did not show higher rates of impairment on the RAVLT immediate $\chi 2$ (1) = 0.47, p = .64, or delayed, $\chi 2$ (1) = −0.71, p = .47, Stroop $\chi 2$ (1) = 2.72, p = .12, or MAT, $\chi 2$ (1) = 0.26, p = .61. In examining global cognitive impairment, indexed as being impaired on two or more tests, the PTSD group was more likely to be impaired than the comparison group on two or more tests, $\chi 2$ (1) = 5.43, p < .01, OR = 1.31, 95% CI = 1.09–1.57.

Predictors of Global Impairment

To identify the extent to which social support may predict global cognitive impairment, binary logistic regressions were run on the dichotomous variable "global cognitive impairment," entered as the dependent variable, and the four social support subscales (emotional, tangible, affectionate, and positive social interaction) were included as predictors. The logistic regression was run separately for the comparison and PTSD groups. As indicated in Table 4, for the PTSD group, none of the social support subscales predicted global impairment (ps > .10). However, for the comparison group, an increase of one point on the emotional support (OR = 0.96, 95% CI = 0.95–0.97), or on the tangible support subscale (OR = 0.98, 95% CI = 0.97– 0.99), was associated with a 4% and a 2% decrease in the odds of being classified as impaired, respectively, $\chi 2$ (4) = 150.44, p < .01, Nagelkerke R2 = 0.01.

Table 4

Logistic Regression Model for Social Support as Predictor of Global Impairment Across Participants

	Comparison Group (*n* = 22158)		PTSD+ (*n* = 1096)	
	OR	95% C.I.	OR	95% C.I.
Social Support Subscales				
Emotional support	**0.96**	**0.95, 0.97**	0.98	0.95, 1.02
Affectionate support	1.01	0.98, 1.04	0.96	0.88, 1.04
Positive social interactions	1.01	0.98, 1.05	1.01	0.92, 1.12
Tangible support	**0.98**	**0.97, 0.99**	1.02	0.96, 1.08

Note. PTSD+ = screened positively for posttraumatic stress disorder.

Discussion

The current study examined a community-based sample of adults aged 45–85 and provided evidence that participants who screened positive for PTSD had a worse performance on multiple cognitive tests than the comparison group, consistent with previous research (Aupperle et al., 2012; Brewin et al., 2007; Jak et al., 2016; Johnsen & Asbjørnsen, 2008; Scott et al., 2015). The group mean differences indicate subtle deficits that may not meet the standard for clinically significant impairment (effect sizes ranged from d = 0.00 to 0.02); these results are in line with research investigating clinically significant impairments in participants with PTSD (Samuelson et al., 2017).

When examining the proportion of participants who exhibit global neurocognitive impairment (defined as 1.5 standard deviations below the comparison group mean on more than two tests), rates are higher for the PTSD group (15.6%) than for the comparison group (10.4%). It has been hypothesized that most participants with PTSD have minor deficits in cognition that likely represent noticeable changes in functioning compared to their pre-trauma performance but do not meet standards for clinically significant impairment (Samuelson et al., 2017). Our results

suggest that a subset of participants who screened positive for PTSD may exhibit greater levels of impairment.

With respect to specific cognitive domains, we found that the PTSD group exhibited higher impairment rates on tests of executive function (COWAT, AFT) and prospective memory (MPMT). Interestingly, no significant differences between groups were found for impairment rates on tasks of declarative memory (RAVLT immediate and delayed). Our results seem to indicate that some tasks may be more sensitive in detecting specific cognitive impairments in participants who screen positive for PTSD.

The current results are largely consistent with recent meta-analyses (Schuitevoerder et al., 2013; Scott et al., 2015); however, effect sizes were smaller here than in previous studies. It is probable that differences in effect size are due to variations in participant samples. Small sample sizes are predominant in this research field and are likely to show larger effect sizes than larger studies. In meta-analyses, these can lead to small study effects (Egger et al., 1997). Furthermore, in most studies, participants are recruited from clinical settings, which often reflect greater levels of impairment, contributing to larger effects. The current study used a community sample and the sample size is quite large, meaning that our results may yield a more accurate representation of the magnitude of cognitive deficits exhibited by participants who screen positive for PTSD.

Social Support, Cognition, and PTSD

Consistent with previous studies, our findings revealed that participants in the PTSD group reported perceiving less social support overall compared to the comparison group (Durai et al., 2011; Seil et al., 2019). This finding held across all subscales of social support, including affectionate support, positive social interaction, emo tional support, and tangible support. We also aimed to assess if perceived social support could act as a cognitive reserve factor by mitigating cognitive deficits in PTSD; our results revealed that social support had no influence

on neuropsychological test scores for participants in the PTSD group, while being associated with better test performance in the comparison group.

One possible explanation for this finding is that trauma victims with PTSD often show impairment in interpersonal functioning and difficulties interacting with intimate social partners (Cook et al., 2004; Lambert et al., 2012). Symptoms of emotional numbing, including feelings of estrangement and detachment from others, are often present in PTSD and appear to be associated with altered interpersonal functioning (American Psychiatric Association, 2013; Kashdan et al., 2007). Furthermore, researchers have found that participants diagnosed with PTSD have deficits in social cognition skills: they have difficulty understanding and sharing other peoples' emotional experiences (i.e., empathy) and exhibit difficulty in interpreting other peoples' mental states (i.e., theory of mind; Mazza et al., 2011; Nietlisbach et al., 2010; Stevens & Jovanovic, 2019). If people with PTSD experience social relationships in a less profound way, it is possible that social contact becomes less mentally stimulating, thus attenuating its effect on cognitive functioning.

Furthermore, higher levels of perceived social support did not lead to better scores on any neuropsychological measures. Similarly, Andrews et al. (2003) have found that positive social support had no influence on the course or severity of PTSD symptoms. However, negative social support appeared to increase PTSD symptom severity. The interaction between neuropsychological functioning and positive social support appears to follow the same trajectory; positive social support was not associated with better scores on neuropsychological measures. It could be hypothesized that negative social support could have more of an impact on neuropsychological functioning in participants with PTSD rather than positive social support. It remains to be determined how negative social support interacts with neuropsychological functioning in participants with PTSD.

The current study had several limitations. First, PTSD status was determined using self-report questionnaires, which depend on participants to understand the language used to determine which events are deemed traumatic and to interpret the severity of symptoms without clinical guidance. Therefore, structured clinician-administered interviews are usually preferred over self-report questionnaires to insure proper comprehension and categorization of clinical concepts. Moreover, time since onset of PTSD symptoms is unknown. The specific nature of the traumatic event was unavailable and could have impacted moderation analyses, because interpersonal traumatic experiences have been shown to have greater impact on interpersonal functioning post- trauma than other types of trauma (Charuvastra & Cloitre, 2008). Furthermore, it is possible that for certain participants, PTSD symptoms could have affected the accuracy of their responses on the social support scale due to its self-report nature. Finally, these results should be interpreted with caution because studies suggest cognitive deficits are bidirectional, meaning they are both a risk factor and a consequence of PTSD (Jacob et al., 2019; Vasterling & Brailey, 2005).

Clinical Implications

The present study found that participants who screened positive for PTSD exhibit higher impairment rates than the comparison group on tests of executive functioning and prospective memory. Social support is an important protective factor in the development of PTSD and its absence has been deemed a risk factor. However, we found that social support did not influence neuropsychological functioning in participants experiencing symptoms of PTSD. Previous research suggests that participants with PTSD often show impairments in interpersonal functioning and difficulties interacting with others, which may attenuate the benefits of social support (Nietlisbach et al., 2010). This study also suggests that participants who screened positive for PTSD do not experience nor benefit from social support in the same ways as their

healthy counterparts. These findings are important to consider in treatment, because deficits in cognition have been shown to lead to impaired treatment outcomes (Nijdam et al., 2015), and impairment in social functioning could impact the therapeutic alliance, the strongest predictor of treatment outcome (Norcross & Lambert, 2018). Furthermore, a reduction in social support has been associated with increased risk in suicidal ideation and intent (Panagioti et al., 2014). Further research needs to be done exploring other lifestyle factors that could help mitigate neuropsychological impairments in middle-aged and older adults with PTSD to help inform treatments at an institutional level.

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Study 2: Cognitive Change and Cognitive Reserve in Post-traumatic Stress Disorder: Findings From the Canadian Longitudinal Study on Aging

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Abstract

Objective*:* Meta-analyses have demonstrated that people with PTSD have a higher risk of developing dementia than people without PTSD. Identifying modifiable risk factors for dementia is crucial. However, there is insufficient research examining the benefit of cognitive reserve proxies in the context of PTSD to understand if they can attenuate cognitive decline. The current study evaluates the longitudinal cognitive performance of middle-aged and older adults with symptoms of PTSD and examines the influence of lifestyle factors on cognitive performance over time. ***Method:*** The study used data from the first two waves of the Canadian Longitudinal Study on Aging (three-year interval), which included 614 participants with PTSD and 14,235 participants as comparisons. Participants completed neuropsychological tests and questionnaires on lifestyle factors (cognitive stimulation, education, social support, physical activity and social participation). ***Results:*** Relative to the comparison group, the PTSD group included a greater proportion of participants exhibiting cognitive deterioration from T1 to T2 on memory tasks. Moderation analyses revealed the comparison group performed better on the RAVLT delay and COWAT with higher perceived social support; however, for participants in the PTSD group, higher social support was linked to worse performance on these measures. Furthermore, *education was associated with higher scores on the RAVLT delay for the comparison group, although the relationship was weaker for the PTSD group.* ***Conclusion:*** A greater proportion of participants with PTSD experienced cognitive decline on tasks of memory relative to the comparison group. Social support and education were found to moderate the relationship between group membership and neuropsychological performance.

Keywords: PTSD; neurocognition; cognitive reserve; CLSA; cognitive decline; older adults

Introduction

As the aging population grows in many parts of the world, age-related cognitive impairment has been of increasing public health concern. Studies investigating cognitive function in older adults must consider how different health conditions—which may themselves be associated with cognitive impairments—interact with the aging process to further impact cognition. While both physical and mental health problems can interact with age to impact cognition (Trivedi, 2006), research to date has focused more on the role of physical rather than mental health.

Posttraumatic stress disorder (PTSD) is a psychiatric disorder that alters the complex system in the brain responsible for self-protection in individuals who have experienced or witnessed a traumatic incident that threatened their physical and/or psychological safety (American Psychiatric Association, 2013). While PTSD is most often discussed in terms of emotional dysregulation, it is also associated with cognitive deficits. A large body of research has provided robust evidence of deficits across numerous cognitive domains, including attention, working memory, episodic memory, processing speed, executive functioning, and learning (Aupperle et al., 2012; Jak et al., 2016; Johnsen & Asbjørnsen, 2008; Scott et al., 2015).

While the impacts of PTSD on cognition are better understood in younger adults, the literature investigating PTSD in older adults is limited (Cook & O'Donnell, 2005). One meta-analysis found that older adults with PTSD exhibited worse performance in all cognitive domains studied (processing speed, attention, working memory, learning, language, visuospatial abilities and executive functioning) compared to older adults without PTSD (Schuitevoerder et al., 2013). However, most studies included in the meta-analysis had a cross-sectional design, limiting the conclusions about the cognitive impacts of PTSD as individuals age.

Longitudinal studies examining the symptom course of PTSD have shown that symptom severity appears to decrease with age, potentially reducing the risk of cognitive decline (Yehuda et al., 2006). However, few longitudinal studies have assessed how the cognitive performance of individuals with PTSD is influenced by the course of the illness, age, and PTSD-associated vulnerabilities (Schuitevoerder et., 2013). One longitudinal study found a discrepancy in the pattern of performance on two tests of memory, the California Verbal Learning Test (CVLT) and the paired-associated learning test, following an improvement of PTSD symptoms (Yehuda et al., 2006). In the PTSD group, performance on the CVLT improved over time and was correlated with PTSD symptom improvement (i.e., group differences at the follow-up were no longer detected). However, the PTSD group still exhibited a decline in paired associated learning, which was not correlated with symptom severity. These results suggest a possible distinction between aspects of memory function associated with aging and trauma exposure and aspects related to PTSD symptom severity.

Evidence that older adults with PTSD have greater decline in certain domains of cognitive performance than those without PTSD has led investigators to believe that PTSD and aging may interact, leading to accelerated age-related cognitive decline (Lapp et al., 2001; Yehuda et al., 2006). In the last decade, numerous studies have examined the link between PTSD and the development of dementia (Desmarais et al., 2020; Qureshi et al., 2010; Yaffe et al., 2010). A recent meta-analysis has demonstrated that individuals with a diagnosis of PTSD had a 1.61-1.99 times higher risk of developing dementia compared to individuals who did not have a diagnosis of PTSD (Günak et al., 2020).

Given the current dearth of disease-modifying interventions and medications, identifying and preventing modifiable risk factors for dementia is crucial for public health initiatives (Anderson, 2019). The cognitive reserve model has been of increasing interest, because it proposes that the brain's networks are flexible and adaptable, allowing it to maintain cognitive function despite damage or disease. Researchers have found that some people have higher

cognitive reserve, facilitating the formation of alternate neural networks, and delaying the functional impairments associated with dementia neuropathology (Nelson et al., 2021; Stern, 2012).

Typically, cognitive reserve is measured using proxies that recapitulate lifestyle factors or experiences that are said to impact reserve (Stern et al., 2019). Cognitive reserve proxies can include factors such as educational attainment, social support, and cognitively demanding activities. Although these measures help to moderate the link between brain changes and functional impairments, they are not direct measures of cognitive reserve and do not reflect the underlying brain mechanisms that contribute to cognitive reserve (Stern et al., 2019). Nevertheless, a large body of evidence has found that people with higher levels of cognitive reserve proxies have milder functional impairments with more advanced Alzheimer's type pathology, compared to people with lower levels of cognitive reserve proxies (Bennett et al., 2003; Ewers et al., 2013; Stern et al., 1999). However, there is insufficient research examining the benefit of cognitive reserve proxies in the context of PTSD to understand if they can attenuate cognitive decline (Ranger et al., 2022; Seil et al., 2019). There is a need for more longitudinal studies to understand when PTSD begins to interact with age and which modifiable risk factors could slow the decline of cognitive deficits (Lapp et al., 2011).

The current study aims to evaluate the neuropsychological performance of a large sample of middle-aged and older adults with symptoms of PTSD and to quantify the decline in cognition across cognitive domains over three years. Furthermore, we will aim to identify if cognitive reserve proxies may mitigate decline in participants with symptoms of PTSD.

Method

Data Source and Procedures

The data are taken from the Comprehensive Cohort of the Canadian Longitudinal Study on Aging (CLSA). The CLSA collects data at 3-year intervals to capture the transitions, trajectories, and aging profiles. The present study used data from the baseline and three-year follow-up waves. Demographic, clinical, and cognitive data were collected through 90-minute home interviews and/or assessments that were conducted at one of the 11 data collection sites across Canada. For more detailed information on procedure and sampling in the CLSA, please refer to Raina et al. (2019). Ethical approval was obtained for the CLSA protocol by the Canadian Institutes of Health Research (CIHR) and approval was acquired from each research site before data collection. Furthermore, the current study was also approved by the Bruyère Research Institute and the University of Ottawa Research Ethics Boards and is in accordance with the ethical standards of the Declaration of Helsinki and its subsequent amendments.

Participants

Approximately 30,000 participants participated in both the Baseline and Follow-Up One data collection waves. The participants were recruited as part of a stratified random sample of Canadians between the ages of 45 and 85 who were fluent in English and/or French. Participants were excluded from the current analyses if they were diagnosed with a neurological disorder (e.g., Alzheimer's, Parkinson's, multiple sclerosis), did not participate in the Maintaining Contact Questionnaire (interviews with additional health-related questions that were completed approximately 18 months after baseline and included, among other, questions related to physical activity), did not participate in Follow-Up One, did not complete the DCS visit or the cognitive module data was not administered, did not complete the Primary Care PTSD Screen, or had missing data on the variables of interest (see Figure 1). Participants were divided into two groups

based on their Primary Care PTSD Screen (PC-PTSD) scores. Participants who earned a score of three or higher on the PC-PTSD were categorized in the PTSD group. In contrast, participants who earned a score of two or lower on the PC-PTSD were categorized in the comparison group. According to prior research, using study-specific comparison groups yields better normative criteria than utilizing normative reference groups (Clapp et al., 2018). The sample sizes used in the CLSA are bigger than any previously conducted study using the neuropsychological tests listed below (Bleecker et al., 1998; Kempler et al., 1998; Morrow, 2021). Please refer to Tuokko et al. (2017) for a thorough comparison of published standards with CLSA norms on neuropsychological tests.

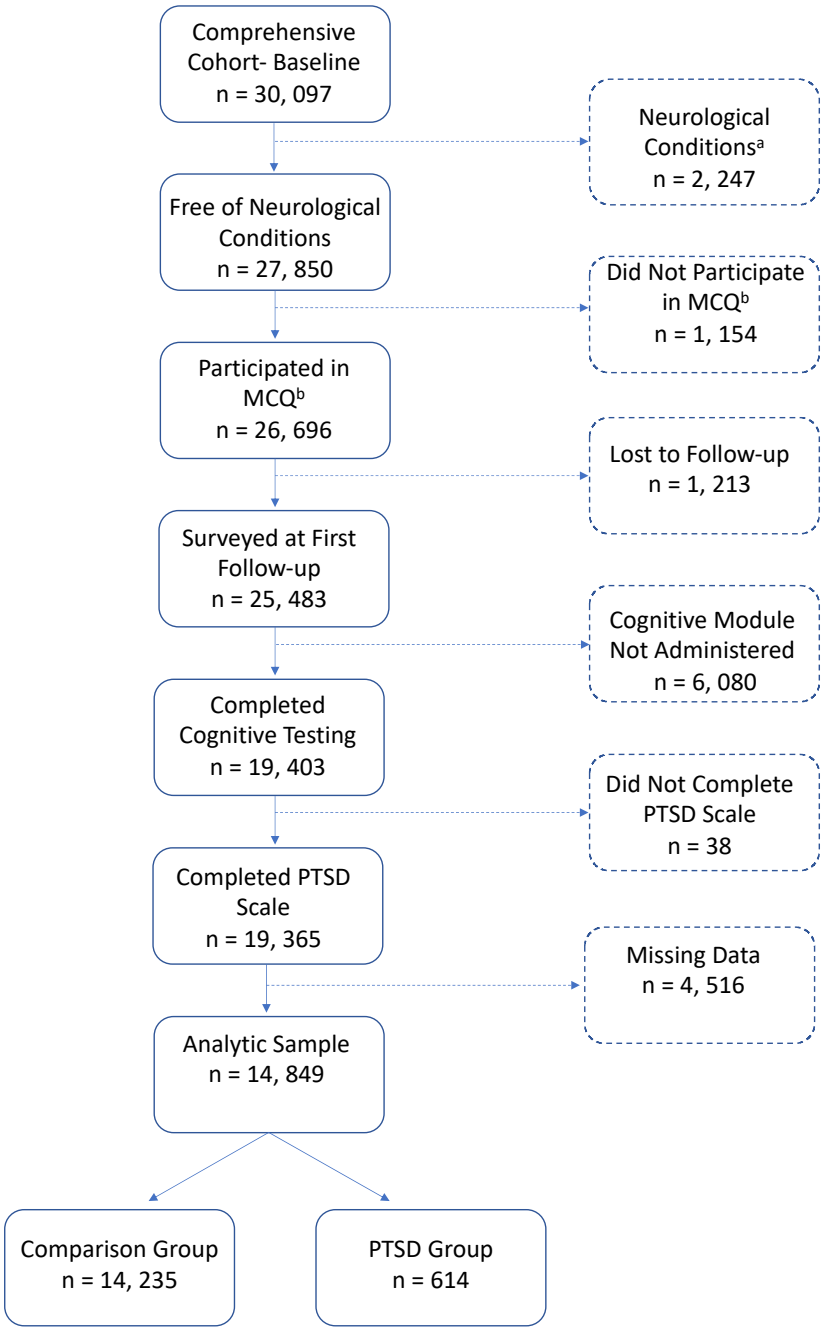


Figure 1. Flow diagram of participants in the Canadian Longitudinal Study on Aging (CLSA) included in the analysis. a = Alzheimer's disease, dementia, multiple sclerosis, epilepsy, Parkinson's disease, transient ischemic attack, and cerebrovascular accident. b = Maintaining Contact Questionnaire.

Measures

Demographic Data and Lifestyle Factors

In-person structured interviews were used to gather demographic data pertaining to age, alcohol consumption, depression, education, and sleep time. The frequency of alcohol use was determined by asking participants how frequently they consumed alcohol in the previous 12 months. Their responses ranged from "never" to "nearly every day." The Center for Epidemiologic Studies Short Depression Scale (CES-D10) was used to evaluate depression. The scale ranges from 0 to 30 ($\alpha = 0.79$), with a score greater than 10 indicating depression (Andresen et al., 1994). Sleep time was assessed by asking participants how many hours of actual sleep they received per night, on average, during the previous month. Alcohol consumption, sleep time, and depression levels were collected at T1(baseline) and T2 (three-year follow-up).

Posttraumatic Stress Disorder

The PC-PTSD (Prins et al., 2003) was used to assess PTSD symptoms. The PC-PTSD is a short self-report screening test for PTSD that consists of four questions aimed at detecting the presence of the four major symptom clusters: re-experiencing, numbing, avoidance, and hyperarousal. The total score ranges from 0 to 4 ($\alpha = 0.64$). A score of 3 or higher indicates clinically significant PTSD symptomatology, with a sensitivity rate of 0.78 and a specificity rate of 0.87. It was found to have good test-retest reliability ($r = .83$) and predictive validity against the Clinician-Administered PTSD Scale ($r = .83$; Prins et al., 2003). Other studies have found the PC-PTSD to have good discriminatory strength (*C*-statistics=.82; Ouimette et al., 2008). The PC-PTSD was only collected at T1 (i.e., baseline).

Cognitive Reserve Proxies

Social Support. The Medical Outcomes Study (MOS) Social Support Survey was used to assess social support (Sherbourne & Steward, 1991). The scale includes four social support subscales and 19 items that are answered on a five-point Likert scale: (1) emotional/information support (i.e., empathetic understanding, support of expression of feelings, and expression of positive affection, advice, guidance, and information) (2**)** tangible support (i.e., cognitive or physical assistance) (3) positive social interaction (i.e., availability to join in leisurely activities) (4) affectionate support (i.e., expression of love and affection). A higher score indicated greater preserved social support. The scale has good internal consistency, with overall and subscale Cronbach alphas ranging from 0.91 to 0.97, and good test-retest reliability (ICC=0.78 after one year) and convergent validity (ranging from 0.72-0.87; Sherbourne & Steward, 1991).

Social Participation. Social participation was measured by asking participants their frequency of involvement over the past 12 months in the following community-related social activities: 1) activities with family or friends outside the home; 2) church or religious activities; 3) sports or physical activities; 4) education or cultural social activities; 5) service clubs or fraternal organizations; 6) neighborhood, community or professional association activities; 7) volunteer or charitable work, and 8) other recreational or social activities (e.g., gardening, hobbies, playing cards). Items were recorded using a 5-point Likert scale (i.e., 1 = daily; 2 = weekly; 3 = monthly, 4 = yearly, and 5 = never). Scores were reversed to facilitate interpretation of results. The total social participation scale score represented a participant's highest score in any of the eight categories described above. Therefore, the total score ranged from 1 (never) to 5 (daily). This measure was adopted from the Canadian Community Health Survey – Healthy Aging and the English Longitudinal Study on Aging.

Physical Activity. Physical activity was assessed using the Physical Activity Scale for the Elderly (PASE) questionnaire (Washburn et al., 1993). This self-report questionnaire collects information pertaining to the amount of walking and/or light, moderate, and vigorous-intensity activities participants engage in a week on average. A higher score was indicative of greater levels of physical activity. The PASE demonstrates good test-retest reliability with a coefficient of 0.75 and good construct validity (r=0.25-0.42) when correlated with a measure of physiological variables and health status (Washburn et al., 1993).

Cognitive stimulation. Cognitive stimulation was measured by asking participants how much time they spent playing board games, cards, crossword puzzles, jigsaw puzzles, or Sudoku**.** Items were recorded using a 5-point Likert scale (i.e., 1 = daily; 2 = weekly; 3 = monthly, 4 = yearly, and 5 = never). Scores were reversed to facilitate interpretation.

Education. Participants' education level was categorized according to degrees completed, including no high school degree, high school degree, college degree, undergraduate degree, and graduate degree.

Neuropsychological Measures

Executive Functioning. The Controlled Oral Word Association Test (COWAT; Spreen & Benton, 1977) is a measure of phonemic verbal fluency using three letters: *F, A,* and *S.* Participants are given one minute to name as many words as they can that begin with each of the supplied letters, earning one point for each word. Each letter is given its own trial, and the results of the three trials are added together to generate a global score. The Animal Fluency Test (AFT; Rosen, 1980) is a semantic verbal fluency test in which participants are asked to list as many animals as they can in one minute, earning one point for each word. A higher score on both verbal fluency tests was indicative of better performance.

The Victoria Stroop Test (Stroop; Regard, 1981) assesses inhibition, mental speed, and mental control. The test consists of three trials: 1)Participants are asked to name the ink colour of dots (Dot Trial), 2)Participants are asked to read a list of neutral words printed in different ink colours (Word Trial), 3) Participants name the colour of the ink in which the words are printed rather than read the word (Color Trial). The time, in seconds, it takes the participant to complete the 100 items in each trial determines the score. From this data, a ratio interference time score is calculated and consists of dividing the time on the Color Trial by the time of the Dot Trial, to account for the influence of cognitive slowing (Strauss et al., 2006; Troyer et al., 2007). A shorter interference time is indicative of better performance. Errors were not analyzed in the present study.

The Mental Alternation Test (MAT; Teng, 1994) assesses set-shifting. Participants are asked to count aloud for 30 seconds, alternating between numbers and letters in ascending order (i.e., 1-A, 2-B, 3-C, etc.). The number of correct alternations comprised of each correct number-letter sequence determines the total score. The score can range between 0 and 52, with higher scores indicating better executive function.

Memory. The Rey Auditory Verbal Learning Test **(**RAVLT; Rey, 1964) is a two-part test designed to assess verbal learning and retention. It includes an immediate recall score and a delayed recall score. At a rate of one word per second, fifteen nouns are read to the participants. Participants are asked to recall as many words as possible, in any order (immediate recall). In the CLSA administration, participants are asked again after 5 minutes to recall as many of the words (delayed recall). The number of correctly recalled words determines the score, with a maximum of 15 points available for each trial. A higher score indicates better performance.

Statistical Analyses

Statistical analyses were performed using SPSS version 28 (Armonk, NY, USA: IBM Corp.). All continuous variables were checked for normality with Q-Q plots and skew statistics (i.e., remain between -2 and 2), as recommended when using large datasets (Curran et al., 1996; Tabachnik & Fidell, 2013). Stroop time was positively skewed and was normalized with the use of a logarithmic transformation.

We conducted a comparison between respondents who were lost to follow-up and those who were retained, utilizing chi-square tests of independence ($\chi 2$) and independent sample t-tests. Group differences on continuous demographic and clinical data were analyzed with univariate analysis of variance (ANOVA). Ordinal data were examined with Mann-Whitney U, and categorical data were analyzed with chi-square test. Repeated measure analyses of covariance (ANCOVA) were run, with T1 and T2 neuropsychological test scores as within-subjects factors and group (i.e., PTSD group and Comparison group) as the between-subjects factor. Age (T1), education (T1), sex (T1), testing language (T1), sleep time (T2), alcohol frequency (T2), and depression level (T2) were used as covariates. Age, education level, gender, and tested language are known to significantly influence cognitive performance. Additionally, levels of depression, duration of sleep, and frequency of alcohol consumption are common factors that can be affected or comorbid with PTSD, which in turn can impact cognition.

To determine the proportion of participants that demonstrated decline on neuropsychological tests over time (i.e., three years) in each group, Reliable change indices (RCI) were calculated. The RCI was set at two-tailed z-score cut-off value of ± 1.645. The upper limit signifies clinically significant improvement, whereas the lower limit signifies a clinically

significant decline. The formula used to calculate RCI was adjusted for practice effects. A detailed explanation and mathematical formulation can be found in Duff (2012). Mann-Whitney U tests were used to identify group differences on the dichotomized declined vs. collapsed no change/improved RCIs across individual tests.

Moderation analyses were conducted to investigate whether the relationship between being part of the PTSD group (independent variable) and cognitive functioning at T2 (dependent variable) was influenced by various cognitive reserve proxies (moderator variables), such as cognitive stimulation, education, physical activity, social participation, and social support. Covariates including age, alcohol frequency, depression, sleep time, sex, and testing language were also used. Model 1 of Hayes's PROCESS macro (v.4.2; Hayes, 2022) for SPSS (IBM, v.28) was used to conduct the moderation analyses. Bootstrap resampling (5,000 samples) was employed to estimate 95% confidence intervals. This analysis was performed for each raw neuropsychological test score.

Results

Respondents Lost to Follow-Up

A comparison of respondents lost to follow-up versus those retained in the CLSA at first follow-up revealed that those lost to follow-up were more likely of older age (M= 66.28, SD = 9. 99) (t = 13.26, p <0.001) and had worst performance, than those retained, on all neuropsychological measure including, RAVLT, COWAT, AFT, MAT, and Stroop (ps <0.001).

Demographic and Clinical Characteristics

Demographic and clinical characteristics of the sample are displayed in Table 1. The present study included 614 participants who screened positive for PTSD and 14,235 comparison participants. Relative to the comparison group, the PTSD group had a larger proportion of

females relative to males ($p < .01$, $d = 0.52$), participants were younger ($p < .01$, $d = 0.10$), reported less formal education ($p < .01$, $d = 0.08$), more depressive symptoms at T1 ($p < .01$, $d = 0.45$) and T2 ($p < .01$, $d = 0.36$), less sleep at T1 ($p < .01$, $d = 0.06$) and T2 ($p < .01$, $d = 0.04$), and consumed alcohol less frequently at T1 ($p < .01$, $d = 0.11$) and T2 ($p < .01$, $d = 0.12$). A Time x Group interaction was not significant for sleep time ($p = .16$). However, the PTSD group had lower levels of depression over time ($p = < .01$, $d = 0.10$) relative to the comparison group. A larger proportion of the comparison group was assessed in English, relative to French, as compared to those in the PTSD group ($p < .01$, $d = 0.37$). The PTSD group did not differ from the comparison group with respect to veteran status ($p = .31$).

Table 1

Participant Demographic and Clinical Characteristics

	Comparison Group (n=14235)		PTSD Group (n=614)	
	T1	T2	T1	T2
Age, mean (SD)	61.1 (9.6)		58.38 (7.8)	
Sex				
Female (%)	49.1		65.0	
Male (%)	50.9		35.0	
Education (%)				
<High school	1.2		1.5	
High school	15.5		17.9	
Some College	9.8		14.3	
College diploma	17.5		22.8	
Some university	3.9		4.2	
University degree	26.7		23.8	
Graduate degree	25.2		15.5	
Marital status (%)				
Married	73.4		60.4	
Widowed	6.8		6.2	
Divorced	9.1		19.2	
Separated	2.6		4.1	
Single	8.0		10.1	
Veteran status (%)	8.7		7.5	
Depression, mean (SD)	4.7 (4.1)	4.5 (4.0)	9.4 (6.3)	8.2 (6.0)
Sleep hours, mean (SD)	6.8 (1.1)	6.9 (1.2)	6.6 (1.4)	6.7 (1.5)
Alcohol frequency (%)				
Never	8.5	7.4	11.4	11.4
<once a month	10.4	10.7	16.8	14.3
About once a month	6.3	6.9	9.1	9.0
2-3 times a month	10.6	10.2	11.6	12.4
About once a week	12.0	12.4	11.4	15.5
2-3 times a week	23.6	23.1	19.5	17.9
4-5 times a week	11.8	11.6	9.6	8.1
Almost every day	16.9	17.7	10.6	11.4
Social support, mean (SD)				
Total scale score	83.1 (15.9)	83.5(16.0)	76.1 (19.4)	77.4 (19.4)
Tangible subscale	82.3 (19.9)	83.4 (19.6)	74.5 (24.1)	76.4 (24.3)
Affection subscale	88.0 (18.0)	88.0 (18.2)	81.8 (22.5)	82.0 (22.7)
Positive interaction subscale	84.1 (17.5)	84.4 (17.4)	76.6 (21.5)	77.9 (20.3)
Emotional subscale	82.0 (17.5)	82.2 (17.5)	75.5 (21.1)	76.9 (20.8)
Social participation (%)				
Once a day	17.2	16.4	21.2	19.1
Once a week	70.3	69.7	64.2	66.6
Once a month	11.6	12.5	13.8	11.9
Once a year	0.9	1.3	0.8	2.1
Never	0	0.1	0	0.3
Physical Activity, mean (SD)	149.6 (73.0)		149.5 (75.9)	
Mental stimulation (%)				
Every day	34.8	34.6	33.1	31.9
Several times a week	19.1	18.5	18.9	20.2
Several time a month	14.3	13.2	14.0	12.2
Several times a year	12.0	12.1	11.4	10.4
Once a year or less	19.7	21.6	22.6	25.2
Testing language (%)				
French/ English	19.1/ 80.9		27.4/ 72.6	

The PTSD group also indicated perceiving less social support overall at T1 ($p = 0.1$, $d = 0.16$) and T2 ($p < 0.1$, $d = 0.14$) than the comparison group. However, the Time x Group interaction was not significant ($p = .24$). When social support subscales were examined separately, the PTSD group reported perceiving less social support at T1 and T2 on all the subscales ($ps < .01$) relative to the comparison group. The Time x Group interactions on all the social support subscales were not significant ($ps > .05$), with the exception of the emotional subscale ($p < .01$, $d = 0.03$). Levels of physical activity were similar between groups at T1 ($p = .96$). In addition, both groups were similar in terms of frequency of social participation at T1 ($p = .34$) and T2 ($p = .35$), and mental stimulation at T1 ($p = .17$) and T2 ($p = .13$).

Longitudinal Neuropsychological Functioning

Neuropsychological and reliable change score data are presented in Table 2. A repeated measure analysis of covariance (ANCOVA) did not reveal a significant three-way interaction between Groups, Type of Neuropsychological Tests (i.e., RAVLT, COWAT, AFT, MAT, and Stroop) and Time-Point, $F(5, 74200) = 0.21$, $p = .96$. The interaction between Group and Type of Neuropsychological Tests was not significant, $F(5, 74200) = 2.04$, $p = .07$. However, there was a significant interaction between Time-Point and Type of Neuropsychological Tests, $F(5, 74200) = 4.71$, $p < .01$. Bonferroni corrected pairwise-comparisons revealed that scores on RAVLT immediate, RAVLT delay, and COWAT were significantly higher at T2 than T1, $ps < .01$. Contrasts also indicated that scores on Stroop interference and mental alternation test were significantly lower at T2 than T1, $ps < .01$. (Note that for the Stroop interference, lower scores represent better performance). The main effect of Group was not significant, $F(1, 14840) = 2.32$, $p = .13$.

Table 2

Neuropsychological test and impairment rates across study groups

Tests, mean (SD)	Comparison Group (n=14235)		PTSD Group (n=614)	
	T1	T2	T1	T2
Memory raw scores				
RAVLT immediate	6.13 (1.8)	6.87 (2.1)	6.27 (1.8)	7.09 (2.1)
RAVLT delayed	4.36 (2.1)	4.99 (2.4)	4.55 (2.1)	5.11 (2.2)
RAVLT retention ratio	0.70 (0.3)	0.71 (0.3)	0.72 (0.3)	0.71 (0.2)
RCI Deterioration (%)				
RAVLT immediate		4.1		5.7
RAVLT delayed		5.2		7.0
RAVLT retention ratio		3.4		2.9
Executive functioning raw scores				
Stroop Interference	2.09 (0.5)	2.07 (0.6)	2.13 (0.5)	2.11 (0.52)
Mental Alternation Test	28.00 (8.1)	27.42 (7.3)	26.89 (8.7)	26.32 (7.2)
COWAT	40.85 (12.2)	41.63 (12.0)	40.02 (12.4)	40.89 (11.9)
Animal Fluency Test	22.51 (6.3)	22.32 (5.7)	22.27 (6.1)	22.32 (5.7)
RCI Deterioration (%)				
Stroop Interference		4.7		5.5
Mental Alternation Test		0.6		0.8
COWAT		4.3		4.1
Animal Fluency Test		5.3		5.2

Note. RAVLT = Rey Auditory Verbal Learning Test; COWAT = Controlled Oral Word Association Test; RCI = reliable change index; Deterioration is indexed as an RCI value of ≤ -1.645.

Reliable Change Indices

When considering the relative dichotomized frequency of deterioration vs. no change/improvement between participants, Mann-Whitney U analyses found a significant group difference on the RAVLT immediate, $U(14235, 614) = 4299399.50$, $p < .05$, $d = 0.03$, and RAVLT delay, $U(14235, 614) = 4291886.50$, $p = .05$, $d = 0.03$. Relative to the comparison group, the PTSD group included a greater proportion of participants exhibiting cognitive deterioration from T1 to T2 on the RAVLT immediate (comparison group = 4.1%; PTSD group = 5.7%) and RAVLT delay (comparison group = 5.2%; PTSD group= 7.0%). There were no group differences on the frequency of deterioration vs. no change/improvement on other neuropsychological measures (*p*s > .05).

Post-hoc Analyses

Post-hoc analyses were conducted to further elucidate which memory process may be impacting the deterioration of the RAVLT immediate and RAVLT delay in the PTSD group. A retention ratio was calculated by dividing the number of words recalled on the RAVLT delay trial by the number of words recalled on the RAVLT immediate. This analysis aimed to account for initial learning to help clarify whether individuals in the PTSD group have greater deterioration on the RAVLT delay because of poor memory performance or rather attention difficulties contributing to poor initial encoding. When considering the relative dichotomized frequency of deterioration vs. no change/improvement between participants, Mann-Whitney U analyses found no significant group difference in the retention ratio of the RAVLT, U (14235, 614) = 4325229, $p = .52$.

Moderation Analyses

Physical Activity

Moderation analyses demonstrated that the interaction between group membership and physical activity was not significant for any of the neuropsychological measures *(p*s >.05*)*. These results indicate that physical activity does not moderate the relationship between PTSD and neuropsychological performance.

Social Participation

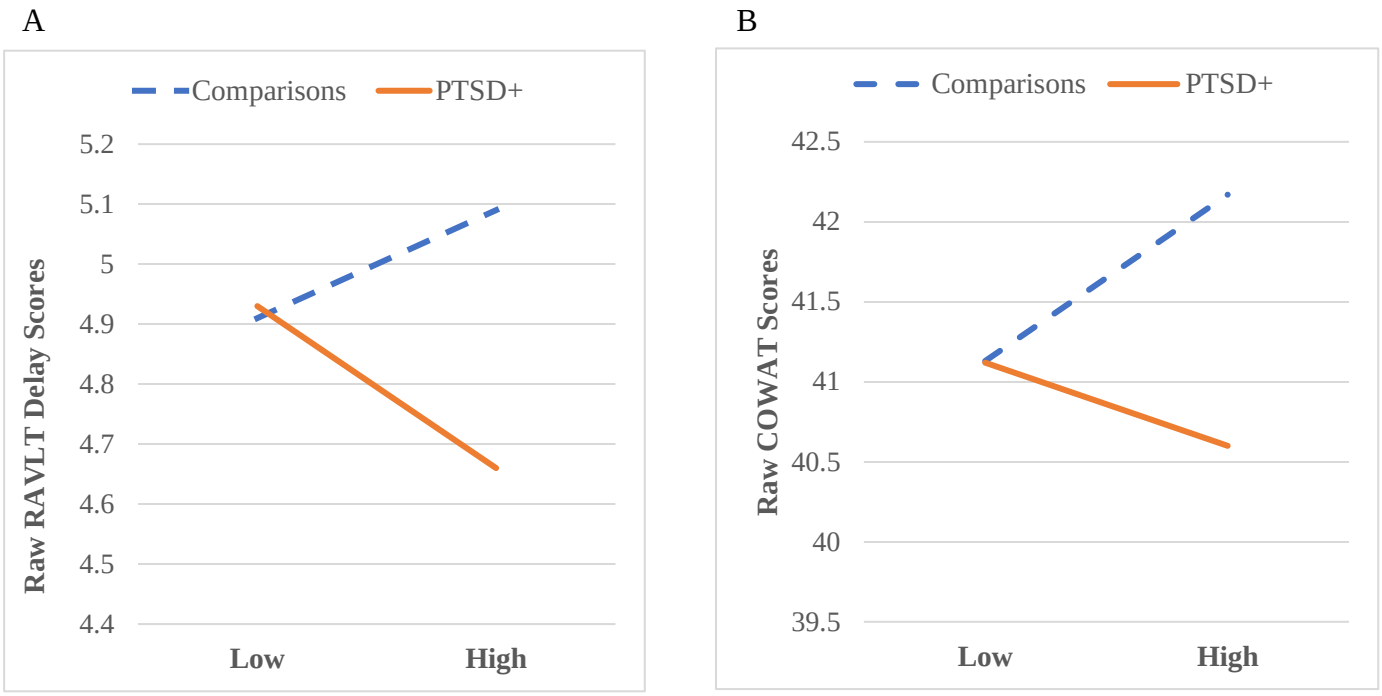
Moderation analyses demonstrated that the interaction between group membership and social participation was not significant for any of the neuropsychological measures *(p*s >.05). These results indicate that social participation does not moderate the relationship between PTSD and neuropsychological performance.

Social Support

The interaction between group membership and social support was found to moderate the RAVLT delay scores *(*$\Delta R2 = 0.24$, $b = -.01$, $t(14839) = -3.17$, $p < .01$*)*, and COWAT scores *(*$\Delta R2 = 0.15$, $b = -.05$, $t(14839) = -2.01$, $p = .04$*)* indicating that the effect of group membership on the aforementioned test scores varied depending on the level of social support (see, Figure 2). Simple slope analyses indicated that the comparison group had better performance on the RAVLT delay and COWAT with more perceived social support, while for participants in the PTSD group, higher social support was linked with worse performance on the RAVLT delay *(b* = -.43, $p < .01$*)*, and COWAT *(b* = -1.57, $p = .03$*)*. Social support was not found to moderate the relationship between group membership and other neuropsychological test scores, including on the RAVLT immediate, MAT, AFT and Stroop (*p*s > .05).

Figure 2

Social support moderating the relation between group and neuropsychological scores



Note. With regards to the relation between group membership and social support, panel **A)** shows the relationship for the Rey Auditory Verbal Learning Test- Delayed Trial (RAVLT), Panel **B)** presents the relationship for the Controlled Oral Word Association Test (COWAT). All neuropsychological measure are from T2. PTSD+ = screened positively for posttraumatic stress disorder.

Cognitive Stimulation

Moderation analyses demonstrated that the interaction between group membership and cognitive stimulation was not significant for any of the neuropsychological measures *(ps >.05).* These results indicate that cognitive stimulation does not moderate the relationship between PTSD and neuropsychological performance.

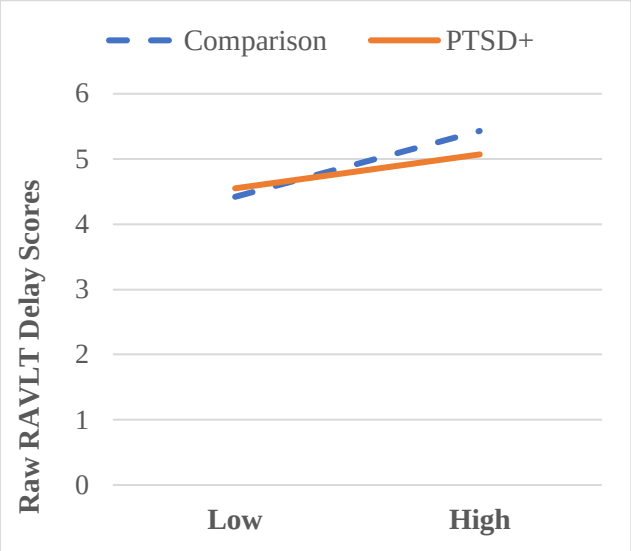
Education

The interaction between group membership and education was found to moderate the RAVLT delay scores *(*$\Delta R2 = 0.24$, $b = -.10$, $t(14839) = -2.03$, $p = .04$*)*, indicating that the effect of group membership on the RAVLT delay scores varied depending on the level of education

(see, Figure 3). Simple slope analyses indicated that the effect of group membership did not have a significant impact on RAVLT delay scores at low levels of education *(b* = 0.11, *p* = .44*)*. However, higher levels of education were associated with higher scores on the RAVLT delay for the comparison group, although this relationship was not as strong for the PTSD group *(b* = -0.37, *p* = .01*)*. Education was not found to moderate the relationship between group membership and the other neuropsychological test scores, including on the RAVLT immediate, MAT, COWAT, AFT, and Stroop.

Figure 3

Education moderating the relation between group and RAVLT delay scores



Note. The relation between group membership and education on the Rey Auditory Verbal Learning Test-Delayed Trial (RAVLT) at T2. PTSD+ = screened positively for posttraumatic stress disorder.

Discussion

The current study examined a community-based sample of participants aged 45-85 and found no evidence that the performance of those who screened positive for PTSD differed from the comparison group across several cognitive tests over three years. However, post-hoc RCI analyses that accounted for practice effects found that a greater proportion of participants who screened positive for PTSD showed decline in immediate and delayed recall relative to the comparison group. Regarding the impact of cognitive reserve proxies, the comparison group performed better on neuropsychological measures with higher levels of social support, although for the PTSD group, more social support was linked to worse performance. Greater education was related to better performance on a memory task for the comparison group, but the relationship was not as strong for the PTSD group.

Examining the results more closely, we found that performance on all neuropsychological tests was superior at T2 compared to T1, except for the mental alternation test (MAT), which declined significantly in both groups. It is likely that improved scores at T2 on the RAVLT immediate, RAVLT delay, COWAT, AFT, and Stroop resulted from practice effects: other studies using CLSA data have also found improved scores at T2 on most neuropsychological tests (Bedard et al., 2021; Grant et al., 2021; Tessier et al., 2022*).* Similar to other studies, we found that the MAT is a sensitive measure that can detect subtle levels of cognitive decline in aging populations (McComb et al., 2010; McComb et al., 2011). Our findings also suggest that the MAT may be more robust against practice effects than other cognitive tests, given that it was the only neuropsychological test that did not yield improved performance at T2 compared to T1.

To date, very few studies have examined cognitive performance longitudinally in older populations with PTSD (Schuitevoerder et al., 2013). One such study, Yehuda et al. (2006), examined performance on the California Verbal Learning Test (CVLT) and the paired-associated

learning test at a five-year interval, and also failed to detect a significant Group (PTSD+/PTSD-) by Time interaction. Examining mean group differences may not fully elucidate the extent of cognitive changes across time in individuals with PTSD.

As mentioned above, adjusting for practice effects in post-hoc RCI analyses revealed different results. A greater proportion of participants who screened positive for PTSD showed deterioration on the RAVLT immediate and RAVLT delay (5.7% and 7.0 %, respectively) relative to the comparison group (4.1% and 5.2%, respectively). While a greater proportion of individuals with PTSD showed deterioration on the RAVLT immediate and RAVLT delay, post-hoc analyses revealed that the PTSD group did not differ in the rate of retention between the RAVLT immediate and the RAVLT delay. These results suggest that participants in the PTSD group may experience greater difficulty initially encoding/ learning the information on the RAVLT immediate, yielding lower scores on the RAVLT delay. Similarly, in a meta-analysis conducted by Schuitevoerder and colleagues (2013), they found that the largest effects were found in the domain of memory. However, their results showed large variability in confidence intervals, which led them to consider subdomains of memory (e.g., encoding/learning, retention, retrieval). Further analysis demonstrated that the effect of encoding/learning was about half as strong for participants with PTSD compared to those without PTSD.

While emerging research has shown that a larger proportion of people with PTSD develop dementia compared to people who do not have PTSD *(*Desmarais et al., 2020; Qureshi et al., 2010; Yaffe et al., 2010*).* Alzheimer-type neuropathology is the most common form of dementia, with rapid forgetting being a hallmark symptom of the disease (Lopez et al., 2019). Our results do not seem to suggest that individuals in the PTSD group experience greater accelerated loss of memory traces than the comparison group. Further research should examine

whether participants with PTSD develop increased difficulties with rapid forgetting as they enter older age.

Our second research objective was to determine if cognitive reserve proxies can help mitigate cognitive decline in participants who screen positive for PTSD, as has been shown for people without PTSD *(*Bennett et al., 2003; Ewers et al., 2013; Stern et al., 1999*).* Moderation analyses demonstrated a significant interaction between group membership and social support on two neuropsychological measures (RAVLT delay and COWAT). These results indicate that the comparison group had better performance on neuropsychological measures with more perceived social support (at T2). However, higher social support was linked with worse performance on neuropsychological measures for participants in the PTSD group (at T2). Similar results were found in our previous study utilizing baseline data from the CLSA. Ranger et al. (2022) found that high levels of perceived social support yielded better neuropsychological performance for the comparison group, while for the PTSD group, increased social support had either no influence or had a negative effect on neuropsychological performance. These findings demonstrate that participants who screen positive for PTSD do not benefit from increased social support in terms of their cognitive performance.

Increased disruptions in levels of arousal might explain why participants in the PTSD group may experience social support differently, meaning that it does not yield the same cognitive benefits as in the comparison group. One possible account relates to the concept of the "window of tolerance", which defines an optimal arousal level where a person can effectively manage stressors and perform daily tasks without becoming overwhelmed or dissociated (Siegel, 1999). When an individual's level of arousal falls outside their window of tolerance, they will have difficulty effectively engaging with their environment. In the same vein, the polyvagal theory stipulates that if arousal levels are too elevated, individuals have difficulty engaging the

ventral vagal circuit, which enables social engagement and connections (Porges, 2017). Extensive research has shown that PTSD disrupts the hypothalamic-pituitary-adrenal (HPA) axis, which inherently interferes with levels of arousal (Inslicht et al., 2006; Jovanovic et al., 2010*).* Aligning with this research, people with PTSD have been shown to exhibit deficiencies in social cognition skills, including impaired empathy and difficulty interpreting others' mental states (Mazza et al., 2011; Nietlisbach et al., 2010; Stevens & Jovanovic, 2019).

Secondly, the interaction between group membership and education was found to moderate performance on a memory test (RAVLT delay). Results indicated that higher levels of education were associated with better performance on a memory task for the comparison group, although this relationship was not as strong for the PTSD group. Similarly, Seil et al. (2019) found that groups with greater cognitive reserve proxies (measured using education, marital status, employment, social support, social integration, and physical activity) were less likely to report confusion or memory loss. However, the association was stronger for the comparison group than the group with probable PTSD. These findings suggest that cognitive reserve proxies may play a more important role in modifying or delaying cognitive processes in individuals without PTSD.

The current study had several limitations. First, PTSD status was established utilizing a self-report questionnaire, which relies upon participants to comprehend the language used, decipher events deemed traumatic, and determine the severity of symptoms without clinical guidance. Clinician-directed interviews are generally considered the gold standard to determine the presence of PTSD. Moreover, PTSD symptoms were only collected at baseline; therefore, it is possible that participants no longer met the cut-off score for PTSD at follow-up (i.e., three years later) or rather experienced a traumatic event between both time points that led to the development of PTSD symptoms. Previous research has demonstrated that PTSD symptom

severity can impact results on neuropsychological measures *(*Yehuda et al., 2006). Finally, the results presented ought to be interpreted with attention since studies propose that cognitive deficits are bidirectional, meaning they are both a risk factor and a result of PTSD (Jacob et al., 2019; Vasterling & Brailey, 2005).

Clinical Implications

Previous studies along, with the current study, have failed to identify group differences in neuropsychological functioning over time between PTSD + and PTSD – using commonly used statistical analysis (repeated-measure analysis of variance; Yehuda et al., 2006). Our study demonstrates the importance of accounting for practice effects when assessing longitudinal change in neurocognitive performance in those with PTSD. A reliable change index, accounting for practice effects (Duff, 2012), may be more suitable to quantify longitudinal within-subject decline on neuropsychological testing in people with PTSD. Studies have shown that older adults with PTSD have worse performance across cognitive measures, with memory having the strongest effect (Schuitevoerder et al., 2013). Our current study replicates those findings by demonstrating that a greater proportion of adults and older adults in the PTSD group exhibited decline in memory than the comparison group after three years. While some studies suggest a link between PTSD and the development of dementia *(*Desmarais et al., 2020; Qureshi et al., 2010; Yaffe et al., 2010*)*, the main memory mechanism impacting decline in memory function in the PTSD group appears to be learning/encoding. Future research may wish to examine compensatory strategies such as mnemonic techniques, chunking, or external memory aids that can bypass or mitigate decline in memory for people with PTSD.

In addition, the current study highlights that individuals who screen positive for PTSD do not experience or gain the same benefit from social support as those without. These findings have crucial implications for treatments, as cognitive deficits have been linked to poorer

treatment outcomes, and impaired social functioning can affect the therapeutic alliance, which is a strong predictor of treatment success (Nijdam et al., 2015; Norcross & Lambert, 2018). It is important to consider these factors when developing treatment approaches for individuals with PTSD. Research has shown that addressing cognitive impairments and improving social functioning may contribute to more effective interventions and better treatment outcomes.

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Study 3: Cognitive Change in Veterans and Civilians with Posttraumatic Stress Disorder: Findings from the Canadian Longitudinal Study on Aging

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Abstract

Objective: Canadian veterans differ from the general Canadian population in many aspects of health. Few studies have evaluated whether cognitive functions differ by veteran status and how they evolve with age. Given the high prevalence of PTSD among veterans and the growing number of older veterans, there is a need for longitudinal studies to better understand the long-term impact of PTSD on cognition as veterans age. The study aims to investigate (1) whether veterans with PTSD are more likely to show improvement or decline in cognition over time (i.e., three years) compared to non-veterans with PTSD, and (2) to determine the severity of neuropsychological deficits and the proportion of impairments experienced by veterans with PTSD. ***Methods:*** The study uses data from the first two waves of the Canadian Longitudinal Study on Aging, a nationwide study on health and aging. The study includes 54 veterans and 54 age-and sex-matched non-veterans with symptoms of PTSD, all between the ages of 45-85 at baseline. Symptoms of PTSD were assessed using an adapted version of the Primary Care PTSD Screen Test, and participants completed neurocognitive tests in the domains of executive functioning and memory. ***Results:*** Initial results demonstrated that non-veterans with PTSD performed better than veterans with PTSD across several cognitive tests over a three-year period. However, after controlling for traumatic brain injury (TBI), differences were no longer detected between the groups. ***Conclusion:*** Findings highlight the importance of accounting for the presence or cooccurrence of PTSD and TBI when examining the neuropsychological profile of veterans.

Keywords: PTSD; Neurocognition; Veterans; CLSA; older adults

Introduction

The aging population is increasing in Canada, along with the population of veterans. According to a 2017 study, it is estimated that 33% of the veteran population will exceed 70 years old by 2026 (VanTil et al., 2018). Canadian veterans differ from the general Canadian population in many aspects of health and well-being. Substantial research has compared the life-course ramifications of military service, although fewer studies have evaluated whether cognitive functions differ by veteran status and how it evolves with age (Brown et al., 2014; Wilmoth et al., 2010).

By nature, the military favors an environment that has an impact on multiple characteristics related to cognitive aging (Brown et al., 2014). For example, military service/training is linked to protective factors such as educational attainment, a highly stimulating work environment, physical and mental activity, access to health benefits, and social camaraderie (Padula et al., 2016; Yaffe et al., 2014). Conversely, military service may have more direct, detrimental effects on cognition as a result of service-related accidents, operational stress injuries, substance use, and exposure to dangerous conditions (Brown et al., 2014; Padula et al., 2016; Vantil et al., 2018.). In addition, recruits are disproportionately chosen from underprivileged backgrounds, and early-life disadvantages may have long-lasting effects on cognitive outcomes (Thompson et al., 2016; Wilmoth & London, 2013).

Several studies have compared the cognitive performance of veterans versus non-veterans. Using a subjective measurement of memory, Wilmoth et al. (2011) found that male veterans had lower odds of memory-related disability than non-veteran males using cross-sectional data from the 2000 Census. Building upon these results, Brown et al. (2014) used longitudinal data from the Health and Retirement Study to examine whether men's cognitive trajectory varied by veteran status. Similarly, they found that veterans performed better on a

cognitive test than non-veterans at a mean age of 75 years; however, as veterans aged, their cognitive scores declined more steeply than non-veterans. Padula et al. (2016) examined the longitudinal cognitive trajectories of women veterans and found similar results. Baseline cognitive scores were comparable between veterans and non-veterans; however, longitudinal analyses revealed a greater cognitive decline in veterans relative to non-veterans.

The occurrence of mental health disorders among veterans is up to three times higher than in the general population (Thompson et al., 2016). When studying cognitive function in older adults, it is crucial to account for the influence of various health conditions, including mental health issues, because they can exacerbate cognitive impairments and interact with the aging process (Trivedi, 2006). Posttraumatic stress disorder (PTSD) is one of the leading causes of disability among veterans. It has been estimated that approximately 12.7% of Canadian veterans have a diagnosis of PTSD, the third most prevalent service-connected disability (Thompson et al., 2016). In addition, early research has also suggested that veterans with PTSD have a twofold increased risk of developing dementia compared to their veterans without PTSD (Yaffe et al., 2010).

Multiple studies have highlighted that PTSD is associated with cognitive deficits in both civilian and veteran populations across multiple domains, including attention, working memory, episodic memory, processing speed, executive function, learning, and memory (Aupperle et al., 2012; Cobb Scott et al., 2016; Johnsen & Asbjørnsen, 2008; Yehuda et al., 2005). It is noteworthy that there appears to be a bidirectional link between PTSD and neurocognitive abilities. Studies indicate that lower cognitive functioning before a traumatic event may increase the likelihood of developing PTSD. A study conducted by Sørensen et al. (2016) found that higher pre-deployment cognitive ability scores were associated with a lower risk of PTSD symptoms, and soldiers on a non-resilient PTSD trajectory had significantly lower cognitive

scores compared to those on a resilient trajectory. Nevertheless, there are also indications that pre-traumatic cognitive function alone does not entirely explain the cognitive impairments observed after a traumatic event (Aupperle et al., 2012).

To date, results have been mixed regarding the influence of trauma type on the magnitude of effect size on cognitive performance in those with PTSD. In a meta-analysis conducted by Scott et al. (2015) trauma type (military, interpersonal, state persecution, and mixed/unknown trauma) did not have a significant impact on the magnitude of effect size in terms of cognitive performance. However, a meta-analysis specifically examining cognitive functioning in older adults with PTSD found that combat traumas yielded larger effect sizes (Schuitevoerder et al., 2013). It remains unclear whether trauma type may have a greater impact on cognitive profiles as people with PTSD age.

Among the veteran population, PTSD can be associated with increased severity and clinical heterogeneity owing to combat exposure, injury, help-seeking behaviors, post-deployment stressors, service branch, and duration of service (Gauvin et al., 2022; Gaylord et al., 2009; Lehavot et al., 2018; O'Toole & Catts, 2017) However, to our knowledge, no studies have compared the cognitive profiles of veterans versus civilians with PTSD. There is a need for longitudinal studies to gain a better understanding of the long-term impact of PTSD on cognition as veterans age. While there is a considerable body of research investigating the health of veterans globally, with a particular focus on the United States, there are fewer studies addressing the particularities of the Canadian veteran population (Wolfson et al., 2023).

The current study aims to target this gap by evaluating the neuropsychological performance of Canadian veterans and civilians with symptoms of PTSD over three years. Furthermore, we compare reliable change indices across various neuropsychological measures between both groups.

Methods

Data source and procedures

The data used for this study are sourced from the Comprehensive Cohort of the Canadian Longitudinal Study on Aging (CLSA). The CLSA collects data every three years to document the changes, patterns, and characteristics of aging. The current study used data from the first two waves of data collection: baseline and follow-up one (FU1, three years later). Demographic, clinical, and cognitive data were collected through interviews at one of the 11 data collection sites located across Canada. For detailed information about the CLSA's procedures and sampling, please see Raina et al. (2019). The Canadian Institutes of Health Research (CIHR) granted ethical approval for the CLSA protocol, and approval from each research site was also obtained prior to data collection. Additionally, the present study received approval from the ethics boards of the Bruyere Research Institute and University of Ottawa.

Participants

Roughly 30,000 individuals participated in both the baseline and FU1 collection waves. These participants were selected through a stratified random sampling method from the Canadian population, and were aged between 45 and 85 years, and proficient in either English or French. Participants were excluded from the current analysis if they had a diagnosed neurological disorder (such as Alzheimer's, Parkinson's, or multiple sclerosis), did not complete FU1, did not complete the cognitive testing, or did not screen positive on the Primary Care PTSD Screen (see Figure 1). During the baseline assessment of the CLSA, participants were asked a series of Veteran Identifier Questions regarding their military service and were then categorized into two groups: veterans (including Canadian veterans and non-Canadian veterans) and Civilians (non-veterans). Because active military service was an exclusion criterion for the CLSA, participants who reported current service were not included in the analysis.

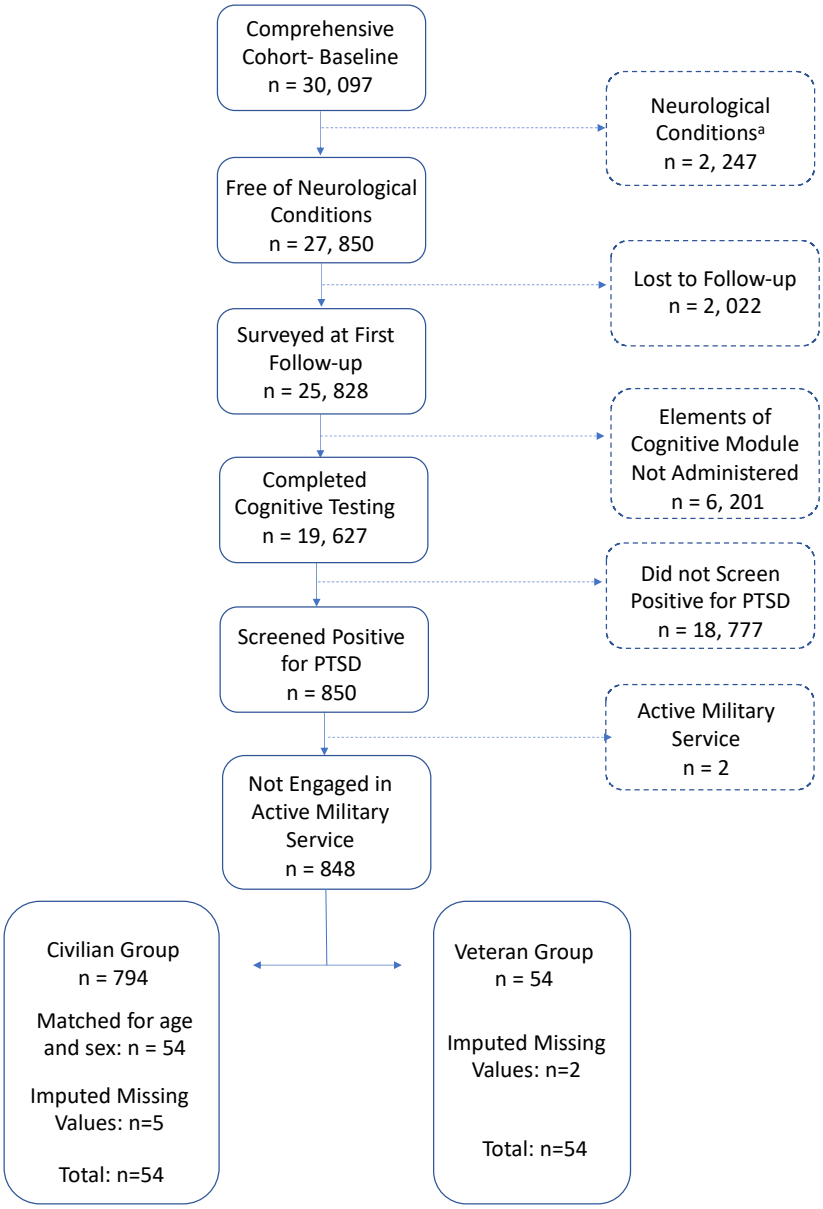

Figure 1. Flow diagram of participants in the Canadian Longitudinal Study on Aging (CLSA) included in the analysis. a = Alzheimer's disease, dementia, multiple sclerosis, epilepsy, Parkinson's disease, transient ischemic attack, and cerebrovascular accident.

Measures

Demographic Data and Lifestyle Factors

Demographic characteristics such as age, education, sex, alcohol use, sleep duration, and depressive symptoms were gathered through structured interviews. Participants were asked about the frequency of alcohol consumption over the past 12 months, ranging from never to nearly every day. Sleep duration was assessed by inquiring about the average number of hours slept per night during the previous month. The Center for Epidemiologic Studies Short Depression Scale (CES-D10) was employed to measure depressive symptoms, with scores ranging from 0 to 30. A score higher than 10 indicates the presence of depression (Andresen, 1994) Information about TBI was collected using the Brief Traumatic Brain Injury Screen (BTBIS; Schwab et al., 2007). Information regarding alcohol consumption, sleep duration, and depressive symptoms was collected at both time points (T1 (baseline) and T2 (FU1)).

Veteran Identifier Questions included details such as the branch of service (i.e., Army, Navy, Air Force, Reserves, or other branches) and the year of joining and leaving the military. The duration of military service was calculated by subtracting the reported join year from the release year. For non-Canadian veterans, the specific country of service was not recorded.

Posttraumatic Stress Disorder

The presence of PTSD symptoms was assessed using the PC-PTSD (Prins et al., 2003), which is a brief self-report screening tool designed to identify PTSD symptoms. It consists of four questions that target the key symptom clusters: re-experiencing, numbing, avoidance, and hyperarousal. The total score on the PC-PTSD ranges from 0 to 4, with a higher score indicating a higher level of PTSD symptomatology. A score of 3 or above suggests clinically significant PTSD symptomatology, with a sensitivity rate of 0.78 and a specificity rate of 0.87. The PC-PTSD demonstrates good test-retest reliability (r = .83) and has shown predictive validity when

compared to the Clinician-Administered PTSD Scale (r = .83; Prins et al., 2003) Previous studies have also indicated that the PC-PTSD has strong discriminatory power (C-statistics=.82; Ouimette et al., 2008) The PC-PTSD was administered only at T1 (baseline).

Neurocognitive Measures

Cognition was assessed using the Rey Auditory Verbal Learning Test (RAVLT; Rey A., 1964) immediate and delayed recall, the FAS Controlled Oral Word Association Test (COWAT; Spreen, 1977), Animal Fluency Test (AFT), The Mental Alternation Test (MAT; Teng, 1994), and the Victoria Stroop Test (VST; Regard, 1981) from which a ratio interference time score is computed by dividing the time taken for the color-word trial by the time for the dot trial. This calculation is done to accommodate the impact of cognitive slowing that is associated with aging (Troyer et al., 2007) A lower ratio interference time indicates better performance. It is important to note that errors were not examined in the current study. Please refer to Tuokko et al. (2017) for more details on the neurocognitive measures used in the CLSA.

Statistical Analyses

Data analysis was conducted using SPSS version 28 (Armonk, NY, USA: IBM Corp.). Normality checks were performed on all continuous variables using Q-Q plots and skew statistics. In the case of Stroop time, which exhibited positive skewness, a logarithmic transformation was applied to normalize the data (i.e., $\log_{10}(X + 1)$). In order to balance the numbers of individuals in the two groups (veteran and civilian) and reduce the variance in the parameters of interest (Rose & Van Der Laan, 2009), case-control matching was employed (matched for age and sex). A Little's Missing Completely at Random (MCAR) test was completed to determine the pattern of missing data on neuropsychological measures (<2.0 %). Results indicated that data were MCAR, $\chi 2$ (30, N = 108) = 27.714 p = 0.586. Expectation-maximization with 250 iterations was completed to replace missing values.

Differences between groups on continuous demographic and clinical variables were assessed using the univariate analysis of variance (ANOVA). For ordinal data, the Mann-Whitney U test was utilized, while categorical data were analyzed using chi-square test. Repeated measures analyses of covariance (ANCOVA) were conducted, considering T1 and T2 neuropsychological test scores as within-subject factors and group (veteran/civilian) as between-subject factors. Covariates including testing language (T1), sex (T1), age (T1), education (T1), sleep duration (T2), alcohol frequency (T2), depression symptoms (T2), and TBI (T2) were included in the analysis. Age, education level, gender, and tested language are known to significantly influence cognitive performance. Additionally, levels of depression, duration of sleep, and frequency of alcohol consumption are common factors that can be affected or comorbid with PTSD, which in turn can impact cognition.

To determine the proportion of participants who experienced a change in neuropsychological test performance over a three-year period in each group, Reliable Change Indices (RCI) were computed. A sample of 14,235 cognitively healthy participants (absence of neurological conditions) who screened negative for PTSD from the comprehensive cohort of the CLSA was used to determine normative cognitive change. The RCI was established using a two-tailed z-score cut-off value of ± 1.645. A z-score above this threshold indicates clinically significant improvement, while a z-score below this threshold indicates clinically significant decline. The RCI formula used for calculation was adjusted to account for practice effects. (For a more comprehensive understanding of the calculation method, including the detailed explanation and mathematical formulation, please see Duff (2012)). Mann-Whitney U tests were employed to identify group differences in the proportion of participants who exhibited decline (based on dichotomized RCI values) compared to those who demonstrated no change or improvement across individual tests.

Results

Demographic and Clinical Characteristics

Table 1 presents the demographic and clinical characteristics of the sample. The study included 54 veterans and 54 age-and sex-case-matched civilians. Relative to the civilian group, the veteran group reported less formal education ($p < .009$, $d = 0.52$), had sustained more traumatic brain injuries ($p = .052$, $d = 0.61$), and reported more depressive symptoms at T1 ($p = .020$, $d = 0.46$) and T2 ($p = .035$, $d = 0.42$). The Time x Group interaction was not significant for sleep time ($p = .18$) and depressive symptoms ($p = 0.68$). However, both groups reported fewer depressive symptoms from T1 to T2 ($p = 015$, $d = 0.48$). The veteran group did not differ from the civilian group with respect to testing language ($p = 0.06$), sleep duration at T1 ($p = 0.06$) and T2 ($p = .55$), and alcohol consumption at T1 ($p = 0.67$) and T2 ($p = 0.30$).

Table 1

Participant Demographic and Clinical Characteristics

	Civilian Group n=54		Veteran Group n=54	
	T1	T2	T1	T2
Age, mean (SD)	59.7 (9.9)		59.6 (9.8)	
Sex, (%)				
Female	13.0%		13.0%	
Male	87.0%		87.0%	
Testing language				
English	61.1%		77.8%	
French	38.9%		22.2%	
Education				
<High school	0.0%		1.9%	
High school	9.3%		20.4%	
Some College	13.0%		20.4%	
College diploma	9.3%		20.4%	
Some university	5.6%		3.7%	
University degree	24.1		24.1%	
Graduate degree	31.5%		7.4%	
Missing	7.4%		1.9%	
Marital status				
Married	53.7%		68.5%	
Widowed	14.8%		5.6%	
Divorced/ Separated	14.8%		16.7%	
Single	11.1%		9.3%	
Missing	5.6%		0.0%	
Traumatic brain injury		39.1%		60.9%
Missing		0.0%		1.9%
Depression, mean (SD)	8.5 (5.8)	7.4 (6.0)	11.53 (7.0)	10.1 (6.8)
Sleep hours, mean (SD)	7.0 (1.2)	6.93 (1.3)	6.52 (1.6)	6.8 (1.6)
Alcohol frequency				
Never	13.0%	7.4%	9.3%	14.8%
<once a month	5.6%	9.3%	13.0%	9.3%
About once a month	7.4%	7.4%	3.7%	11.1%
2-3 times a month	13.0%	16.7%	20.4%	11.1%
About once a week	14.8%	16.7%	14.8%	11.1%
2-3 times a week	22.2%	7.4%	16.7%	20.4%
4-5 times a week	7.4%	11.1%	3.7%	3.7%
Almost every day	16.7%	24.1%	18.5%	18.5%
Branch of military service				
Army			18.5%	
Navy			7.4%	
Air force			3.4%	
Reserve			13.0%	
Other*			7.4%	
Duration of military service, mean (SD)				
<2 years			33%	
2-9 years			22.2%	
10-19 years			7.4%	
>20 years			37.0%	
Country military service				
Canadian military			88.9%	
Military outside of Canada			11.1%	

Longitudinal Neuropsychological Functioning

Neuropsychological score data are presented in Table 2. A repeated measure analysis of covariance (ANCOVA) revealed a significant three-way interaction between Group (civilian, veteran), Neuropsychological Test (i.e., RAVLT, COWAT, AFT, MAT, and Stroop), and Time-Point, $F(5, 495) = 2.27$, $p = 0.046$, $d = 0.21$ while including testing language (T1), sex (T1), age (T1), education (T1), sleep duration (T2), alcohol frequency (T2), and depression symptoms as covariates. Bonferroni-corrected pairwise comparisons revealed that the civilian group performed significantly better on the MAT at T1 than the veteran group ($p = .025$, $d = 0.45$, 95% CI [0.48, 6.89]). In addition, the civilian group performed significantly better on the RAVLT immediate test ($p = .009$, $d = 0.52$, 95% CI [0.24, 1.65]), and Stroop interference at T2 than the veteran group ($p < .001$, $d = 0.71$, 95% CI [-0.25, 0.08] (note that for the Stroop interference, lower scores represent better performance). Scores on the RAVLT delayed test were significantly higher at T2 than at T1 for the civilian group only ($p < .001$, $d = 0.49$). Contrasts also indicated that scores on AFT, MAT, and Stroop interference (ps < .03, $d = 0.49$; note that for the Stroop interference, lower scores represent better performance) were significantly lower at T2 than T1 for the civilian group, although these results were not significant for the veteran group (ps = >.05).

Given the elevated risk of TBI in the veteran population, we added TBI (T2) to the list of covariates. With the addition of TBI as a covariate, the repeated measure analysis of covariance (ANCOVA) revealed a non-significant three-way interaction between Group, Neuropsychological Test, and Time-Point, $F(5, 495) = 2.08$, $p = 0.07$. Interactions were not significant between Group and Neuropsychological Test, $F(1, 99) = 0.61$, $p = .43$, and Time-Point and Neuropsychological Test, $F(5, 495) = 0.68$, $p = .64$. The main effect of Group was also not significant, $F(1, 99) = 2.48$, $p = .12$.

Table 2

Neuropsychological test and impairment rates across study groups

Tests, mean (SD)	Civilian Group (n=54)		Veteran Group (n=54)	
	T1	T2	T1	T2
Memory raw scores				
RAVLT immediate	6.09 (1.71)	7.06 (2.13)	5.47 (1.54)	6.15 (1.92)
RAVLT delayed	4.09 (2.05)	4.80 (2.45)	3.68 (1.93)	4.23 (2.18)
RCI Deterioration				
RAVLT immediate		1.9%		5.6%
RAVLT delayed		3.7%		3.7%
Executive functioning raw scores				
Stroop Interference	2.04 (0.66)	1.82 (0.46)	2.11 (0.48)	2.14 (0.58)
Mental Alternation Test	31.0 (8.76)	28.02 (8.36)	27.25 (8.72)	26.96 (7.52)
COWAT	42.28 (12.89)	42.89(9.75)	43.47 (11.8)	43.47 (11.82)
Animal Fluency Test	24.54 (6.54)	23.09 (6.59)	23.06 (7.60)	23.06 (6.34)
RCI Deterioration (%)				
Stroop Interference		13.0%		3.7%
Mental Alternation Test		1.9%		0.0%
COWAT		3.7%		7.4%
Animal Fluency Test		13.0%		5.6%

Note. RAVLT = Rey Auditory Verbal Learning Test; COWAT = Controlled Oral Word Association Test; RCI = reliable change index; Deterioration is indexed as an RCI value of ≤ -1.645.

Reliable Change Indices

Mann-Whitney U analyses found no group differences in the frequency of deterioration vs. no change/improvement on any neuropsychological measure (RAVLT immediate, U = 1404.00, p = .31; RAVLT delay, U = 2943.00, p = 1.00; COWAT, U = 1404.00, p = .40; AFT, U = 1350.00, p = .19; MAT, U = 1431.00, p = .32; Stroop, U = 1323.00, p = .083). RCI rates for the veteran and civilian groups can be found in Table 2.

Discussion

The current study examined a community-based sample of participants aged 45-85 and found evidence that the cognitive performance of veterans versus civilians who screened positive for PTSD differed across several cognitive tests over a period of three years. The civilian group showed better performance than the veteran group on the MAT (T1), RAVLT immediate (T2),

and Stroop (T2). In addition, the civilian group demonstrated better performance on the RAVLT delay, and Stroop from T1 to T2, suggesting that they benefited more from practice effects than the veteran group. However, after controlling for TBI, differences were no longer detected between both groups. TBI leads to cognitive symptoms, such as difficulties in executive functioning and disinhibition, slower processing speed, and impaired attention and concentration (Dolan et al., 2012; Rice et al., 2020). Consistent with prior research, the current study found that the veteran group had a higher prevalence of TBI compared to the civilian group, with rates of 60.9% and 39.1%, respectively. These results suggest that the initial differences observed on neuropsychological tests were likely attributable to the effect of TBI or the co-occurrence of TBI and PTSD.

Previous studies have found that the co-occurrence of TBI and PTSD among members of the military poses a significant health challenge due to the intricate array of symptoms and characteristics that exhibit substantial overlap. These include impaired attention, memory, and executive functioning, as well as sleep disturbances, depression, and hyperarousal (Dolan et al., 2012; Shor et al., 2022; Vasterling et al., 2018). Previous research has indicated that the combined neuropsychological profile of comorbid TBI and PTSD is more severe than that of either condition individually (Dolan et al., 2012). Similar to our results, one study found that veterans who had both PTSD and TBI performed worse on the Stroop compared to those who were diagnosed with PTSD alone (Brenner et al., 1995). The findings of our study highlight the importance of accounting for the presence or co-occurrence of PTSD and TBI when examining the neuropsychological profile of veterans.

As mentioned above, after controlling for TBI, no significant differences in cognitive profiles were found between veterans and civilians who screened positive for PTSD. These findings align with previous studies that indicate veterans have similar baseline cognitive scores

to non-veterans but experience a steeper decline as they age, compared to non-veterans. Stern's theory of cognitive reserve has been proposed as a potential explanation for the impact of military recruitment and service on the trajectory of cognitive performance in veterans (Padula et al., 2016; Stern, 2009). This model suggests that the brain can maintain cognitive function by forming alternate neural networks or better utilizing existing networks, protecting against the functional effects of neuropathology. Hence, individuals with lower cognitive reserve would exhibit signs of impairment earlier, while those with higher reserve would perform better for a longer duration (Stern et al., 2019).

Although the aforementioned studies did not account for PTSD (Brown et al., 2014; Padula et al., 2016), our results indicate that veterans and civilians with PTSD may follow a similar trajectory, as both groups demonstrate comparable scores at baseline and three years later. Future research should focus on comparing the longitudinal neuropsychological profiles of veterans and non-veterans with PTSD as they enter older age, while considering the impacts of cognitive reserve.

Reliable change indices failed to detect any differences in deterioration rates over a three-year period across various neuropsychological measures between the veteran and civilian groups. Early research suggests that PTSD increases the risk of developing dementia compared to individuals without the diagnosis (Yaffe et al., 2010). Following cohorts of veterans and civilians for longer periods as they enter older age may depict a different emerging cognitive profile between the groups. Building on previous research, it is hypothesized that veterans may reach a point in time where they experience a more rapid decline in cognitive functioning (Brown et al., 2014; Padula et al., 2016). Future studies should focus on determining if and when the steeper decline in cognition begins in veterans. Considering the scarcity of disease-modifying

interventions and medication, the identification and prevention of modifiable risk factors for dementia play a pivotal role in public health initiatives.

Our study has provided insight into the neuropsychological profile of veterans and civilians. However, certain limitations need to be considered. One constraint of this study relates to survivor bias, wherein the sample of veterans may not be fully representative of the entire veteran population due to the exclusion of individuals with more severe cognitive impairments or those who did not survive. As a result, the findings might underestimate the actual prevalence and severity of neuropsychological performance issues experienced by veterans. In addition, the determination of PTSD status relied on a self-report questionnaire, which required participants to understand the language used, interpret traumatic events, and assess the severity of symptoms without professional guidance. Generally, clinician-led interviews are considered the most reliable method to establish the presence of PTSD. Additionally, PTSD symptoms were only assessed at the beginning of the study; it is possible that participants no longer met the criteria for PTSD at the follow-up three years later. Alternatively, they may have experienced a traumatic event between the two-time points, resulting in the development of PTSD symptoms. Lastly, enhanced statistical power could be achieved by increasing the sample size in future studies, potentially leading to more robust and generalizable findings. While the proportion of female veterans in our sample aligns with lower enrolment of women in the Canadian military, the limited size of our study's sample prevents us from adequately considering the influence of sex and gender on these findings.

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General Discussion

Summary of Research

While a substantial body of research has explored the cognitive abilities of younger adults affected by PTSD, the situation differs when considering middle-aged and older adults. This particular age group, distinct from their younger counterparts, demonstrates an increased vulnerability to persistent physical ailments, a gradual decline in social connections, and significant life transitions (Lapp et al., 2011). Each of these factors, coupled with the inherent cognitive decline linked to the normal aging process, has the potential to engender a unique cognitive manifestation within older adults affected by PTSD (Lapp et al., 2011).

To date, most studies have focused on a cross-sectional design with relatively small sample sizes. In addition, owing to the dearth of studies in this area, there are a limited number of distinct samples used, resulting in participant redundancies across studies (Schuitevoerder et al., 2013). While various meta-analyses have identified differences in cognitive performance between people with and without PTSD (Scott et al., 2015; Schuitevoerder et al., 2013), these differences exhibit a range of magnitudes, spanning from small to medium (Cohen's d = -0.29 to -0.62). Despite this, the differences do not typically surpass the threshold denoting a clinically significant impairment (scores 1.5 or 2 standard deviations below the mean scores of broader populations) (Gilbertson et al., 2001; Nijdam et al., 2013; Samuelson, 2011; Samuelson et al., 2016; Scott et al., 2015; Vasterling et al., 1998). The use of group analyses may have hindered the identification of clinically significant impairments for a subset of individuals with PTSD. However, conflicting results from other studies have raised questions about the presence and extent of cognitive impairments associated with PTSD. (Crowell et al., 2002; Elsesser &

Sartory, 2007; Gurvits et al., 1996; Neylan et al., 2004; Pederson et al., 2004; Twamley et al., 2004).

Although some cross-sectional studies have indicated a link between PTSD and reduced cognitive function, few longitudinal studies have explored how cognitive changes unfold as individuals with PTSD age. The few studies available report discrepant results in terms of the rate of decline on neuropsychological measurements and the particular cognitive domains impacted (Roberts et al., 2022; Samuelson et al., 2009; Schuitevoerder et al., 2013; Vasterling et al., 2018; Yehuda et al., 2006). Additional longitudinal studies incorporating comparative groups are imperative to evaluate whether age exacerbates cognitive changes linked to PTSD, potentially resulting in faster decline. Such investigations would aid in managing cohort-related influences and addressing the recurring pattern of symptom fluctuations frequently observed in people with PTSD (Roberts et al., 2022; Schuitevoerder et al., 2013).

Existing research suggesting faster cognitive decline in older adults with PTSD compared to their non-PTSD counterparts has prompted researchers to hypothesize an interplay between PTSD and aging, which could potentially result in an accelerated age-associated cognitive decline (Lapp et al., 2011; Yehuda et al., 2006). A multitude of studies over the last decade have examined the association between PTSD and the development of dementia (Desmarais et al., 2020; Qureshi et al., 2010; Yaffe et al., 2010), and a recent meta-analysis indicates that people diagnosed with PTSD exhibit a 1.61-1.99 times higher susceptibility to developing dementia compared to people without PTSD (Günak et al., 2020).

Given the current shortage of interventions and medications that can modify the course of dementia, public health initiatives have focused on prioritizing the identification and prevention of modifiable factors that delay the onset of symptoms (Anderson, 2019). The cognitive reserve model has received increasing attention due to cognitive reserve factors having the ability to

mitigate cognitive decline (Stern et al., 2019). Although most research concerning cognitive reserve has revolved around dementia, cognitive reserve factors have demonstrated efficacy in delaying or alleviating cognitive impairment arising from other conditions (e.g., multiple sclerosis, Parkinson's, HIV, and traumatic brain injuries; Stern & Barulli, 2019). To date, only a single study has explored the influence of cognitive reserve among individuals with PTSD (Seil et al., 2009). This study employed subjective self-report questionnaires to gauge the impact of cognitive reserve on cognition, rather than using objective neuropsychological tests. Consequently, delineating the true effect of cognitive reserve factors and understanding the extent of their influence on individuals with PTSD remains challenging. There exists a need for further investigations into cognitive reserve among individuals with PTSD to ascertain whether these factors could potentially mitigate the progression of cognitive deficits as individuals age.

The current dissertation is oriented around three primary objectives: 1) to use a large population-based sample to quantify the magnitude of cognitive change, encompassing clinically significant impairment, associated with PTSD in diverse samples of middle-aged and older adults, including veterans; 2) to compare the magnitude of cognitive decline over time between people with and without symptoms of PTSD; 3) to explore if any lifestyle elements can act as cognitive reserve factors by mitigating cognitive decline over time.

Study 1

Drawing on the baseline data from the Canadian Longitudinal Study on Aging, Study 1 aimed to analyze neuropsychological performance within a sizable group of middle-aged to older adults displaying symptoms of PTSD. Specifically, the study focused on investigating the prevalence of impairment rates, defined as performance scores falling 1.5 or more standard deviations below the population's mean. In addition, Study 1 served as a preliminary study to

inform the plausibility of Study 2 by assessing if a cognitive reserve factor (i.e., social support) could mitigate performance deficits on neurocognitive tests in both the PTSD group as well as the comparison group.

Study 1 provided evidence indicating that participants who screened positive for PTSD exhibited poorer performance on various cognitive tests (MAT, MPMT, and Stroop) compared to the comparison group at baseline. These findings are in line with prior research studies (Aupperle et al., 2012; Brewin et al., 2007; Jak et al., 2016; Johnsen & Asbjørnsen, 2008; Scott et al., 2015). Concurrent with previous research that have used group analysis, group means revealed only slight differences (effect sizes ranged from d = 0.00 to 0.02) that did not reach the threshold for clinically significant impairment (Samuelson et al., 2017).

However, when first calculating individual neuropsychological impairment rates and subsequently conducting group analysis on dichotomized results of impaired versus not impaired, findings offered a broader view of the potential neuropsychological profile of individuals with PTSD. The proportion of participants displaying global neurocognitive impairment (defined as scoring 1.5 standard deviations below the mean of the comparison group on more than two tests) was higher in the PTSD group (15.6%) in relation to the comparison group (10.4%). Previous research postulated that individuals with PTSD exhibited slight cognitive deficiencies, which reflect a discernible alteration in functioning compared to their cognitive performance before the arrival of their PTSD symptoms, but these changes did not surpass the criterion for clinically significant impairment (Samuelson et al., 2017). Our findings suggest that a subgroup of participants who experience symptoms of PTSD might potentially display heightened levels of impairment.

Regarding our second research objective, results indicated that social support did not exert an effect on the neuropsychological test scores among participants in the PTSD group;

however, it was linked to improved performance within the comparison group. These findings suggest that people in the PTSD group may not benefit from cognitive reserve factors in the same way or to the same extent as the comparison group.

Study 2

Utilizing data from the first follow-up wave of the Canadian Longitudinal Study on Aging, Study 2 sought to evaluate the longitudinal neuropsychological performance, over three years, in middle-aged to older adults displaying symptoms of PTSD. Building upon the foundation laid by Study 1, Study 2 sought to broaden its scope by exploring additional cognitive reserve factors such as physical activity, cognitive stimulation, education, social participation, and social support. The objective was to ascertain whether these factors could ameliorate the performance on neurocognitive tests and examine whether individuals in the PTSD group would derive comparable benefits from those in the comparison group.

Study 2 results demonstrated that the performance of those who screened positive for PTSD did not differ from the comparison group on any of the cognitive tests across a period of three years. A previous study looking at the longitudinal performance in older adults with PTSD also failed to detect a significant group differences (PTSD+/PTSD-) by time interaction (Yehuda et al., 2006). As identified in Study 1, merely analyzing average group differences might not provide a comprehensive understanding of the scope of cognitive change among individuals with PTSD.

After adjusting for practice effects in RCI analyses, different results were obtained. The findings revealed that a higher percentage of participants who screened positive for PTSD displayed noteworthy clinical deterioration in both the RAVLT immediate and RAVLT delay tasks (5.7% and 7.0%, respectively), compared to the comparison group (4.1% and 5.2%, respectively). Further analyses revealed that the PTSD group did not differ in the rate of

retention between the RAVLT immediate and the RAVLT delay suggesting that participants in the PTSD group experienced greater difficulty initially encoding/learning or retrieving the information on the RAVLT immediate. Consistent with our findings, other studies have reported analogous results concerning challenges in encoding/learning or retrieving new information in individuals with PTSD (Golier et al., 2006; Schuitevoerder et al., 2013; Scott et al., 2015).

Our second research objective yielded similar results as found in Study 1. In terms of moderation analyses, it was observed that the comparison group exhibited enhanced performance on neuropsychological assessments with a higher level of perceived social support (at T2). Conversely, within the PTSD group, greater social support was associated with reduced performance on neuropsychological measures (at T2). These results further support that individuals who screen positive for PTSD do not experience improved cognitive performance as a result of heightened social support. Similarly, an exploration into the influence of alternative cognitive reserve factors on cognitive performance among individuals who screened positive for PTSD yielded comparable outcomes. The findings revealed that the comparison group exhibited improved performance on a memory task in association with higher levels of education, whereas this relationship was comparatively weaker within the PTSD group. In the sole other study that evaluated the influence of cognitive reserve factors on cognitive performance among individuals with PTSD, it was determined that groups with stronger cognitive reserve indicators exhibited a decreased likelihood of reporting confusion or memory loss. However, this association displayed greater robustness within the comparison group when contrasted with the probable PTSD group (Seil et al., 2019). These results propose that cognitive reserve indicators might exert a more significant influence on modifying or postponing cognitive processes in individuals without PTSD.

Study 3

Considering the divergence of Canadian veterans from the general population across various dimensions of health and well-being, along with their heightened susceptibility to PTSD, the objective of Study 3 was to delve deeper into the subgroup of individuals who screened positive for PTSD and assess if the cognitive profile of veterans with PTSD versus non-veterans with PTSD differed. This was achieved by integrating the objectives of both Study 1 and Study 2. It involved quantifying the longitudinal neuropsychological performance of veterans with PTSD over a span of three years and investigating whether they exhibited heightened clinical deterioration on neurocognitive measures in comparison to civilians with PTSD after three years.

Initially, the civilian group showed better performance than the veteran group on multiple neurocognitive measures, including the MAT, RAVLT, immediate, and Stroop. However, once adjustments were made for TBI, differences ceased to be discernible between the two groups. In addition, reliable change indices also failed to detect any differences in deterioration rates over three years across various neuropsychological measures between the veteran and civilian groups. Echoing our results, a separate study reported that veterans afflicted with both PTSD and TBI exhibited poorer performance on the Stroop task relative to individuals diagnosed solely with PTSD (Brenner et al., 1995). Previous research has suggested that the collective neuropsychological profile of concurrent TBI and PTSD is more severe compared to each condition taken separately (Dolan et al., 2012). These results imply that the initial differences in neurocognitive performance observed between both groups may be rather associated with TBI or the co-occurrence of TBI and PTSD. The results from Study 3 underscore the significance of considering the existence or co-occurrence of TBI and PTSD when analyzing the neuropsychological profile of veterans.

Implications and Future Research

Neurocognitive function

Group differences emerged between the PTSD and the comparison group in domains of executive functioning and prospective memory (i.e., MAT, MPMT and Stroop) at baseline. Strategies employed to enhance prospective memory skills have been linked to improved executive functioning (Rabin et al., 2014). These results are largely consistent with previous studies that have examined the cross-sectional cognitive performance of individuals with PTSD (Aupperle et al., 2012; Brewin et al., 2007; Jak et al., 2016; Johnsen & Asbjørnsen, 2008; Scott et al., 2015). Moreover, these outcomes are in line with the cognitive functioning models that propose that individuals with PTSD might allocate an excessive amount of resources toward affective processing and the associated regulation networks, while not dedicating sufficient resources to cognitive control networks. This imbalance is posited to compromise neurocognitive integrity, particularly affecting executive functioning (Aupperle et al., 2012; Jacob et al., 2019; Scott et al., 2015).

In comparison to our findings, a pertinent meta-analysis focusing on cognitive functioning in older adults with PTSD demonstrated noteworthy differences across all assessed cognitive domains (i.e., attention, working memory, learning, language, visuospatial abilities, and executive functioning; Schuitevoerder et al., 2013). In these domains, significant differences emerged between the individuals with PTSD and the control groups, characterized by notably larger effect sizes that emerged in Study 1. The dissimilarities in effect sizes are likely attributed to variations in participant samples. The prevalence of predominantly small sample sizes within this research domain tends to magnify effect sizes compared to larger-scale studies. In the context of meta-analyses, these circumstances can give rise to what is known as small study effects (Egger et al., 1997). In this study, a community sample of a considerable size was

employed, enhancing the potential for our results to provide a more precise portrayal of the extent of cognitive deficits observed among individuals who screened positive for PTSD.

Despite the group analysis revealing only minor differences in neuropsychological functioning between participants in the PTSD group relative to the comparison group (effect sizes ranged from d = 0.00 to 0.02), further investigations into neuropsychological impairment rates revealed that a subset of individuals in the PTSD group (15.6%) experienced global neurocognitive impairment (scoring 1.5 standard deviations below the mean of the comparison group on more than two tests). These findings suggest that a subgroup of participants who experience symptoms of PTSD might potentially display heightened levels of cognitive impairment. This discovery contributes to the expanding body of literature delving into the cognitive profiles of individuals with PTSD. Moreover, these results indicate the likelihood of distinct disease-related characteristics exerting a more pronounced influence on cognition. Such factors that have been proposed are dissociative symptoms and depression (Cohen et al., 2013; McKinnon et al., 2016). Further research is needed to elucidate what characteristics are associated with the proportion of individuals with PTSD who experience cognitive impairment and examine if the nature and/or intensity of their PTSD symptoms vary.

Looking at cognitive differences between the PTSD group relative to the comparison group at FU1 revealed different results. Similar to a previous study examining the longitudinal differences between participants with and without PTSD, Yehuda et al. (2016) results' revealed that group differences on neurocognitive measures between both groups (i.e., PTSD+/PTSD-) were no longer discernible during the follow-up period. To our knowledge, no other studies have examined RCI rates in individuals with PTSD. Our results revealed that a greater proportion of participants in the PTSD group (5.7%; 7%) experienced clinically significant decline in relation to the comparison group (4.1%; 5.2%) in the domain of learning and memory (i.e., RAVLT

immediate and RAVLT delay respectively). Similarly, a recent study explored the association between PTSD and cognitive deterioration over time (Roberts et al., 2022). Their findings revealed that an elevated count of PTSD symptoms corresponded to a more pronounced degradation in cognitive functioning over time, with the largest differences observed in the domain of learning and memory (Roberts et al., 2022). Other studies have also noted greater decline in the domains of learning and memory (Vasterling et al., 2018; Schuitevoerder et al., 2013).

To delve deeper into memory processes that potentially suffered a more pronounced impact among participants screening positive for PTSD, post-hoc analyses were conducted. These analyses aimed to explore whether the PTSD group exhibited a more significant decline in the rate of retention between the RAVLT immediate and RAVLT delay tasks. This investigation was driven by the heightened susceptibility of individuals with PTSD to developing dementia, as indicated by previous research (Günak et al., 2020). The findings indicated that the PTSD group did not exhibit any differences in the rate of retention between the RAVLT immediate and the RAVLT delay. These outcomes imply that individuals within the PTSD group might encounter heightened challenges in the initial encoding or learning phase of information during the RAVLT immediate task. This difficulty in early information acquisition is likely to lead to lower scores on the RAVLT delay task.

Other studies have also employed cognitive psychology models highlighting the stages of episodic memory processing—encoding, storage, and retrieval. Numerous other studies have demonstrated that individuals with PTSD exhibit deficiencies in initial learning. However, they tend to experience minimal forgetting over time. Additionally, during recognition trials, these individuals often recall supplementary information, reducing the demands on retrieval. This trend is evident in various studies (Scott et al., 2015; Golier et al., 2006). This collective body of findings

strongly indicates that PTSD-related episodic memory deficits are linked to issues in strategically encoding and retrieving information. In line with previously mentioned cognitive functioning models of PTSD, prefrontal systems (executive functioning) are also likely contributing to the memory dysfunction observed in PTSD (Scott et al., 2015; Golier et al., 2006).

When considering both studies collectively, Study 1 underscores that participants in the PTSD group display lower performance levels at baseline on certain aspects of executive functioning relative to those in the comparison group . Moreover, a substantial subset within the PTSD group encounters clinically significant impairment on measures of executive functioning or on cognitive tasks relying on prefrontal systems, such as prospective memory. In tandem, Study 2 reveals that a larger subset of participants in the PTSD group undergoes a decline that initially seems to manifest within the memory domain. However, delving deeper into memory processes demonstrates that the challenges are intertwined with the encoding or retrieval of information processes which are reliant on the functioning of prefrontal systems. Both studies converge in suggesting that PTSD is linked to greater difficulties in higher-order cognitive processes hinging on prefrontal systems. However, the transition of the neurocognitive tasks on which these primary challenges manifest appears to shift over time.

Future studies should investigate, over a prolonged period, how the trajectory of cognitive change evolves with time and age in individuals with PTSD. This could be achieved by conducting longitudinal studies spanning multiple years incorporating comparison groups and recurrently evaluating symptom severity. Such investigations would serve to mitigate the influence of cohort-related variables and address the typical variation in symptom progression that impacts cognition.

Study 3 set out with the objective of focusing on a specific characteristic within the PTSD group, seeking to discern whether this approach would yield variations in the pattern of

cognitive change. To our knowledge, Study 3 was the first study that examined the differences in cognitive performance between veterans with PTSD and civilians with PTSD. After accounting for TBI, there were no significant differences observed in cognitive profiles between veterans and non-veterans who screened positive for PTSD. These results are in line with prior research suggesting that, while veterans and non-veterans initially exhibit similar cognitive scores, veterans tend to experience a more rapid cognitive decline as they age, unlike their non-veteran counterparts (Brown et al., 2014; Padula et al., 2016). Although these earlier studies didn't factor in PTSD, our findings suggest that individuals with PTSD, regardless of their veteran status, might follow a parallel trajectory as both groups demonstrate comparable scores at baseline and three years later. Subsequent research should concentrate on contrasting the longitudinal neuropsychological profiles of veterans and non-veterans with PTSD as they enter older age. Such investigations should also consider the potential influence of cognitive reserve, as suggested by previous authors (Brown et al., 2014; Padula et al., 2016). The outcomes of our study emphasize the significance of taking into account the presence or co-occurrence of PTSD and TBI when evaluating the neuropsychological characteristics of veterans.

Cognitive Reserve

Our secondary research goal was to assess whether cognitive reserve proxies might offer a means to alleviate cognitive decline in participants who screen positive for PTSD, mirroring findings in individuals without PTSD (Bennett et al., 2003; Ewers et al., 2013; Stern et al., 1999). In summary, the outcomes from Study 1 and Study 2 collectively suggest that cognitive reserve proxies might exert a more significant influence on altering or postponing cognitive processes in individuals without PTSD than in those with PTSD. Incorporating findings from both Study 1 and Study 2, the moderation analyses revealed a notable trend: higher levels of perceived social support were linked to enhanced neuropsychological performance within the

comparison group. However, for the PTSD group, the impact of increased social support was either negligible or, in some cases, associated with a decline in neuropsychological performance. Heightened disturbances in arousal levels could potentially account for why individuals in the PTSD group might experience support in a distinct manner, in that it doesn't confer the same cognitive advantages as observed in the comparison group. As highlighted in Study 2, numerous theories shed light on how heightened arousal can hinder individuals' capacity to engage and connect socially in a meaningful and advantageous manner. The "window of tolerance" and the "polyvagal theory", for instance, converge in describing that excessively heightened arousal levels can impede effective engagement with both others and the environment (Siegel, 1999; Porges, 2017). These theories align well with cognitive functioning models, which posit that individuals with PTSD might disproportionately allocate their resources to affective processing and the associated regulation networks, at the expense of dedicating resources to higher-order cortical networks that are needed in social engagement/ support (Aupperle et al., 2012; Jacob et al., 2019; Scott et al., 2015). Supporting the latter, researchers have observed deficits in social cognition skills among participants diagnosed with PTSD, meaning that they struggle with comprehending and sharing others' emotional experiences (empathy) and encounter difficulties in interpreting other people's mental states (theory of mind; Mazza et al., 2011; Nietlisbach et al., 2010; Stevens & Jovanovic, 2019). These social cognitive abilities rely on prefrontal networks, which are also integral to executive functioning, known to be impacted in individuals with PTSD (Cristofori et al., 2019; Walker, 2009).

In addition, the interaction between group membership and education was found to moderate performance on a memory test (RAVLT delay). The results indicated that for the comparison group, higher levels of education were linked to enhanced performance on a memory task, although this relationship was not as strong for the PTSD group. This aligns with a similar

discovery made by Seil et al. (2019), who found that groups possessing greater levels of cognitive reserve proxies (assessed using education, marital status, employment, social support, social integration, and physical activity) were less prone to reporting confusion or memory loss. However, this association displayed a more pronounced impact on the comparison group compared to the PTSD group. These observations reinforce that cognitive reserve proxies might exert a more significant influence on altering or postponing cognitive processes in individuals without PTSD.

Strengths

Our studies had strengths that allowed us to further understand the neurocognitive profile of individuals who screened positive for PTSD and how cognitive reserve proxies may impact such profile with age. Most studies examining the neurocognitive profiles of individuals with PTSD draw participants from clinical settings, where higher levels of impairment are often present. In contrast, our present study used a community sample. This choice allows our results to potentially offer a more precise depiction of the average severity of PTSD symptoms and, consequently, the extent of observed cognitive deficits. In conjunction with the substantial sample sizes in both Study 1 and Study 2, the CLSA utilized a nationally stratified sample that encompassed participants from the 10 Canadian provinces. This comprehensive approach provides a more precise representation of cognitive challenges potentially faced by Canadians who screen positive for PTSD. This is particularly noteworthy because most previous studies have focused on investigations conducted within the United States that employ convenience sampling. Lastly, owing to the extensive array of variables collected within the framework of the CLSA, we were able to control for a multitude of factors that impact cognitive performance.

Limitations

We must also acknowledge some limitations to the studies reported here. In terms of internal validity, it is worth considering the potential threats posed by mortality and attrition. Given the longitudinal nature of the study, the attrition or loss of participants over time could introduce bias to the results. Participants who experience escalating cognitive impairment might opt to withdraw due to the increasing demands of the study, resulting in their exclusion from follow-up data. To address this, we conducted analyses to examine the characteristics of participants lost to follow-up at FU1. Furthermore, the issue of repeated testing surfaces due to the use of the same neuropsychological measures every three years (Raina et al., 2019). To counteract this issue, we made efforts to account for practice effects in the RCI calculations, as suggested by Duff (2012).

In addition, a cautious interpretation of these results is warranted due to the secondary data analysis design, which precludes assumptions of causality. Existing research indicates that cognitive deficits and PTSD are interconnected in a bidirectional manner, wherein they both serve as risk factors and consequences (Jacob et al., 2019; Vasterling & Brailey, 2005). Therefore, our study cannot definitively ascertain whether PTSD causes cognitive decline or if pre-existing cognitive deficits predispose individuals to developing PTSD.

Furthermore, certain limitations are associated with the specific measures employed in the three aforementioned studies. Initially, the determination of PTSD status relied on self-report questionnaires, which inherently hinge on participants' comprehension of the language used to identify traumatic events (i.e., meeting DSM diagnostic criteria A) and their ability to assess symptom severity without clinical guidance. For this reason, clinician-administered structured interviews are generally favoured. Additionally, the duration since the onset of PTSD symptoms,

and the nature of the traumatic incident(s) are not recorded. Notably, interpersonal traumatic experiences have a greater impact on post-trauma interpersonal functioning than other types of trauma (Charuvastra & Cloitre, 2008). Furthermore, the symptoms were only captured at the baseline assessment, introducing the possibility that participants may no longer have met the threshold for PTSD at the follow-up assessment (three years later). Alternatively, participants might have encountered a traumatic event between the two assessment points that triggered the emergence of PTSD symptoms. Previous studies have underscored that the severity of PTSD symptoms can affect outcomes on neuropsychological measures (Yehuda et al., 2006).

Both Study 1 and Study 2 have strong external validity due to their use of expansive sample sizes. However, it is worth acknowledging that the limited time-points of measurements could potentially influence the external validity of these studies. Cognitive decline is not a static phenomenon; an individual's performance can vary from one day to the next, and a single follow-up measurement of cognitive abilities might not accurately capture the participant's genuine experience of decline. Regrettably, cognitive measurements were not yet available for the FU2 data of the CLSA. In forthcoming research, it would be prudent to explore growth curve analysis, incorporating multiple time points to thoroughly assess the trajectory of cognitive change as individuals with PTSD as they age.

Within the scope of Study 3, the external validity is notably weaker due to the constraints imposed by the limited number of participants. Statistical power should be enhanced in future studies by expanding the sample size of veterans with PTSD, which could contribute to more robust and broadly applicable findings. Although the proportion of female veterans in our sample mirrors the lower representation of women in the Canadian military, the restricted scale of our study's sample hampers a comprehensive examination of how sex and gender might influence these findings.

Conclusions

In conclusion, this thesis sought to quantify the extent of cognitive changes associated with PTSD across a diverse array of middle-aged and older adult samples, including veterans. Additionally, it delved into the exploration of potential lifestyle factors that could serve as cognitive reserve mechanisms, potentially mitigating cognitive decline as participants with PTSD age. The outcomes revealed compelling evidence that a subgroup within the PTSD cohort exhibited initial impairments in tasks necessitating executive functioning. Notably, these participants also demonstrated a clinically significant decline in executive function tasks at the first follow-up assessment. Interestingly, it emerged that within the PTSD group, veterans' cognitive profiles did not diverge significantly from those of non-veterans over the span of three years, after controlling for TBI. Regarding cognitive reserve, Studies 1 and 2 suggest that cognitive reserve proxies may have a more significant impact on modifying or delaying cognitive processes in individuals without PTSD compared to those with PTSD.

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