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Cognitive changes during the menopause transition

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Thesis Abstract

Menopause is a natural stage in the reproductive ageing process for midlife women. The transition to this stage leads to the reduction in and fluctuation of oestrogen which leads to the development of many symptoms including cognitive symptoms. The primary aim of this study was to examine how menopause stage influences cognitive performance as during this transition, many women report cognitive challenges such as forgetfulness, poor concentration, foggy thinking, working memory changes, changes in retrieval speed and increased distractibility. This is the first study to use a comprehensive self-report tool to assess executive functions alongside laboratory-based cognitive tasks, enabling a broader understanding of cognitive performance across different menopause stages.

Participants in this study were women aged between 35-65 years, who were either premenopausal, perimenopausal or postmenopausal. This study involved two distinct groups of women. For the online study, a self-report measure was used to assess executive function by way of a questionnaire which also asked various lifestyle questions. For the in-person study, women took part in laboratory-based tasks assessing processing speed, working memory and selective attention and inhibitory control alongside completion of the same self-report measure of executive functions.

Chapters 1 of the thesis begins by providing background on menopause and reviewing the literature on cognitive challenges commonly experienced by midlife women. This Chapter also includes a review of measures used to assess cognition in existing menopause research. The section concludes by outlining the aims of this thesis and how it seeks to contribute and build on existing literature.

Chapters 2 and 3 of this thesis examine the relationship between menopause stage and cognitive performance in midlife women. Chapter 2 presents findings from an online study that examined executive function across menopause stages, revealing that

perimenopausal women reported poorer executive functioning than premenopausal women, independent of age. In contrast, Chapter 3 describes an in-person study that found no significant differences in cognitive performance across menopause stages in domains such as processing speed, verbal working memory, selective attention, and inhibitory control.

Importantly, both studies demonstrated that menopause symptoms significantly influenced cognitive performance, suggesting that symptom severity may play a more influential role than menopause stage alone. Additionally, socio-behavioural factors such as caring responsibilities, alcohol consumption, diet quality and sleep quality were also found to influence cognitive outcomes. Chapter 4 further explored the relationship between subjective and objective measures of cognition and found no significant correlations between self-reported cognitive performance and its corresponding laboratory-based tasks.

Taken together, these findings highlight that while menopause stage may have some influence, menopause symptoms and other external factors are also associated with cognitive performance during midlife. This thesis contributes to the existing literature by examining a range of cognitive domains, including executive functions by considering the broader context of reproductive ageing. The results also highlight the need for further research into the cognitive effects of menopause while considering modifiable lifestyle factors. This research has the potential to inform decision-making within the context of menopause while reassuring women by validating their concerns.

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Psalm 94:18–19: *When I thought, "My foot slips," Your steadfast love, O LORD, helped me up. When the cares of my heart are many, your consolations cheer my soul.* Thank you for seeing me through

Abbreviations

Analysis of Covariance (ANCOVA)

Backward Digit Span (BDS)

Behaviour Rating Inventory of Executive Function - Adult (BRIEF-A)

Behaviour Regulation Index (BRI)

Building Research Establishment (BRE)

Chartered Institute of Personnel and Development (CIPD)

Confidence Interval (CI)

Executive Function (EF)

Final Menstrual Period (FMP)

Follicle Stimulating Hormone (FSH)

General Practice Physical Activity Questionnaire (GPPAQ)

Greene Climacteric Scale (GCS)

Hormone Replacement Therapy (HRT)

Lower Limit (LL)

Luteinising Hormone (LH)

Menopause Transition (MT)

Metacognitive Index (MI)

National Education Opportunities Network (NEON)

National Institute of Child Health and Human Development (NICHD)

National Institute on Aging (NIA)

North American Menopause Society (NAMS)

Number (N/n)

Office of National Statistics (ONS)

Pittsburgh Sleep Quality Index (PSQI)

Polycystic Ovary Syndrome (PCOS)

Prefrontal Cortex (PFC)

Primary Ovarian Insufficiency (POI)

Stages of Reproductive Aging Workshop (STRAW)

Standard Deviation (SD)

Study of Women's Health Across the Nation (SWAN)

Symbol Digit modality Task (SDMT)

The National Institute of Clinical Excellence (NICE)

Upper Limit (UL)

Wechsler Adult Intelligence Scale (WAIS)

Working Memory (WM)

World Health Organization (WHO)

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Conference presentations

- Conference Presentations: Sections of Chapter 2 and Chapter 3 have been presented at the following conferences:
- Poster Presentation: International Menopause Society 2024
- Applied Vision Association (AVA) Spring Meeting 2025
- European society for cognitive psychology 2025
- Oral Presentation: University of Nottingham Doctoral Training Partnership Conference 2024

1 Chapter 1 The menopause transition

1.1 Significance and focus

There is a growing awareness of menopause and how it affects women in their relationships at work, home and within their social circles. For many healthy women, this transition is uneventful (Hunter & Rendall, 2007), However, with more women speaking up about their journey, it is becoming clear how negatively menopause associated symptoms affects some working women (CIPD, 2023). Previously, women had inadequate knowledge around the issue of menopause, but the current climate suggests a shift in behaviour. This is being driven by healthcare professionals, employers, celebrities and some government officials encouraging more women to speak publicly about the topic of menopause in order to normalise the experience for many women. Channel 4's documentary on Menopause by Davina Mcall, Dame Kelly Holme's discussions about her struggles with perimenopause and Carolyn Harris (MP) (Chair of the All-parliamentary group on menopause) are just a handful of the people encouraging a wider public discussion of menopause. There is still a fair way to go in defining what it means to experience a 'normal' menopause, but the work is ongoing and further research is needed to better understand this universal experience. Understanding menopausal experiences is essential, particularly as previous research highlights the potential neurological implications of this transition for some women.

Menopause, marked by hormonal fluctuations is a natural stage of reproductive aging and each woman has a unique experience. While many women navigate menopause without facing long-term adverse effects and continue to enjoy good overall health, a considerable number are susceptible to neurological challenges that may emerge during this transition (Brinton et al., 2015). Some women report menopausal brain fog, characterised by cognitive challenges such as concentration difficulties, difficulty in recalling words or numbers,

forgetting events such as appointments, being easily distracted, misplacing items such as keys and forgetting the purpose of a behaviour such as entering a room and forgetting why (Sullivan Mitchell & Fugate Woods, 2001). According to Epperson et al. (2015), reports of cognitive challenges especially within the domains of executive functions (EFs) are frequently observed in menopausal women and have been linked to a decline in quality of life (Greendale et al., 2020).

Executive functions refer to an umbrella term for cognitive processes that is utilised daily in our lives. These include initiation, planning and organisational skills, regulating emotional responses, problem solving and also being able to retain information and use it at a later date (Gioia et al., 2001 & Chan et al., 2008). Research on these cognitive processes in menopausal women is limited in scope with some studies not fully capturing the experiences of women across the reproductive stages. The primary aim of this thesis to examine how menopause stage influences cognition through the of use self-report and laboratory-based measures to assess cognition. The research in this thesis is one of few studies that has used both measures to assess cognition. This thesis also goes further to expand on the cognitive domains assessed and explore how other menopause-associated factors influence cognition.

To fully comprehend the cognitive implications of menopause, it is essential to consider the underlying biological changes that occur across reproductive stages. In the following sections, I will discuss key aspects of menopause including its aetiology, staging criteria and role of oestrogen on brain function. The cognitive experience of menopausal women will also be discussed. I will also broaden the discussion to include menopause-associated factors and how this impacts cognition while importantly expanding the cognitive focus to include executive functions as this is a focus in this research.

1.2 Aetiology

Menopause transition (MT) refers to the period when the first signs of menopause appear right up until at least 12 months after the final menstruation period (Burger et al., 2002). The menopause transition is characterised by a significant variability in ovarian follicle development, bleeding patterns and fluctuations in oestrogen levels (Hall, 2015). The ovaries and their follicles play a central role in determining the timing of menopause with number of ovarian follicles determined to be around 6-7 million by 20 weeks gestation and depleted to around 300,000 by puberty by apoptosis (Davis et al., 2015). A woman experiences about 400 to 500 menstrual cycles during her reproductive lifespan (Nejat & Chervenak, 2010). During this time, most of the oocytes or eggs in the ovaries break down naturally and undergo a programmed cell death. This eventually leads to a gradual decline of viable egg cells till there are none left. This decline ultimately causes the ovaries to lose their reproductive function, resulting in menopause which usually begins between the ages of 45 and 55 (Nejat & Chervenak, 2010).

Thus, across the various stages of a woman's life, starting from gestation and ending after menopause there is a steady decline in ovarian follicle numbers (Block, 1952). The reason for ovaries beginning their functionality at puberty and ceasing this at menopause remains unclear (Broekmans et al., 2009; Davis et al., 2015). The functional lifespan of ovaries has been attributed to factors such as genetic, hormonal, lifestyle and environmental factors (Davis et al., (2015). In addition, reproductive ageing is not a discrete event but a process with several stages that involves physiological changes such as hormonal and ovarian changes which are part of broader neuroendocrine events. These neuroendocrine events are discussed in the next section.

1.3 Physiology

The physiological process of menopause in ageing women is mediated by the hypothalamic-pituitary-ovarian (HPO) axis. The hypothalamic-pituitary-ovarian (HPO) axis is a closed-loop negative feedback system responsible for controlling reproduction and is considered critical for immune system function, puberty and reproduction (Ellington et al., 2022). Two hormones, luteinizing hormone (LH) and follicle-stimulating hormone (FSH) help regulate the reproductive system. These hormones are released by gonadotrophs in the anterior pituitary which is triggered by another hormone called the gonadotropin-releasing hormone (GnRH) released from the brain's hypothalamus (Burger, 2008).

LH and FSH regulate ovarian function by stimulating the growth of ovarian follicles and triggering ovulation. In response, the ovaries send signals that lead to the production of oestrogen and progesterone in women (Ellington et al., 2022). These hormones regulate the menstrual cycle and provide feedback to the brain to regulate LH and FSH. As primary ovarian follicles start to diminish during menopause, there are not enough follicles to secrete oestrogen to modulate the effects of FSH (Peacock et al., 2023). This results in no LH surge and ovulation leading to a decline in the production of oestrogen and cessation of menstruation eventually (Peacock et al., 2023). The clinical manifestations of menopause result from these neuroendocrine changes as the transition to menopause is a period of hormonal instability (Ellington et al., 2022).

The critical factor during the phase leading up to menopause known as the menopause transition is the decline in ovarian function which leads to the change in oestradiol circulating in the blood. There is a dramatic change in oestradiol and follicle-stimulating hormones during the transition to menopause, and this oestradiol begins to drop noticeably as a woman approaches the final menstrual period (FMP). The FMP can only be recognised in retrospect as a woman is confirmed to have

reached menopause when she has gone 12 consecutive months without experiencing a period. Typically, the levels of oestradiol begin to decline around two years prior to FMP and continues to do so for approximately two years after menopause with stabilisation also being achieved during this period (El Khoudary et al., 2019). The trajectory for FSH is different with levels of FSH increasing much earlier, approximately seven years prior to menopausal transition with stable levels being achieved two years after FMP (El Khoudary et al., 2019). On average, increased levels of FSH detected via serum assays and decreased oestradiol levels are observed during the menopause transition (Randolph et al., 2011) but serum markers on their own cannot be used to diagnose menopause. To fully understand the physiological changes associated with menopause it is important to look beyond hormone levels alone. The following section discusses the timings and progression of menopause as well as the role of genetic factors.

1.4 Timings of menopause

The phase leading up to complete cessation of menstrual cycles (i.e. FMP) typically spans about two to eight years and is referred to as the perimenopause phase or menopause transition (Ellington et al., 2022). The changes observed during this period are attributed to the variability in LH/FSH secretion, oestrogen decline and lack of follicular development (Ellington et al., 2022) and this leads to the gradual changes women experience with regards to their menstrual cycle regularity and monthly fertility (Broekmans et al., 2009). Tepper et al. (2012) also demonstrated that all women demonstrate the same pattern of oestradiol and FSH decline. Soules et al. (2001) note that this process is marked by hormonal shifts and clinical characteristics, with manifestations of reproductive ageing seemingly differing by race, ethnicity, cultural background, geographic region and socioeconomic status. This could somewhat explain the variation in menopause experiences for different women as they transition to menopause.

Genetic factors have also been implicated in the timings of menopause and involved in the processes that direct reproductive ageing. A complex interaction of genetic, epigenetic, lifestyle factors such as smoking, never having given birth and socioeconomic factors also influence menopause timing (Davis et al., 2015). There is also a lack of consistency in these factors in explaining menopause timings (Kok et al., 2005). However, the role of genetic factors in determining menopausal timings is of increasing interest and Morabia et al. (1998) and Murabito et al. (2005) have discussed how associations have been made between menopausal age of mothers and daughters as also with sister pairs. Genetic effects have been attributed to an estimated 50% of the inter-individual variability in menopausal age (Murabito et al., 2005). A study of 551 women by Torgerson et al. (1997) showed that there was a strong relationship between mothers and daughters when it comes to menopausal age. That is, the likelihood of some women reaching early menopause is high when their mothers or other close relatives have previously undergone early menopause. The estimates for the heritability in menopausal age range from as low as 30% to as high as 85% (Kok et al., 2005). The genetic traits that underlie this heritability has not been clearly identified and studies showing links between genes encoding factors involved in menopause have also not revealed this (Davis et al., 2015).

To conclude, the loss of ovarian follicular function which marks the end of monthly periods signals the transition to menopause (Maki & Henderson, 2016; Shanmugan & Epperson, 2014). A woman is said to have reached natural menopause when she has gone 12 consecutive months without experiencing a period and there is no obvious physiological or pathological cause as it is a natural life stage for women. This also marks the beginning of the postmenopause phase. At this point, the ovaries would have stopped releasing eggs for fertilisation. The period between reproductive stage and non-reproductive stage is referred to as the menopause transition or perimenopause stage and culminates in the final menstrual period.

Women in the perimenopause stage experience irregularities or variabilities in duration of their menstrual cycle. The endocrinology and biology of the menopause which marks the end of a woman's reproductive years transition is complex and it is also not possible to predict when a woman will experience menopause but associations between age at menopause, genetic factors and demographic factors exist. Menopause is a multistage process that unfolds over several years. There are several distinct phases associated with this process. In the following section, I explore these stages and outline how they are defined in research as this allows for better interpretation of cognitive and symptom changes.

1.5 Menopause definition and staging

As previously mentioned, menopause is defined as when a woman has not had a menstrual period for 12 consecutive months, with no other underlying cause. In all these cases, there is a marked decline in ovarian-derived sex hormones such as oestrogen and progesterone (Prakapenka & Bimonte-Nelson, 2018). According to the British Menopause Society (2024), natural menopause occurs at the approximate age of 51 years in the UK. Soules et al. (2001) notes that menopause typically occurs at a relatively broad age range (42-58) in healthy women. Menopause is deemed premature if it occurs before the age of 40. Globally, menopause occurs at an earlier age in women from Latin America, Asia, Africa and the Middle East whereas women from North America, Europe and Australia experience it later (Palacios et al., 2010 & Davis, 2015). According to Santoro, (2005) menopause transition occurs in stages and can last for several years.

The stages of menopause can be classified into three main groups based on menstrual or bleeding patterns. The premenopause stage is defined as regular monthly cycles, perimenopause stage is defined as having irregular monthly cycles and finally the postmenopause stage as not experiencing a monthly cycle for 12 consecutive months and

more. The perimenopause stage is the transitional phase that precedes menopause and is associated with significant symptom burden (Cunningham et al., 2025). Research studies on menopause have previously used the World Health Organization (WHO) criteria, menstrual patterns, or their own criteria to stage women going through the menopause. In recent times however, the Stages of Reproductive Aging Workshop (STRAW) classification method has been recommended by the American Society for Reproductive Medicine in conjunction with the National Institute on Aging (NIA), the National Institute of Child Health and Human Development (NICHD) and the North American Menopause Society (NAMS). This standardised system of classification provides a consistent classification of natural menopause status from the reproductive years to the time of menopause and as such has been adopted in this thesis project. Just as there is a useful staging system for girls going through puberty (Marshall-Tanner staging), (Marshall and Tanner, 1969), there is a similar staging for women going through the menopause.

The STRAW system also assists the research community to have uniform scientific data regarding events correlated with menopause leading to less inconsistencies in findings. In this study, the STRAW system was used whereby menstrual cycle or bleeding patterns is used to classify a woman's reproductive age into three main stages: reproductive or premenopause, menopausal transition/perimenopause and postmenopause. This approach relies on observable changes in menstrual regularity which are considered reliable indicators of reproductive ageing. Each of these stages are further broken down into substages which includes: the early, peak and late reproductive stage (premenopause); the early and late menopause transition (perimenopause), and finally the early and late postmenopausal phase (postmenopause). In this research, I categorised women based on self-reported menstrual cycle patterns into the three main reproductive stages as participant numbers were insufficient for substage distinctions. Although the STRAW also includes biomarkers such as

FSH and symptom characteristics for menopause staging, this study focused mainly on menstrual patterns due to practical and methodological considerations. This approach aligns with previous research (Unkenstein et al., 2016; Jaff et al., 2020; Martino et al., 2022) which also utilised menstrual cycle data alone and thus allows for comparisons across other studies.

However, future studies should consider including STRAW substages as Greendale et al. (2010) highlighted significant differences between early and late perimenopause. These differences may reflect distinct hormonal environments, which could have varying implications for symptom presentation and cognitive outcomes. As discussed earlier in Section 1.3, there is a dramatic change in oestradiol levels during the menopause transition. This period of physiological and hormonal changes also involves the development of various symptoms associated with menopause.

Few studies have considered how the menopause experience riddled with changes including menopause-associated factors relate to cognitive change including executive functions. Aside cognitive impairments, there are factors associated with menopause which may potentially influence executive functioning and are discussed in the following section.

1.6 Relationship between menopause-associated factors and cognition

While some women transition through menopause with minimal discomfort, others experience a range of symptoms, with a small proportion reporting them as severe. Some women experience a myriad of symptoms including physical, vasomotor, sexual and affective changes which could have adverse effects on EF. Some studies have shown executive function changes served by the prefrontal cortex being sensitive to oestrogen (Joffe et al., 2006; Rapp et al., 2003). However, it is important to consider whether menopause symptoms themselves play a broader role in influencing executive function than hormonal fluctuations associated with menopause stage and this was of

interest in this thesis. The observed changes in executive function may not be directly caused by oestrogen decline alone but could result from the indirect impact of menopause-associated factors such as sleep disturbances, psychological issues and menopause symptoms. These symptoms rarely occur in isolation and are often present concurrently with other symptoms (Duralde et al., 2023). A review report by El Khoudary et al. (2019) noted that up to 80% of women of 3,302 women in the Study of Women's Health Across the Nation (SWAN) study reported vasomotor symptoms and sleeping difficulties. These symptoms were most prevalent in perimenopausal women which is consistent with findings reported by Gold et al. (2000).

The range of symptoms reported by women are seemingly unrelated but can be grouped into four categories according to Greene (1998). These are psychological, physical/somatic, vasomotor and sexual symptoms. In fact, the list of symptoms associated with menopause are numerous and the Greene (1998) scale for example tracks a comprehensive list of 21 items associated with menopause. Clinical studies have shown that the symptoms that are commonly associated with menopause are vasomotor symptoms such as hot flushes and night sweats, vaginal dryness and sleeping difficulties (National Institute of Health, 2005). Other symptoms include depression, headaches, irritability, joint and muscular pain, tiredness, panic attacks and loss of libido (Greene,1998; National Institute of Health, 2005). The barrage of symptoms that some women suddenly must contend with when they reach this stage in their midlife means some women are often dismayed and puzzled by these changes in their memory, behaviour, sleep patterns and urogenital habits (O'Leary, 1998; Harper et al., 2022). This was a common theme found in conversations with women during recruitment outreach (see Appendix 1) with details of some recruitment events for this current project. Thus, women navigating menopause are often faced with a range of issues such as physical, low moods and cognitive challenges which can contribute to strained relationships. While it can be difficult to distinguish symptoms directly linked to menopause from those linked to broader factors like

cognitive ageing, the increased number of women seeking clinical support during midlife underscores the significance of this transition (Maclellan et al., 2023).

Nevertheless, what remains clear is that during midlife when menopause occurs, more women seek help from clinicians to cope with menopause transition (Maclellan et al., 2023) and these symptoms are valid and cannot be ignored. While potential associations between menopausal symptoms and cognition have been explored, most studies have focused primarily on affective and vasomotor symptoms (Zhu et al., 2022) rather than examining the overall symptom burden. For instance, a study in the US by Greendale et al. (2010) of 1903 midlife women with a mean age of 45.64 showed depressive symptoms being significantly associated with processing speed. Another study in the US by Weber et al. (2012) of 75 perimenopausal women with a mean age of 49.3 years also showed significant associations between memory complaints and anxiety, depression and somatic complaints. In terms of vasomotor symptoms Jaff et al. (2020) in a study of 702 sub–Saharan African pre-, peri- and postmenopausal women also found significant associations between hot flushes and processing speed. Taken together, these findings demonstrate a negative association between menopause symptoms and cognition. However, as mentioned earlier, menopause symptoms rarely occur in isolation, and it is important to consider the overall effect of the various menopause symptoms on cognition with a focus on both subjective and objective measures of cognition. This gap is important and warrants further investigation, which is addressed in the present research.

Another menopause-associated factor to consider is sleep disturbances especially as sleep disorders are among the most commonly reported issues during the menopausal transition (Lee et al., 2019; Joffe et al., 2010; Maki et al., 2024). Poor sleepers complain of cognitive impairment, and this can result in poor performance professionally and broader societal consequences (Garbarino et al.,

2016). This is especially important to consider since studies by Xu and Lang (2014) and Maki et al. (2024) have shown a high prevalence of menopause-associated sleeping difficulties. Given its widespread occurrence and potential for modification through lifestyle interventions, sleep disturbance was a particular focus in this research due to its broad impact and possible independent effects on cognitive functioning.

Several studies have explored the relationship between sleep quality and cognitive function in older adults. For example, a cross-sectional study by Wiranto et al. (2024) examined the relationship between self-reported sleep quality and executive functions in females (n = 118) and males (n = 89) all aged 60 and above. Findings from the study showed that poor sleep quality was associated with poorer executive function in females, but not in males. Similarly, Jelicic et al. (2002), using a population-based sample of 838 adults over 50, showed that self-report sleep complaints predicted cognitive decline over a period of 3 years in middle-aged and older adults even after controlling for age, sex, health factors, and length of follow-up interval. Additionally, Nicolazzo et al. (2021) found that individuals reporting poorer sleep quality also experienced subjective cognitive concerns, particularly in working memory and attention. Their sample consisted of 1421 middle-aged male and female Australian residents aged 40 to 70 who completed self-report questionnaires on sleep. This finding highlights the impact of sleep quality on cognition and the importance of considering this factor in menopause research.

While many studies have examined sleep quality across both sexes, others have focused on specific menopausal stages such as postmenopause (Regestein et al., 2004) or perimenopause (Weber et al., 2012). In research focused on these menopausal populations, the findings are more nuanced. Regestein and colleagues (2004) showed that in 88 healthy postmenopausal women, self-report scores for low sleep quality were associated with poorer cognitive performance. Weber at al. (2012) also in a study of 75 perimenopausal women found

that sleep disturbances were linked to self-report memory challenges. Interestingly, Berent-Spillson (2012), in a study of 67 menopausal women aged 42–61, reported no significant differences in self-reported sleep quality across different menopausal groups although lower cognitive performance was observed in the perimenopause group. These mixed findings suggest that the relationship between sleep quality and cognition may be influenced by menopausal stage but the mechanism underpinning this relationship remains unclear. Although sleep quality has been linked to cognitive decline in existing literature, its impact on executive functions in menopausal women is underexplored. It is unclear whether sleep disturbances directly impair executive functions or whether menopause stage also plays role. This gap in the literature warrants further investigation and is one of the foci of Chapters 2 and 3, where I examine the relationship between sleep quality and cognition in midlife women across different menopausal stages.

Another factor that may influence executive function difficulties during perimenopause is Hormone Replacement Therapy (HRT). This is recommended by The National Institute of Clinical Excellence (NICE) as a coping mechanism for some of the symptoms associated with menopause transition such as vasomotor symptoms, sexual dysfunction and genitourinary syndrome of menopause. In a 2002 survey by Social Issues Research Centre (SIRC) of 200 women, 50% of the respondents continued in their careers as a result of being able to manage their menopause symptoms through the use of HRT. Results from studies investigating the effect of HRT on cognition have been mixed with some reporting positive effects (Shaywitz et al., 2003; Tierney et al., 2009). However, a study by Lethaby et al. (2008) concluded that HRT did not protect against cognitive decline in menopausal women. These studies have focused on postmenopausal women. Studies on effect of HRT on cognitive performance is needed in perimenopausal women as these women during the transition report the worst symptom burden (Ho et al., 1999 & Rautenberg et al., 2023).

As such an exploratory analysis on the role of HRT on executive functions was examined in this study as many perimenopausal women indicated being on HRT during the subjective measure study in Chapter 2.

Several socio-behavioural factors such as age and educational attainment, physical activity, alcohol consumption, diet and hours spent working and caring responsibilities (looking after elderly relatives) have been associated with cognitive performance in the general literature. These modifiable lifestyle factors were explored in this thesis to better understand their potential influence on cognition during the menopausal transition, an area with limited studies. In terms of physical activity and alcohol consumption for instance, a study by Cassidy et al. (2004) used a self-report questionnaire to investigate associations between some modifiable lifestyle factors such as alcohol consumption and physical activity on cognition in a community sample of 278 women aged 70 years and over. In this study, moderate levels of alcohol consumption were linked to better performance on some executive function tasks such as mental flexibility. However, Cassidy and colleagues found no significant associations between physical activity and cognition. In contrast, Yaffe et al. (2001) reported the benefits of physical activity on cognition in 5925 of community dwelling women who had no physical limitations and cognitive impairment. Yaffe and colleagues demonstrated that women with greater physical activity were less likely to experience a decline in cognition. This difference in finding could be as a result of the latter study relying on standardised and objective measures of physical activities as opposed to a self-report measure used by Cassidy et al. (2004).

Unlike previous generations, many women today are likely to be employed and working full time during the menopausal transition. Understanding the impact of long working hours is also important as evidence suggests that long working hours may impact cognitive performance. For instance, a longitudinal study by Virtanen et al. (2009) of 2214 British civil servants found that working longer hours

(>55 hours/week) in comparison to shorter hours (40 hours/week) was associated with a decline in cognitive performance. As well as balancing work, women may have caregiving responsibilities.
Most women will transition to menopause at a period when they take on multiple roles such as caregiving for elderly relatives (Saadedine et al., 2025). Mallya and Fiacco (2018) examined the effect of caregiving for people with dementia on cognitive function. Their samples included 57 informal caregivers of whom 81% were female and a comparison group of 97 non-caregivers of whom 72% were female. Mallya and Fiacco found that caregivers performed significantly worse than non-caregivers in cognition (mental flexibility and verbal fluency) and reported worse psychological well-being.
Diet quality is a modifiable lifestyle factor that may be beneficial for cognitive performance (Jia et al., 2023). A mini-review by Klimova et al. (2020) concluded that a healthy diet may potentially be one of the ways in which cognitive decline can be slowed as we age. In another review of impact of education on cognition Lovden et al. (2020) found that the years spent in formal education is positively correlated with cognitive performance. Taken together, these findings demonstrate how various socio-behavioural factors contribute to cognitive performance. Aside menopause and its associated potential challenges, these factors were examined to get a better understanding of midlife women's experience during this period in the presence of other lifestyle behaviours.

Despite the wide-ranging physiological and psychological changes associated with menopause along with the potential influence of socio-behavioural factors, few studies have examined how these experiences relate specifically to cognitive changes in particular executive functions which are essential for daily living and is of interest in this research. The following section discusses women's cognitive experience of menopause in existing literature.

1.7 Cognitive impairment during menopause: Expanding to executive functions

Some women experience a variety of symptoms including complaints of reduced cognitive functioning during this period of transition as discussed previously. A tendency towards poorer cognitive performance has been reported by some women to their healthcare providers during menopause (Maki & Henderson, 2016; Shanmugan & Epperson, 2014). Brinton et al. (2015) reported that while many women transition through perimenopause without experiencing any lasting negative effects, a significant number also emerge from the transition with an elevated risk of cognitive decline.

In studies conducted by Betti et al. (2001) and by Mitchell and Woods (2001), between 70% and 72% of women reported experiencing cognitive difficulties during perimenopause. In analysing data from the Study of Women's Health Across the Nation (SWAN), Gold et al., 2000 reported that in a sample of 12,425 women aged 40-55 years, 86% of menopausal women complained of forgetfulness in comparison to 31% of premenopausal women. This was before controlling for socio-demographic factors. However, after controlling for factors such as age, education, race, poor sleep and body mass index for example, perimenopausal women were still more likely to complain of forgetfulness in comparison to premenopausal women.

Some examples of menopausal women's complaints include difficulty with words or number list learning and recall i.e., verbal working memory, forgetting events and items such as appointments, household keys, disorganised behaviour and planning and concentration difficulties (Santoro, 2015; Mitchell & Woods, 2001). Warga (1999) categorised areas of cognitive difficulty experienced by women to include thinking (e.g. foggy thinking, mental slowness and difficulty prioritising), memory (e.g. forgetfulness, memory problems, mental flexibility, working memory retrieval speed and agility), speech problems (e.g. loss of words and word-finding difficulties, inefficiency in organising words and sentences, naming difficulties), behaviour and

praxis (e.g. forgetting how to write words and losing automatic skills and reduced fine motor coordination skills), attention (e.g. concentration difficulties, blanking out and easily distracted, listening but not actually engaging), spatial skills (e.g. changed navigation and planning skills, altered spatial skills for remembering faces and experiencing previously familiar places as unfamiliar) and lastly time management (e.g. experiencing a shift in time perception, a diminished ability to predict events with the same clarity). These examples are similar to the later findings by Santoro et al. (2015), Epperson et al. (2011) and Mitchell & Woods (2001). Some of these examples such as working memory, difficulties focusing and concentrating, mental flexibility and disorganisation are aspects of executive function. Taken together, this suggests a need to focus beyond commonly assessed domains such as memory and concentration difficulties but to include other related processes that work alongside these domains such as executive functioning which is discussed in the next section.

Another cognitive domain to consider is processing speed which has been examined in several studies on menopause-related cognitive changes (Jaff et al., 2020; Karlamangla, et al., 2017; Greendale at el., 2010). Kibby et al. (2020) defines processing speed as comprising of many components including perceptual, cognitive and decision-making. Hochstrasser et al. (2021) also discussed how processing speed tasks generally show the accuracy and speed with which participants perform tasks which can include visual or auditory processing, as well as naming and coding tasks. In summary, it demonstrates proficiency in automatic task execution, how information is accessed, encoded and processed, with most tasks requiring either a motor or oral response (Weiss et al., 2015). Performance on a processing speed task has been shown to predict performance across other cognitive tasks (Salthouse & Ferrer-Caja, 2003). This cognitive domain was therefore of interest, as it may provide valuable insights and serve as a basis for understanding other cognitive abilities. It has also been widely

examined in menopause research, though findings have varied and this is further explored in Section 1.11.

Given its relevance, processing speed has been included in various studies examining cognitive changes across the menopause stages including in this present research as it serves as a baseline in predicting performance across other tasks. For instance, Karlamangla et al. (2017) utilised longitudinal data from the SWAN study to assess cognitive processes including processing speed in 2,124 midlife community-based women. Karlamangla and colleagues reported significant within-women decline in processing speed. Similarly, Greendale et al. (2009) found a decline in processing speed during the menopause transition in a study of 2362 women categorised into premenopausal, early perimenopausal, late perimenopausal, postmenopausal and postmenopausal with current hormone use. Processing speed scores did not improve for late perimenopausal women in comparison to premenopausal, early perimenopausal, and postmenopausal women. Unkenstein et al. (2016) after covarying for age, also did not find any significant difference in processing speed in 130 premenopausal, perimenopausal and postmenopausal women. Schaafsma et al. (2010) also examined effect of processing speed in 120 pre-, peri- and postmenopausal women aged 45 to 60 years and found no differences in processing speed performance across the groups similar to Luetters et al. (2007) and Jaff et al. (2020), who also observed no group differences in processing speed related to menopausal stage.

These mixed findings in the literature may be attributed to differences in menopause staging criteria, the specific stages assessed, and the presence of co-morbid conditions such as HIV infection reported in the study by Jaff et al. (2020). Given the importance of processing speed as a foundational cognitive domain and its mention by women as a source of cognitive difficulty according to Conde et al. (2021), it was essential to examine this domain across menopause groups. It would also be useful for future research to also include not the core but also

the substages of menopause. This is particularly relevant given the findings by Greendale et al. (2009).

The cognitive complaints common during the menopause transition may be linked to the decline in ovarian function resulting in fluctuating oestrogen levels and cyclical hormonal changes. This cycle of hormonal changes, which takes place over several years, is responsible for a cascade of neurological changes that affect some women (Brinton et al., 2015). Additionally, according to Conde et al. (2021), cognitive changes occur more frequently in women than in men and as such this has been attributed to hormonal factors. Although cognitive complaints are not necessarily considered a key menopause symptom, their prevalence in research studies has been consistently reported and validated in research studies. For example, a study by Schaafsma et al. (2010) of 120 pre-, peri- and postmenopausal women aged between 45 and 60 years found that women's self-reporting of attention and memory problems in their daily lives was significantly associated with scores on memory and attentions tests. Another study by Weber et al. (2012) of 75 perimenopausal women of average age 49.3 also showed that memory complaints were associated with objective tests of working memory and complex attention. These suggest that during the transition, the cognitive complaints experienced by some women are valid and warrant further investigation.

Furthermore, most studies on subjective cognitive decline in adults have focused primarily on memory (Rabin et al., 2015). Rabin et al. (2015), in a review of 34 self-report measures across 19 international studies, found that approximately 60% of items assessed memory, followed by 16% on executive functions and 11% on attention. He et al. (2025), reviewing 28 menopause-related studies using self-report measures, identified that of the 15 cognitive domains assessed, majority focused on memory (n = 8), attention (n = 2), and multiple domains (n = 5) with the latter heavily skewed toward general memory and perceived cognitive impairment. Only five studies examined

executive functions, and just one assessed them across different menopause stages. Despite being a critical aspect of cognition, executive functions remain underexplored subjectively. Given this gap, my thesis includes a focused examination of executive functions which are discussed in more detail in the following section. While executive functions were briefly mentioned here and in sections 1.6 and 1.7 to provide context, Section 1.8 provides an overview of this cognitive domain including its relevance to daily life and characteristics.

This underexplored aspect of cognition warrants further examination given emerging evidence of menopause-related changes in this domain. For instance, Epperson et al. (2015) reported that menopausal women experience new-onset executive function difficulties, with symptoms resembling those of attention-deficit/hyperactivity disorder (ADHD), despite no prior diagnosis. Epperson et al. (2011) explored these concerns and results showed that cognitively intact perimenopausal and early postmenopausal women reported cognitive complaints in the executive function domains of organisation, working memory, focus and attention. As previously noted, common cognitive complaints during menopause such as difficulties with planning, organisation and working memory are core components of executive functioning. These complaints may be underpinned by disruptions in executive function domains which are closely linked to cognitive processes. As such, it is important to consider the neurobiological mechanisms that may underlie these cognitive changes and this is discussed in Section 1.9. One key factor is oestrogen, which has been shown to influence brain regions involved in executive functioning, particularly the dorsolateral prefrontal cortex (Shanmugan & Epperson, 2014). The following section discusses executive functions in general and its importance in our daily lives.

1.8 Executive Functions

Executive function involves cognitive skills that allow individuals to adapt to changing circumstances and pursue long-term life goals (Burgess & Simons, 2005). Diamond (2013) elaborated on key components of executive function relevant to these symptoms. As defined by Diamond (2013), working memory involves holding information in mind and using it later, mental flexibility refers to adapting to new rules or priorities, inhibitory control involves maintaining focus and regulating one's attention while resisting distractions. Additionally, Burgess & Simons (2005) describes executive functions as a range of skills such as the capacity to plan and organise over extended periods, make complex, abstract decisions, and manage and regulate memory processes. Various conditions are associated with executive function deficits or impairments. Individuals who are neurodivergent, have attention deficit hyperactivity disorder (ADHD), or experience dementia often face challenges related to executive functioning (Diamond, 2005; Shogren et al., 2021; Voss & Bullock, 2004). On the other hand, stronger executive functions are linked to better academic performance, higher quality of life, and greater success in the workplace (Bailey, 2007; Cragg et al., 2017; Davis et al., 2010).

These processes are particularly pertinent to the menopause transition, as they are largely dependent on the prefrontal cortex. This brain region has been implicated in the performance of a set of coordinated activities such as planning and organising an event and resisting temptation or inhibiting distractions from the environment (Shanmugan & Epperson, 2014). The neural structure and function of this brain region are modulated by ovarian hormones, notably oestrogen. The ability to concentrate on a task, recall names and numbers are examples of processes executed daily by many individuals as part of our daily lives and these are some of the examples (Santoro et al., 2015) that were given by menopausal women with complaints about their memory and concentration. These are closely linked to executive

functions which governs cognitive processes essential for managing our daily lives.

The important role of EF in our everyday life cannot be understated as EFs enable us focus on our attention on various tasks while planning and organising various activities essential for success in school or at work for example. Individuals with better EFs have a better quality of life (Davis et al., 2010), are better at resolving problems and more productive in the work environment (Bailey, 2007).

In literature, these executive functions can be divided into three core areas according to Miyake et al. (2000). These three core areas are inhibition and interference control, working memory (WM) and cognitive/mental flexibility (Diamond, 2013). On the basis of these core areas, higher order EFs which involve problem solving, planning, shifting, monitoring, organisational and reasoning skills are also developed (Diamond, 2013).

Summary of EF models

There are several models of EF processes such as working memory, response inhibition, attention shifting and from different perspectives such as a neurochemical, statistical and neuroanatomical angles (Hunter & Sparrow, 2012). According to Hunter & Sparrow, (2012), the definition of EF has either been by a description of its functions or its neuroanatomical links. Current models of executive function (EF) are increasingly informed by research examining both its development and decline across the lifespan, whereas earlier models were primarily based on studies of fully matured adult brains (Wiebe & Karbach, 2017).

An EF model proposed by Miyake et al. (2000) both demonstrated the unity of executive processes and the uniqueness of individual EF components by using simple experimental tasks that predominantly tasked specific EFs. In the study by Miyake and colleagues, 137 university students were recruited to perform tasks related to three key EFs – working memory, cognitive or mental flexibility and inhibitory

control. Confirmatory factor analysis approach was employed in the study by Miyake and colleagues in their study. This approach led to the extraction of an underlying commonality across different tasks being employed and to also identify underlying subcomponents or non-control processes that contribute to individual differences in executive function. Findings from the study demonstrated that despite each of the specific EF being substantially correlated (shared variance), they could also be seen as being distinct (correlations were far from perfect). This model also circumvented the task impurity and construct validity executive function research problem (Miyake et al., 2000). Miyake and Friedman's (2012) review expanded on the original 2000 framework by incorporating new findings and insights from research on individual differences in executive function. Their review discussed four key conclusions and focused on underlying cognitive mechanisms: first, it introduced a new focus on 'unity' or 'common EF' that is, a general control ability that is common across updating, shifting and inhibition; second, that genetic factors contribute substantially to the individual differences in EFs at both 'common EF' and 'diverse' levels, third, the individual differences in EFs are stable over time despite major life changes and lastly, EFs are strong predictors of behavioural outcomes such as successful dieting and exercise intentions. In summary, examining executive functions through this framework offers valuable insight into the structure and variability of cognitive control and role of internal factors such as genetic influences. In addition to this executive function framework by Miyake and colleagues, Baddeley and Hitch (1974) also provided another perspective for understanding how different cognitive systems interact and contribute to cognitive functioning with a focus on working memory.

A three-component or multi-component model of working memory for example was proposed by Baddeley and Hitch in 1974. In a 2010 review by Baddeley, Baddeley stated that the reason why this model continues to gain prominence is because of its simplicity and the possibility to further develop it theoretically. He stated that earlier

models had proposed that, information was stored in a short-term compartment before it was transferred to a long-term compartment. The model proposed by Baddeley and his colleague consisted of a restricted attentional capacity system which was known as the ‘central executive’. Their model proposed that the central executive worked in part or was supported by a phonological loop (acoustic and verbal material) and visuospatial sketchpad. In the experiment by Baddeley & Hitch (1974) which was used to develop the multi-component model, short-term memory was disrupted to determine if people could still perform on working memory tasks such as comprehension, reading and learning. Baddeley & Hitch showed that there was a consistent decline in performance the longer the number of digits that had to be remembered but this was not in any way catastrophic (Baddeley, 2010). However, this model of a unitary attentional system was challenged by findings that showed that in patients with severe long-term impairment, these patients still had an immediate recall capacity and thus were able to perform normally on short-term memory tasks (Hunter & Sparrow, 2012). However, Baddeley (2010) discussed in a later article how a supplementary fourth component known as the episodic buffer which was included later to the model also played a role. Figure 1-1 shows the multicomponent working memory model as proposed by Baddeley (2010) which includes the episodic buffer. In this case, the buffer provided a means of holding a limited amount of information temporarily before being integrated (Hunter & Sparrow, 2012).

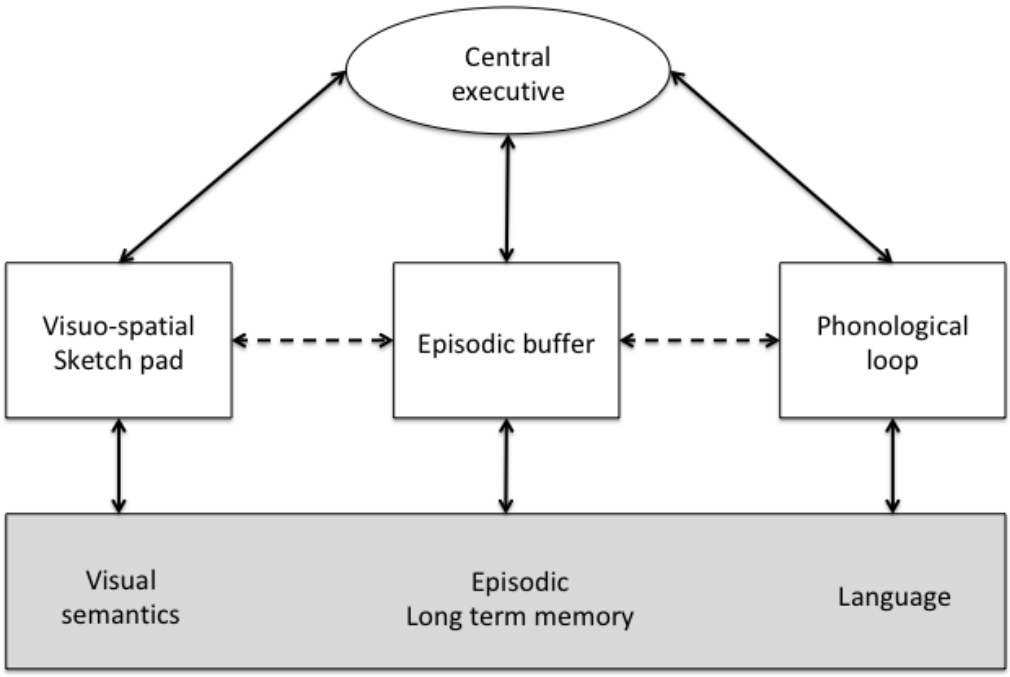

Figure 1-1 Baddeley's revised Working Memory Model (Baddeley, 2000, 2012).

Note: Baddeley's model consists of a central executive that coordinates and controls actions This central executive controls three systems known as the visuospatial and phonological loop and episodic buffer.

This research does not seek to dismiss or discriminate between established models of executive function such as those proposed by Baddeley and Miyake and colleagues. It rather builds upon them to develop a more context-sensitive understanding of cognitive processes in midlife women. The models described above highlight control processes that regulate cognitive processes and link these to neural systems such as the prefrontal cortex which is discussed in the following section.

To better understand executive functions, each model breaks down the cognitive process into separate components with a specific functionality. Baddeley (2010) focuses on a working memory model with the central executive controlling cognitive domains while Miyake et al. (2000) focused on using laboratory-based tasks to show how EF components are separate and also correlated.

This research draws on key principles from these models to use self-report measures and laboratory tasks to assess key executive

functions in the context of menopause transition. The self-report measure utilised in this study provided participants with the opportunity to reflect on behaviour from real-life examples to assess a range of executive functions, which include behavioural regulation items such as self-monitor and emotional control. Laboratory based tasks that assess selective attention and inhibitory control, working memory and processing speed were adopted in this research. The inclusion of processing speed in this study is based on prior research by Nilsson et al. (2014) and Salthouse (1996), which demonstrated that cognitive processing speed is highly sensitive to early age-related changes. As it serves as a basis for other cognitive processes, it warrants inclusion in this research to assess potential impairments associated with midlife transition to menopause as discussed in Section 1.7. EF, though complex is crucial to our development and success in all aspects of our lives. It has broad and significant implications in aspects such as maintaining relationships, job success and quality of life for example. This also translates to women transitioning to menopause especially where changes in executive functioning may influence personal and professional wellbeing.

Understanding the role of oestrogen provides a crucial foundation for interpreting executive function changes during menopause. The following section explores the relationship between oestrogen and brain cognitive function during the menopause transition.

1.9 Oestrogen, the brain and menopause

Several researchers have hypothesised that the decline in oestrogen during menopausal transition may contribute to cognitive changes in women (Russell et al., 2019, Au et al., 2016, Reuben et al., 2021, Jett et al., 2022). Oestrogen, which declines with age and drops significantly during menopause has been widely implicated in both the structure and function of the prefrontal cortex which is a brain region critical for executive function and higher-order cognition (Shanmugan & Epperson, 2014). The hormonal fluctuations that characterise the

various stages of menopause are thought to contribute to the cognitive complaints frequently reported by women during this transition. Shanmugan and Epperson (2014) suggest that these cognitive difficulties may stem from impaired modulation of oestrogen in the prefrontal cortex.

Supporting this hypothesis, McEwen (2012) in a review discussed how oestrogen enhances neurotransmitter activity, promoting synaptic growth and plasticity in brain regions associated with cognition. These brain regions are rich in oestrogen receptors which support cognitive processes. The prefrontal cortex is an essential structure in the brain which plays a key role in executive functions (Funahashi & Andreau, 2013). This region of the brain is also sensitive to oestrogen (Rapp et al., 2003). In a controlled study of 16 ovariectomised Rhesus monkeys, Rapp et al. (2003) demonstrated that those that received oestrogen treatment improved in areas of cognition such as visuospatial working memory; a part of execution function served by the prefrontal cortex. Additionally, a neuroimaging study by Jacob et al. (2017) showed increased activation in the prefrontal cortex of midlife women during cognitive tasks, suggesting that the brain may be recruiting additional resources to maintain function amid hormonal change. In their study of 142 midlife men and women, Jacobs and colleagues showed that postmenopausal women recruited the prefrontal cortex and hippocampus more strongly than premenopausal women during working memory tasks. Similarly, a study by Frey et al. (2010) of 67 menopausal women aged 42-61 years grouped into premenopausal, perimenopausal and postmenopausal women showed that there were differences in brain regions such as the prefrontal cortex during verbal tasks and this persisted across menopause stage, independent of age. Frey and colleagues suggested that the influence of menopause stage on brain regional activation may be due to the fluctuating levels of oestrogen during menopause. As mentioned earlier, oestrogen has a stimulatory effect on prefrontal cortex functions which support cognitive functions including executive functions.

For executive function tasks to be accomplished, the prefrontal cortex is responsible for monitoring tasks or events in the cortical and subcortical structures (Funahashi & Andreau, 2013). The dorsolateral prefrontal cortex (DLPFC), a region of the PFC has been shown in studies to be crucial in attention and working memory tasks. For example, Baeg et al. (2003) demonstrated in monkeys how PFC injuries affect working memory performance and to be more specific, the dorsolateral PFC was implicated by Lemire-Rodger et al. (2019). While in human subjects, Diwadkar et al. (2000) also showed in their work focusing on the DLPFC and the parietal cortex how brain activity volume and intensity increased in working memory tasks. These studies demonstrate how different areas of the PFC play a role in EF. Current literature takes into consideration how this vast network is interconnected and is involved in the different aspects of executive function such as working memory and attention (Szczepanski and Knight, 2014). Szczepanski and Knight in a 2014 review article discussed how the PFC is involved in one or a combination of tasks. A close relationship could exist between oestrogen effects on the PFC and its influence on executive dysfunction and serves as a basis for this research. Taken together, these findings suggest that executive functions deserve more attention in menopausal research to gain an understanding of the cognitive experience of midlife women. In the subsequent section a review of the various measures used in menopause research to assess cognition including executive functions, and its findings are discussed.

1.10 Measurements of executive functions

Self-report and laboratory-based tasks have both been used to assess cognition including executive function in research examining cognition in menopausal women. A review of both measures which have been used in literature is discussed below. Most studies have relied on one type of measure, either self-report or laboratory-based tasks to assess cognitive complaints. For those that have relied on self-report, the

majority have focused on one cognitive domain - memory - as reviewed by He et al. (2025). Others that have used laboratory-based tasks have a limited battery of measures or have focused on one cognitive domain (Epperson et al., 2013). The research in this thesis employed a self-report measure that focuses on a broader array of cognitive domains as well as laboratory-based tasks to assess cognition. The rational for this research is also provided following the review of measures used to assess cognition.

Laboratory tasks

As mentioned earlier, executive functions are closely linked to the frontal lobe with research showing that lesions in the prefrontal cortex can negatively impact executive functioning (Baeg et al., 2003). Given this connection, menopause-related cognitive complaints may share many similarities with executive dysfunction, as hormonal shifts, particularly the decline in oestrogen, can affect brain regions involved in cognitive control. Several laboratory-based tasks have been developed to assess executive functions and a review of some of these tasks along with their findings in menopause research is discussed in the following section.

1.11 Review of laboratory-based tasks to assess cognition

Researchers have used objective measures in the form of laboratory-based tasks to assess executive function performance in menopause-related cognitive studies. These measures are administered in highly controlled and standardised environments. For example, the presentation of a stimulus in computer-based experiments is carefully controlled so that each participant experiences and finishes the task in the same manner as all other participants. To assess performance, variables such as accuracy and response time are measured. These tasks are also sensitive and target specific EF components thereby assessing one’s behaviour in a structured environment. Even though

the research in this thesis employed a cross-sectional method, an overview of cross-sectional and longitudinal studies which examined cognitive performance in menopausal women are presented in the subsequent sections. Table 1-1 outlines the tasks employed across studies reviewed in Table 1-2 and is discussed in the following section.

Table 1-1 Brief description of laboratory tasks and domain assessed

Task – (Study reference)	**Description**	**Domain assessed**
Symbol Digit Modality Test (SDMT) - (Greendale et al.,2009)	Participants match symbols to numbers as quickly as possible using a reference key provided	Processing speed
Eastern Boston Memory Test (EBMT) – (Greendale et al.,2009)	Participants hear a short story. Subsequently, they are asked to remember as much detail from the story as possible	Verbal episodic memory
Digit Span Backwards (DSB) - (Kilpi et al., 2020) and Digit Span Forwards (DSF) – (Lee et al.,2020)	Participants were asked to repeat a sequence of numbers either backwards or forwards. The sequence gets increasingly longer	Working memory
Trail Making Test (TMT) Consists of Part A and Part B - (Lee et al.,2020)	Participants have to connect a randomly series of numbers (Part A) or letter and numbers (Part B) as quickly as possible on a page	Attention and mental or cognitive flexibility,
Paced Serial Addition Test (PASAT) - (Elsabagh et al., 2007)	Participants add up consecutive pairs of single numbers that are read from a list.	Sustained attention, working memory, calculation ability, processing speed

Task – (Study reference)	**Description**	**Domain assessed**
Cambridge Neuropsychological Test Automated Batteries (CANTAB) - (Elsabagh et al., 2007)	A computerised test consisting of 25 tests which assess various cognitive functions	Executive function and other cognitive processes such as memory, attention
Stroop - (Lee et al., 2020)	Participants are presented with a list of colour names printed in discordant ink. Participant must ignore the words and name the ink colour as quickly as possible	Response Inhibition; Interference control
Porteus Labyrinth – (Martino et al., 2022)	Participants trace a path through a set of mazes without backtracking	Planning
Rey Auditory–Verbal Learning Test (RAVLT) – (Fuh et al., 2006)	Participants learn 15 words over 5 trials. Delayed recall after 15 min. After, 15 target and 15 distractor words shown, participant identify original items.	learning, immediate memory, and delayed memory.

In a longitudinal study conducted by Greendale and colleagues (2009), 2,362 women from the Study of Women's Health Across the Nation were assessed using three cognitive tasks: the Symbol Digit Modalities Test (SDMT) to measure processing speed, the East Boston Memory Test (EBMT) for verbal memory, and the Digit Span Backwards (DSB) task for working memory. Greendale and colleagues aimed to evaluate whether menopause stage influences cognitive performance. The findings revealed that perimenopausal women experienced declines in verbal memory (EBMT) and processing speed (SDMT). Additionally, cognitive performance in these areas rebounded to premenopausal levels in postmenopause, leading the researchers to propose that the cognitive challenges associated with the menopausal transition may be temporary. In contrast, no significant effects of menopause stage were observed on working memory performance as measured by the DSB task.

A cross-sectional study conducted by Lee et al. (2020) utilised the Digit Span (Forwards and Backwards) task to evaluate working memory, the Trail Making Test to assess cognitive flexibility, attention and executive function and the Stroop task to measure selective attention and inhibitory control in mid-life women. The findings revealed that menopausal women performed significantly worse on laboratory-based measures when compared to non-menopausal women. However, the study did not differentiate between premenopausal and perimenopausal women, instead categorising them collectively as non-menopausal and comparing their cognitive performance to that of postmenopausal women. This makes it challenging to draw firm conclusions with regards to the self-reported cognitive challenges experienced by perimenopausal women. Other studies such as Greendale et al. (2009) and Henderson et al. (2003) employed alternative menopausal staging methods, which also makes direct comparisons with research utilising the STRAW criteria, such as Martino et al. (2022) and Elsabagh et al. (2007) challenging.

In contrast to the above study, a cross-sectional study by Martino et al. (2022) investigated cognitive performance in 100 healthy, 18-79 year old premenopause, perimenopause and postmenopausal women using Digit Span Backwards (working memory), Stroop Colour-Word Interference (Inhibitory control), verbal fluency task, Part B of the Trail Making (Cognitive flexibility), Porteus Labyrinth (Planning). Findings from the study showed no significant differences in any of the above-mentioned measures in the menopause groups after adjusting for age. In a separate study involving an older premenopausal cohort recruited from an outpatient menopause clinic, Unkenstein et al. (2016) after covarying for age, also did not find any significant differences in laboratory-based tasks of working memory, selective attention and inhibitory control, shifting, verbal fluency, attentional switching, memory and processing speed. The study consisted of 130, 40–60 year-old premenopausal, perimenopausal and postmenopausal women. Additionally, in a similar study by Luetters et al. (2007), no significant differences in cognitive performance were also observed. This cross-sectional study by Luetters et al used a general population sample of 1657 multiethnic women from the SWAN study. Premenopause, perimenopausal and postmenopausal women performed the Digit span backward (working memory), SDMT (processing speed) and EBMT (verbal memory) tasks. Multivariable linear regression analysis adjusted for age showed no statistically significant differences in cognitive performance when premenopausal were compared to the other menopause stage groups.

Finally, Kilpi et al. (2020) examined five cognitive domains in premenopausal, perimenopausal, and postmenopausal women. The data used was from mothers participating in the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort. The study included women aged 36 to 66 years and assessed five domains: verbal episodic memory, working memory, processing speed, verbal intelligence, and verbal fluency. Results showed no significant differences in cognitive scores across the three groups in most

domains, except for a decline in verbal episodic memory. Additionally, processing speed decreased across menopause stages. The authors noted that these declines were subtle and accounted for age as a factor in their analysis.

In summary, the preceding review highlights how variations in staging criteria, menopause groups assessed, and study design contribute to mixed findings. Table 1-2 provides an overview of findings from both cross-sectional and longitudinal studies including menopause groups assessed.

Table 1-2 Summary of studies using laboratory based measures to assess cognition

Author (year)	Sample size	Study type	Age	Menopause stage	Laboratory task - cognitive measure	Analysis	Main Outcome
Elsabagh et al. (2007)	189	Cross-sectional	49-67	Early post Late post (STRAW)	Paced serial addition test (PASAT) - sustained attention, paragraph recall Immediate and delayed test – episodic memory, CANTAB – executive function	ANOVA	There were no differences in attention, verbal fluency and memory. Late postmenopausal women performed significantly worse in executive function.
Kilpi et al. (2020)	2411	Longitudinal	36-66	Pre, peri, post (STRAW)	Immediate logic memory & Delayed logic memory test - Verbal episodic memory, digit span backward (DSB) – working memory, processing speed – digit symbol matching task, spot the word task– verbal intelligence, same letter word test – verbal fluency	ANOVA	No differences in working memory, verbal intelligence and fluency. Decline in immediate and delayed verbal episodic memory and processing speed across menopause stages.

Author (year)	Sample size	Study type	Age	Menopause stage	Laboratory task - cognitive measure	Analysis	Main Outcome
Greendale et al. (2009)	2362	Longitudinal	42-52	pre, early peri, late peri, post, post with HT	Symbol digit modalities test (SDMT) - Processing speed, East Boston Memory test (EBMT) - Verbal memory, Digit span backwards (DSB) - Working memory	Mixed effect model	Perimenopause was linked to a decline in cognitive function, but postmenopausal women improved to premenopausal levels. Declines in processing speed in perimenopausal women in comparison to pre- and postmenopausal women.
Lee et al. (2020)	178	Cross-sectional--	41-70	Menopausal women and non-menopausal women	Digit Span Forwards and Backwards - working memory, Trail Making test -cognitive flexibility, attention and executive function, Stroop - selective attention, inhibitory control	Multiple regression	In all measures assessed. menopausal women had significantly worse performance compared to non-menopausal women
Martino et al. (2022)	100	Cross-sectional	18-79	Pre, peri, post (STRAW)	Digit Span Backwards - working memory,	ANCOVA	No significant differences were

Author (year)	Sample size	Study type	Age	Menopause stage	Laboratory task - cognitive measure	Analysis	Main Outcome
					Verbal fluency tasks - phonological and semantic fluency, Stroop Colour-Word Interference - Inhibitory control, Trail Making test (Part B) - Mental flexibility, Porteus Labyrinth - Planning		observed between groups in all measures in age adjusted analysis
Luetters et al. (2007)	1657	Cross-sectional	50 (mean age)	Pre, peri, post	Symbol Digit Modalities Test (SDMT) - Processing speed, East Boston Memory test (EBMT) - Verbal memory Digit span backwards (DSB) - Working memory	Multiple linear regression	No significant differences observed in any of the processing speed, verbal and working memory tasks
Maki et al. (2021)	443	Longitudinal	42 (median age)	Pre, peri, post	Letter-Number Sequencing (LNS) – working memory, symbol digit modalities test (SDMT) - Processing speed,	General linear-mixed effects regression	Cognitive declines in learning, memory, and attention/working memory from pre- to peri- and from pre- to postmenopause,

Author (year)	Sample size	Study type	Age	Menopause stage	Laboratory task - cognitive measure	Analysis	Main Outcome
					Trail Making test – executive function, animal naming task – verbal fluency, Hopkins Verbal Learning Test-Revised (HVLT-R) – memory and learning		
Henderson et al. (2003)	326	Cross-sectional	52-63	Peri, post, HRT users	Immediate and delayed verbal memory	Multivariable linear regression	No significant difference in verbal memory regardless of menopausal stage
Fuh et al. (2006)	495	Longitudinal	42-50	Pre, peri	Digit Span Forwards and Backwards - working memory, RAVLT learning, immediate memory, and delayed memory, Trail Making test – executive function, animal naming test – verbal fluency	Multiple linear regression	No significant difference in task performance except in verbal fluency where perimenopausal performed worse.

Findings from Table 1-2 demonstrate how some studies have not focused on the three key stages of menopause or have focused on memory. Also, despite the relevance of the findings from above, it is important to think about the role of other assessments of executive function such as self-report measures. As laboratory-based tasks are highly structured and controlled, they often lack ecological validity, meaning they may not accurately reflect how individuals solve real-world problems. In everyday situations, people typically engage multiple components of executive function (EF) simultaneously to adapt and respond effectively. To bridge this gap, self-report or subjective measures have been developed, contributing an ecologically valid perspective on executive function. These tools offer insight into how individuals apply cognitive skills in their everyday lives, It also expands the assessment scope by capturing behavioural manifestations of EF within a single assessment. A combination of self-report and laboratory tasks provides valuable information about women's cognitive performance in different settings. This research employed the Behaviour Rating Inventory of Executive Function-Adult version (BRIEF-A; Roth, Isquith, & Gioia, 2005) and is discussed briefly in Section 1.13. It is a standardised 75-item assessment tool, available in both self and informant report format to evaluate how executive functions manifest in daily life. For now, the focus shifts to discuss existing literature on self-report measures used in menopause to assess cognition.

1.12 Review of subjective measures to assess cognition

As previously discussed, cognitive complaints are commonly reported in mid-life women. Subjective measures in the form of questionnaires are also widely acknowledged as effective instruments for gauging challenges in executive skills or cognitive challenges in both groups and individuals. Within existing literature, questionnaire items highlight the importance of integrating real-life scenarios from everyday

experiences that showcase executive functions as this enhances a study's ecological validity. These items are structured into clinical scales, categorising them into different areas of executive function (EF). The Executive Function Index (EFI) (Spinella, 2005), Learning, Executive and Attention Functioning Scale (LEAF) (Castellanos et al., 2018), Behaviour Rating Inventory of Executive Function-Adult version (Roth, 2005) and Brown Attention Deficit Disorder Symptom Assessment Scale (BADDS) (Brown, 2001) are some examples of subjective measures that have been used in studies to assess executive function.

As mentioned earlier, this study used the Behaviour Rating Inventory of Executive Function – Adult version (BRIEF-A) to assess executive function in adult participants. The BRIEF-A provides a more comprehensive assessment, covering executive function skills, emotional and behavioural regulation. The BRIEF-A is suitable for use with both clinical and nonclinical adult populations, offering broader applicability in assessing everyday executive function challenges.

In contrast, an instrument such as the BADDS was developed as an evaluation tool to assess adults presenting with ADHD symptoms Brown (1996). As it was initially developed for clinical populations, particularly those presenting with ADHD, it may not fully capture the nuanced executive profiles found in a nonclinical sample of women transitioning to menopause (He at al., 2025). As subjective measures rely on individuals' assessments of behaviour across diverse scenarios over time, they can be susceptible to personal biases and differences in self-awareness (Spinella, 2005). In both clinical and research settings, there is considerable interest in measuring executive function to comprehend the behaviours of individuals affected by executive function impairment. Evaluations should typically consist of a combination of subjective and objective measures to get an overall picture of executive function performance, and this was the case in this research project.

Research studies employ either or both types of measures (subjective and objective) to evaluate cognitive complaints and difficulties with concentration reported by menopausal women. Associations have been identified between subjective or self-report complaints and objective measures used to evaluate cognitive complaints experienced by women (Schaafsma et al., 2010; Weber et al., 2012; Weber & Mapstone, 2009). However, the study by Schaafsma et al. (2010) did not find an influence of menopause stage on this association. The subjective measures commonly used to assess cognitive changes in menopausal women include the Memory Functioning Questionnaire (MFQ) which assesses everyday memory function including items such appointments, names and where objects are placed. This has been used in menopause research by Drogos et al. (2013); Grummisch et al. (2023); Weber et al. (2012). There is also the use of the Multifactorial Memory Questionnaire (MMQ) which measures aspects of self-report memory including one's satisfaction with their memory and coping strategies for memory difficulties. The Women's Health Questionnaire (WHQ) and Menopause Rating Scale (MRS) which use single item questions to assess memory and attention difficulties have also been used (Hammam et al., 2012; Heinemann et al., 2004). These measures described have focused mainly on memory and it is important to consider other domains that might be affected during the menopause transition given the range of psychological symptoms described by Warga (1999).

However, these self-assessment questionnaires do not provide a comprehensive range of diverse measurements of cognitive domains that can be used to assess women's perceived cognitive complaints in their everyday environment as outlined in Table 1-3. A few studies have focused on other cognitive domains such as executive functions and not just memory. For example. studies by Epperson et al. (2011) and Page et al. (2023) required participants to use the Brown Attention Deficit Disorder Scale (BADDS) to report executive function. Despite the utility of BADDS in assessing broader domains, it mainly focuses

on assessing symptoms of attention deficit hyperactivity disorder (ADHD) in adults and provides a narrow view on executive function domains when used in otherwise normal menopausal women. Given that executive functions are instrumental in the activities we perform daily and key to our functioning in society, it is crucial for scientific literature that, this aspect of cognition is also covered in menopause research. Executive function domains are very much dependent on the prefrontal cortex which is sensitive to drastic changes in ovarian hormones such as oestrogen (Luine, 2014).

Table 1-3 provides a summary of commonly used measures used to assess cognition including executive functions in menopause research and as mentioned earlier, many of the studies have focused on learning and memory. However, women's report of struggles with cognition includes areas such as learning, recalling names and numbers and words, planning and organisation, attention and focus, increased distractibility and losing train of thought. It also includes disturbances in daily life like forgetting appointments and events and misplacing house hold items like keys, mental slowness and decline in motor coordination skills (Epperson et al., 2011; Mitchell & Woods, 2001, 2011; Santoro et al., 2015, Warga., 1999). These include examples of executive function which relate to one aspect of cognition.

Table 1-3 Summary of some subjective measures used to assess cognitive measures in menopause research

Author (year)	Sample size	Study type	Age	Menopause stage	Subjective measure	Number of domains/items	Domains assessed	Main Outcome
Page et al. (2023)	1971	Cross-sectional	35-65	Pre, peri, natural post and surgical post	Brown Attention Deficit Disorder Scale (BADDS)	5 (40)	Assesses executive functions including interference control, sustained attention and concentration working memory and recall, initiating and organisation, sustaining energy and effort	Difficulties in executive function in peri- and surgical postmenopause group compared to premenopausal group.
Unkenstein et al. (2016)	130	Cross-sectional	40-60	Pre, peri, post	Multifactorial Memory Questionnaire (MMQ)	3 (61)	Assessed frequency of forgetting and contentment with memory	Peri- women reported more frequent forgetting and not being content with their memory compared to

Author (year)	Sample size	Study type	Age	Menopause stage	Subjective measure	Number of domains/items	Domains assessed	Main Outcome
								pre- and postmenopausal women
Drogos et al. (2013)	68	Cross-sectional	44-62	Not specified. Midlife women experiencing at least 35 hot flushes	Memory Functioning Questionnaire (MFQ)	4 (64)	Assessed subjective memory difficulties	Subjective memory performance predicts objective memory performance
Weber at al. (2012)	75	Cross-sectional	40-60	Peri	Memory Functioning Questionnaire (MFQ)	4 (64)	Assessed memory problems in everyday life	Memory complaints were associated with working memory, somatic, psychological and sleeping difficulties
Epperson et al. (2011)	16	Cross-sectional	45-60	Peri, post	Brown Attention Deficit Disorder Scale (BADDS)	5 (40)	Assesses executive functions including interference	Peri- and postmenopausal women with self-report cognitive

Author (year)	Sample size	Study type	Age	Menopause stage	Subjective measure	Number of domains/items	Domains assessed	Main Outcome
							control, sustained attention and concentration working memory and recall, initiating and organisation, sustaining energy and effort	difficulties reported significantly less difficulties while on cognitive impairment medication
Grummisch et al. (2023)	43	Longitudinal	45-55	perimenopause	Memory Functioning Questionnaire (MFQ) Attentional Function Index (AFI)	4 (64) 3 (13)	assessed perceived everyday memory functioning assessed attention and working memory	Oestradiol fluctuations were significantly and positively associated with MFQ (better memory) but not AFI (attention and working memory)

The section has described the various self-report measures used to assess cognition and the following section provides more information about the more comprehensive tool, BRIEF-A that has been used in this research.

1.13 BRIEF-A

Roth et al. (2005) describes the BRIEF-A as a self-report measure that evaluates nine distinct domains linked to behaviour and emotional regulation, as well as metacognitive skills such as working memory and planning and organisational skills. It captures the challenges that adults aged 18-90 years face in applying cognitive control to real-world situations thereby providing an insight into their ability to regulate their thoughts, emotions, behaviours and problem-solving skills. Previous studies have also shown that the BRIEF-A has adequate psychometric properties. Rabin et al. (2006) showed that the measure effectively differentiates adults with mild cognitive impairment from neuropsychologically healthy controls and has also been validated in different population as used by Albuquerque et al. (2025) in a sample of healthy Portuguese adults. Roth et al. (2005) has shown the BRIEF-A to have a moderate to high internal consistency with alpha coefficients ranging from .73 to .90 for the subscales and .93 to .96 for BRI, MI and GEC in a normative sample. In terms of test-retest reliability, the BRIEF-A also scores high on this psychometric property with stable correlation scores of r = .93 for both the BRI and MI and r = .94 for the GEC (Roth et al., 2005).

Notably, using the BRIEF-A which encompasses nine subscales of executive function (Inhibit, Shift, Emotional Control, Self-Monitor, Initiate, Plan/Organize, Task Monitor, Organisation of Materials, and Working Memory) has not been previously explored in menopause research. These nine subscales are grouped into two indices known as the Behaviour Regulation Index (BRI) which is made up of Inhibit, Shift, Emotional Control, Self-Monitor and the Metacognitive Index (MI) which consists of Initiate, Plan/Organize, Task Monitor, Organisation of

Materials, and Working Memory. Together, these domains which reflect different abilities provide a comprehensive measure of executive function skills. The Global Executive Composite score is a combination of BRI and MI and gives an overall summary of executive functioning. This BRIEF-A self-report measure was used in this research, and a description of the various scales will be provided in the methodology section in Chapter 2. BRIEF-A has been used to study clinical and healthy populations with cognitive difficulties (Rabin et al., 2006). Findings from the study by Rabin and colleagues indicated that participants with mild cognitive impairment and those with significant cognitive complaints reported difficulties with selective domains on the BRIEF-A, highlighting distinct patterns of executive function challenges. Though other self-report measures have been used to assess cognitive complaints in menopausal women, BRIEF-A is the first to be employed to target this population. Despite offering a comprehensive assessment of executive functions, the BRIEF-A remains susceptible to bias, consistent with limitations characteristic of self-report measures. Thus, it is equally important to also assess executive functions using laboratory-based tasks to complement findings from self-report or subjective measures. This was an approach that was adopted in this research.

1.14 Overview and constraints

The findings from the various studies described above fail to provide a clear understanding of how reproductive aging or menopause stage influences cognitive performance, as the results are mixed and inconsistent. Different measures have also been used to assess cognition with limited domains assessed especially given the broad description of psychological symptoms described by women. In general, the findings from both subjective and laboratory-based measures do not provide clarity. Several factors may contribute to this lack of clarity. For instance, some studies, such as Elsabagh et al. (2007) and Lee et al. (2020), have only investigated cognitive

performance in one or two menopausal groups without including a control group of premenopausal women. This omission makes it challenging to draw definitive conclusions about cognitive health during the menopausal transition.

Furthermore, while some studies such as Greendale et al. (2009) and Lee et al. (2020) have reported a relationship between menopause stage and cognition, others, like Luetters et al. (2007) and Martino et al. (2022), found no such association. The inconsistency is further complicated by variations in the criteria used to stage menopause. Both longitudinal and cross-sectional research has explored cognitive performance during the menopausal transition relative to premenopausal women. While longitudinal studies have more consistently observed cognitive declines during this transition, findings from cross-sectional studies remain mixed. For instance, Martino et al. (2022) found no differences across menopausal stages, whereas Lee et al. (2020) reported significantly poorer performance on cognitive tests among menopausal women. This project aims to address existing research gaps by using cross-sectional studies to explore the cognitive changes women experience during the menopause transition.

1.15 Rationale for study

Key gaps in cognitive research on the menopause transition include the absence of a control such as a premenopause group in some studies (Drogos et al., 2013) and the lack of standardised criteria for classifying menopause stages (Henderson et al., 2003). Effects of sleep quality, overall menopause symptom burden and socio-behavioural factors on executive functions are examined as very few studies have assessed this across the menopause stages given its prevalence. This study aims to address these limitations, ensuring more precise and representative findings in menopause-related cognitive research.

The Greene Climacteric Scale (Greene, 1998) is a widely used tool for assessing menopause symptoms in the general population, as

demonstrated in studies by Drogos et al. (2013) and Barentsen et al. (2001). Additionally, it serves as a standardised measure for conducting cross-cultural research as highlighted by Thakur et al. (2019). Utilising this scale in menopause studies enhances the ability to compare findings across different populations, ensuring consistency in symptoms assessment and facilitating broader research insights.

Self-report and laboratory-based measures are used typically in many psychological assessments. Thus, a combination of these two measures could potentially increase the reliability, accuracy and predictive power of findings from research studies. In addition, it would be useful to explore if there are associations between similarly named domains on both measures. Both measures have their strengths and weaknesses. Objective measures for example lack ecological relevance and self-report measures are also prone to bias. However, the strength of the two measures such as the natural relevant nature of questions asked in self-report questionnaires and the opportunity to observe participants in controlled environments during experimental measures can augment the validity of research. Furthermore, the BRIEF-A in a single assessment can provide a comprehensive assessment of both behavioural regulation and metacognitive skills across nine subdomains of executive function. Its broad scope allows for a more insightful evaluation of executive function, identifying areas that may be unexplored or underexamined. This makes it particularly valuable in shedding light on women's cognitive complaints offering a more nuanced understanding of executive function challenges.
The self-report measure, BRIEF-A and the objective laboratory-based measures included tasks such as processing speed, working memory and attention and inhibitory response tasks. Most studies have primarily focused on memory problems only, but the use of both measures expands the focus of domains assessed, thereby contributing to existing literature. Details of these tasks are discussed in Chapter 3 but firstly, the subjective study is discussed in the Chapter 2.

1.16 Thesis Aims

Two studies examined the associations between menopause stage, symptoms and sleep quality in relation to executive function performance across different reproductive stages. The first study used a questionnaire to assess executive function performance, while the second study conducted in person, utilised behavioural experimental measures to evaluate executive functions.

Both studies aimed to investigate whether differences in executive function were linked to reproductive aging, with the hypothesis that perimenopausal women would exhibit poorer performance. By examining executive function through both subjective and objective measures across various menopause stages, these studies address a gap in the existing literature, where research on this cognitive domain remains limited.

In conclusion, this thesis primarily aimed to investigate how the impact of the menopause stage influences cognition in midlife women during the transition to menopause. Details of specific objectives or hypotheses are detailed in relevant Chapters of this thesis.

1.17 Summary

In summary, this chapter reviewed the literature on cognitive challenges experienced by women during the menopausal transition. It examined the underlying pathophysiology of menopause, outlined its timing across genetic and geographic contexts, and the importance of using standardised staging criteria that includes a premenopause group to enable meaningful comparisons across studies. Key menopause stages and sub-stages were outlined, alongside associated symptoms which included psychological, somatic, vasomotor, sexual, and sleep-related changes as well as the role of hormone replacement therapy (HRT) and socio-behavioural factors.

The chapter also explored the prevalence of cognitive complaints in midlife and the influence of oestrogen on brain function and cognitive performance. It reviewed both subjective and objective measurement tools used to assess cognition in menopause, highlighting limitations in study design, measurement approaches, and outcome variability across the literature.

While many studies have focused on memory, this research shifts the focus toward executive functions which is a critical set of skills used in daily life that, when disrupted, can significantly impact quality of life. There is a clear need for research that examines how menopause stage, menopause-related factors such as symptom burden, sleep disturbances, HRT, and socio-behavioural influences affect cognitive outcomes. By applying standardised measures for menopause staging, cognitive assessment, and symptom profiling, this thesis aims to build a framework for more consistent and meaningful comparisons by examining the effect of menopause stage on cognition in pre-, peri- and postmenopausal women. It also explores how overall menopause symptom burden, sleep disturbances, HRT and socio-behavioural factors impact cognition.

Given that all women experience menopause, understanding its cognitive impact is essential. This research offers a novel, multifaceted approach to studying cognition during this life stage, with the goal of informing better support and management strategies for women and healthcare providers.

2 Chapter 2 Examining self-reported executive function during menopause

2.1 Abstract

In Chapter 1, I discussed how many women transitioning through menopause report experiencing cognitive challenges, often described as “brain fog” with hormonal fluctuations particularly oestrogen being implicated in both cognitive complains the emergence of menopause symptoms. While previous research has predominantly focused on memory complaints, there is a need to consider that these cognitive difficulties may reflect broader impairments in executive functioning. Despite this, few studies have directly examined executive function in menopausal women, and those that have often relied on limited or non-comprehensive assessment tools.

I also highlighted the various menopausal symptoms associated with this transition and discussed how existing research has tended to explore the impact of individual symptoms on cognition, overlooking the cumulative effect of overall symptom severity. This is an underexplored gap in the literature, as menopausal symptoms rarely occur in isolation and may collectively influence cognitive performance. Additionally, HRT is commonly recommended to alleviate menopausal symptoms, yet its potential cognitive benefits remain unclear and so this was explored in this study. Sleep disturbances, a frequent complaint during midlife, were also discussed in relation to the broader literature on sleep and cognition. Although poor sleep is known to negatively affect cognitive functioning, few studies have examined its role in the menopause-related executive dysfunction context.

In addition to biological factors, it was important to consider socio-behavioural factors such as education, diet quality, alcohol consumption, working hours, caregiving responsibilities and physical activity. These factors could offer insight into the lived experiences of midlife women and may contribute to cognitive outcomes.

Cognitive complaints are frequently reported by women transitioning through menopause, yet research has largely focused on memory, overlooking executive functions such as planning, inhibition, and working memory. The overarching aim of this study was to examine how menopause stage affects executive function performance. Additionally, the study explored the influence of menopause symptom severity, sleep quality, HRT use, and socio-behavioural factors. A total of 979 women who were aged 40 and above completed an online questionnaire. This included 257 premenopausal women, 283 perimenopausal women not using HRT, 161 perimenopausal women using HRT, and 278 postmenopausal women. The study employed the 75-item BRIEF-A to assess executive function, STRAW to assess menopause stage and the Green Climacteric Scale to assess symptom burden. Other questions related to sleep quality and demographic and lifestyle factors were also asked.

Results showed that perimenopausal women not using HRT reported significantly poorer executive function compared to premenopausal women, independent of age. No significant differences in executive function performance were found between perimenopausal and postmenopausal women, nor between premenopausal and postmenopausal women. Menopause symptom severity emerged as a strong predictor of executive function performance across all groups, indicating that greater symptom burden is associated with poorer cognitive outcomes. Although menopause stage showed a significant main effect on executive function, this did not extend to its interaction with sleep quality. Instead, poor sleep quality independently predicted worse executive function performance, regardless of age or menopausal stage. Socio-behavioural factors also played a significant role. Women reporting poorer diet quality, higher alcohol consumption, and caregiving responsibilities reported worse executive function performance. In conclusion, executive function difficulties during menopause appear to be influenced by a combination of biological and lifestyle factors. These findings validated the cognitive complaints in

women transitioning to menopause and demonstrated the need to consider other socio-behavioural factors when assessing cognitive health in midlife women.

2.2 Introduction

In the previous chapter, I discussed how during the menopausal transition, marked by significant hormonal fluctuations, many mid-life women report experiencing cognitive symptoms commonly referred to as ‘brain fog.’ This term encompasses challenges such as difficulty finding words, forgetfulness, losing one’s train of thought, concentration issues and misplacing everyday items (Sullivan Mitchell & Fugate Woods, 2001). Moreover, difficulties in organisation, working memory, focus and attention are key aspects of executive functions that have also been examined in studies on mid-life women (Epperson et al., 2011, 2015). However, the prevalence of these executive function challenges remains underexplored, particularly in subjective or self-reported assessments. The aim of this study is to use a subjective measure to assess executive functions.

I also discussed how the prefrontal cortex, a brain area associated with executive function is sensitive to oestrogen (Joffe et al., 2006; Rapp et al., 2003). The fluctuating and eventual decline in oestrogen has long been suspected to contribute partly to these cognitive changes in these brain regions responsible for cognition such as executive functions and memory (Shanmugan & Epperson, 2014). I therefore reason that a change in executive function may be related to women’s experience of the menopause transition. This thesis examines the role of menopause stage by comparing cognition across the three core menopause stages where premenopausal women are included as a control which has not previously been done in some studies (See Table 1-3). Many studies have overlooked the importance of investigating women at the three different stages of menopause making it challenging to draw meaningful comparisons especially as each stage has unique

hormonal shifts with associated challenges that may affect cognitive performance across a range of cognitive domains.

Importantly, the research in this thesis goes beyond existing literature by using the self-report BRIEF-A, a more comprehensive measure of executive functions to assess women's cognition instead of focusing solely on memory problems which has been the focus of more studies. Roth et al. (2005) divides executive function into two main indices; behaviour regulation index (BRI) and metacognitive index (MI). BRI is the ability to regulate and control one's behaviour when it comes to emotions, thoughts, actions, thinking creatively when solving problems and adapting well to changes. MI on the other hand captures higher order cognitive abilities such as planning and organisational skills to effectively problem solve by using stored information in the working memory to find solutions. By examining both indices, this study aims to gain a more nuanced understanding of the types of executive function challenges women may experience during the menopausal transition. These difficulties may manifest as emotional and behavioural regulation issues (BRI) or as impairments in planning and organisational skills and decision-making (MI). Using BRI and MI separately allows for a more detailed exploration of how different aspects of executive functioning are affected and highlight areas for intervention, rather than relying solely on a global score. The Global Executive Composite (GEC) score was also used to explore the role of socio-behavioural factors on executive functions. GEC combines both the Behavioural Regulation Index (BRI) and the Metacognition Index (MI). The combination of the two indices provides a general summary of executive functioning. This approach was chosen because socio-behavioural influences (discussed in Section 1.6) may potentially affect executive function in a broad and general way and the use of GEC makes the results easier to interpret and avoids unnecessary complexity.

Findings from studies using self-report measures to assess subjective complaints relating to executive function or cognition during the menopause transition have been limited in its scope of EF measurement. Cross-sectional studies by Ford et al. (2004) and Woods et al. (2000), found no significant association between menopause stage and cognitive functioning. However, these studies by Ford et al. (2004) and Woods et al. (2000) focused on perceived memory difficulties. Additionally, the measures used in these previous studies lack the depth needed to provide a comprehensive understanding of subjective changes in executive function during the menopause. Mitchell & Woods (2011) utilised health diary entries to document cognitive challenges such as attention difficulties and forgetfulness. Similarly, some studies, including those by Armeni et al. (2018) and Schaafsma et al. (2010), employed binary 'yes' or 'no' questions to evaluate subjective complaints regarding memory and attention. Reliance on different and non-standardised measures to assess executive function as well as testing limited executive function domains may potentially lead to mixed results.

This study also examined how the overall burden of menopause symptoms influences executive function, beyond the effects of menopause stage alone. While previous research has explored links between individual symptoms such as psychological or vasomotor complaints and cognition (see Section 1.6), these symptoms rarely occur in isolation. Each woman experiences menopause differently and focusing on isolated symptoms may overlook the cumulative impact of symptom burden. Evidence suggests that the perimenopausal stage is associated with the highest symptom load as discussed in section 1.6 and these symptoms can be severe enough to prompt up to 90% of women to seek medical support (Guthrie et al., 2003). To capture this, the current study used the standardised Greene Climacteric Scale (GCS) to assess 21 commonly reported menopause symptoms and their overall association with executive function, while controlling for age. By examining symptom burden in its entirety, this thesis

addresses a gap in the literature, which has largely focused on individual symptoms. This approach offers a more comprehensive understanding of how menopause affects cognitive functioning in everyday life.

As mentioned above, the menopause transition period can be accompanied by a range of distressing symptoms for some women. Hormonal replacement therapy is offered as treatment option for women, yet its effects on cognition is inconclusive as discussed in section 1.6. Given that perimenopause is often associated with the worst symptom burden for some women, this study explored the potential impact of HRT use on executive functions in perimenopausal women while controlling for overall symptom burden.
Despite its clinical relevance, the association between HRT use and cognition is an underexplored area in existing literature that warrants further exploration. It is estimated that by the year 2030, the population of perimenopausal and postmenopausal women will increase to 1.2 billion with an estimated 47 million women beginning the transition each year (Hill, 1996). Therefore, understanding how hormonal treatments may potentially influence cognitive challenges is of timely importance and necessary.

One of the most prevalent issues faced by women during the menopausal transition are sleep disorders (Lee et al., 2019). Complaints about their quality of sleep, not having enough sleep, nocturnal awakenings and sleep apnea have been reported by many women transitioning through menopause (Gava et al., 2019). Observed changes in executive function may not only be directly caused by oestrogen decline alone but could result from the indirect impact of menopause symptoms, such as sleep disturbances.
Some studies examined associations between sleep and executive functions. For instance, Maki et al. (2008) found a negative association between sleep and executive functions. Maki and colleagues found that among 29 midlife women with a mean age of 53, poor sleep

significantly predicted cognitive performance in the domains of verbal memory, working memory and attention. Lastly, a study by Lambiase et al. (2014) found a negative association between sleep and executive function in 122 postmenopausal women. Building on previous findings where sleep disturbances were in some cases assessed in only one menopause stage, this study examined self-reported sleep quality across the key menopause stages. This approach aimed to better understand how sleep disturbances vary throughout the transition and their potential impact on cognitive outcomes.

In addition to menopause-related changes, this study considered a range of socio-behavioural factors that may influence cognition in midlife women during this transitional period. Factors examined included physical activity, working hours, caregiving responsibilities, diet quality, alcohol consumption and education. These factors have shown associations with cognitive performance in previous research as discussed in section 1.6. This study explored the role of these factors on executive function performance due to limited studies exploring many of these factors that have been shown to impact cognitive performance.

In conclusion, this study aims to contribute to existing literature by ascertaining whether cognitive changes observed are directly as a result of menopause stage, or part of a broader picture of the complexities surrounding menopause transition which includes factors such as menopause-associated symptoms, HRT, socio-behavioural factors and cognitive ageing.

2.3 The Current study

This study employed an online questionnaire hosted on the Qualtrics platform to examine executive function performance in pre-, peri- and postmenopausal women. Questionnaires are useful tools used in the collection of data whereby a series of questions relevant to the

research topic are asked of individuals (Denscombe, 2014). The items included in the questionnaire (see Appendix 3) were informed by gaps identified in the existing literature, such as the frequent exclusion of premenopausal women, reliance on narrow cognitive assessment tools that sometimes focused primarily on memory, and limited exploration of executive functions. The study also addressed the underrepresentation of socio-behavioural influences on cognition and prioritised the use of standardised measures for executive function, menopause staging, and symptom severity.

The research was structured around five key aims. First, it examined the impact of menopause stage which is characterised by hormonal fluctuations on executive function, given that many women report experiencing “brain fog” during this transitional period. A premenopause group was included as a comparison group to enable a more nuanced understanding of cognitive changes across stages. Secondly, the study explored the influence of the severity of overall menopausal symptom burden on executive function, building on prior research that has typically focused on individual symptoms rather than collective severity. Thirdly, sleep quality was assessed as a potential contributor to executive performance, given its well-established link to cognitive functioning in the general literature and its prevalence as a concern among midlife women (see Section 1.6).

Fourthly, the study investigated the role of socio-behavioural factors, including alcohol consumption, caregiving responsibilities, educational attainment, working hours, physical activity, and dietary quality as modifiable influences on cognition which is underexplored in existing menopause literature. Finally, the potential cognitive effects of hormone replacement therapy (HRT) were examined in perimenopausal women, particularly in relation to symptom burden. Questionnaire responses indicated a substantial proportion of perimenopausal participants were using HRT. Given the mixed findings in the literature regarding HRT’s cognitive benefits discussed earlier in section 1.6, this study considered whether HRT use may offer

protective effects on executive function as more women turn to this treatment to manage menopause-associated symptoms.

This cross-sectional study employed a comprehensive, standardised assessment tool of executive function to evaluate subjective cognitive performance. According to (Gioia et al., 2000) an adults' assessment of his or her own executive function can provide critical information that can be useful in developing interventions.
BRIEF-A is a standardised self and informant report that was designed to assess the everyday behaviour of adults aged 18-90 years. Toplak et al. 2009 employed the BRIEF-A as it is a reliable tool that can be used to validly measure executive function. The normative samples used to create the BRIEF-A consists of adults from a range of educational and racial backgrounds as well as different geographical regions matched to United States Census data (Roth et al., 2005). The inclusion of a self-report measure that examines executive function alongside the comparison of three distinct menopause groups is a relatively underexplored area within menopause research.
This study broadened the scope of executive functions examined in relation to menopause. It explores not only the cognitive impact of menopause stage itself but also the influence of associated physiological changes and external socio-behavioural factors such as lifestyle, caregiving responsibilities, and occupational demands.

2.4 Aim and Hypotheses

The primary aim of this research was to evaluate the impact of menopause stage on executive function performance. By examining women's subjective perceptions of cognitive challenges collectively referred to as "brain fog", the study offers insight into the cognitive experience of women undergoing the menopausal transition especially as this period has been associated with many challenges. This key life stage is marked by significant hormonal fluctuations, particularly in

oestrogen, which has been implicated in cognitive changes in previous research.

In addition to this overarching aim (included again below), the study also investigated the following hypotheses:

- Hypothesis 1: To investigate the influence of menopause stage on executive functions, while controlling for the effects of chronological age. It was predicted that perimenopausal women would report higher scores (i.e. greater difficulty) on executive functioning in comparison to premenopausal women.
- Hypothesis 2: To investigate the influence of menopausal symptoms on executive function, it was predicted that women with more pronounced symptoms would report greater executive function challenges.
- Hypothesis 3: To investigate whether sleep quality affects executive function performance in premenopausal, perimenopausal and postmenopausal women. It was predicted that women reporting sleep disturbances would report higher executive function scores.
- Hypothesis 4: Exploratory analysis was performed to the role of socio-behavioural factors on overall executive function
- Hypothesis 5: Exploratory analysis was performed to investigate the impact of HRT on EF

These hypotheses were pre-registered (https://osf.io/project/myh5n/files/osfstorage/662ac096d89607244f1b15a7)

2.5 Method

Study design

Given that no menopause related research had previously used the BRIEF A, a smallest effect size approach was used where Cohen's *f* = 0.11 was used to estimate sample size. As small effects are typical in menopause research, this effect size was used for the power analysis to ensure adequate power. The primary effect of interest was the main effect of menopause stage, not the menopause stage × age interaction.

As the aim was to test whether executive function differed across menopause stages while statistically controlling for age, an a priori power analysis was conducted in G*Power 3.1 program (Faul et al., 2007) for an ANCOVA (Fixed effects, main effects and interactions) with three groups and one covariate (age). Using an effect size of f = 0.11, an alpha level of 0.05, and desired power of 0.80, the analysis indicated that approximately 800 participants were required to detect a significant main effect of menopause stage. The final sample of 818 women (premenopausal, perimenopausal not using HRT, and postmenopausal) met this requirement.

Materials and Procedure

This study employed an electronic questionnaire hosted on the Qualtrics platform https://nottinghampsych.eu.qualtrics.com/jfe/form/SV_eRvQZXlA9xSBXZI for women aged 40+ to complete. The online questionnaire was approved by the University of Nottingham School of Psychology Ethics Committee. In the questionnaire that participants completed, it was important to provide valid resources at the end of the questionnaire to assist women negatively impacted by menopause to reach out to these organisations. The questionnaire also included attention checks to ensure data quality. The questionnaire starts with an information sheet which provides respondents with an overview of what the questionnaire entails. This information allowed participants to make an informed decision about whether to complete the questionnaire. The information sheet in this questionnaire provided information about the purpose of the research, what participants will be asked to do, how their data will be used, details of the researcher and who to contact if they have any complaints or further questions. Anonymity, confidentiality and the voluntary nature of participation were highlighted to participants at the beginning of the questionnaire. Questionnaire responses were anonymised by disabling the function that allows the collection of any identifiable information such as IP addresses. Qualtrics XM® software was used to design the questionnaire, and the content of the

questionnaire was informed by the literature review and in discussion with other researchers who have worked on similar study, Griffiths et al., (2013). The questionnaire took approximately 15 minutes. The questionnaire included sections on demographics, menopause staging criteria, menopause symptoms, and other lifestyle-related questions.

Participants

Participants were recruited through advertisements placed in magazines and local newsletters, dental and general surgery practises, private hospitals, supermarkets. Further details of recruitment strategies are detailed in Appendix 2. The flier and advertisement describe a psychological study on attention and memory in women aged 40 years and above and does not specifically target women with attention and memory complaints. Women aged 40 years and above represented women across the pre-, peri- and postmenopausal stages of menopause. Certain groups of participants were excluded from the study. Specifically, individuals who have undergone surgically induced menopause (hysterectomy, removal of ovaries), those whose periods stopped because of cancer treatment and women with polycystic ovarian syndrome (PCOS) and primary ovarian insufficiency (POI) and postmenopausal women on HRT. Women were allocated in pre-, peri- and postmenopausal groups according to Stages of Reproductive Aging Workshop (STRAW+10) criteria by Harlow at al. (2012). This criterion was based on self-reported bleeding cycles in the past 12 months. Participants were classified as premenopause if they answered yes to my period has not changed from how it has always been – regular monthly cycles. Participants were classified as perimenopausal if they answered yes to the following question: In consecutive months, experiencing periods that have been delayed by 7 days or more or my periods have changed or become irregular and I have had a period within the last 12 months or I have skipped cycles for 60 days or more. Participants were classified as postmenopause if they answered yes to the question: I have not had a period in 12 months. Participants who reported using HRT were categorised as

either perimenopause on HRT or postmenopause on HRT based on if they answered yes to the question: I am taking HRT and I am perimenopause or I am taking HRT and I am postmenopause respectively. Additionally, although a substantial proportion of perimenopausal women in the sample reported using HRT, all hypotheses concerning perimenopausal women were restricted to those not using HRT, except for Hypothesis 5, which included perimenopausal women using HRT. For some women using hormonal contraceptives, menstrual cycles were either irregular or absent, making it difficult to determine their menopausal stage based solely on cycle patterns. As a result, these participants were asked to self-classify as premenopausal, perimenopausal. This approach was supported by growing public awareness and media coverage around menopause, which has equipped many women with a broader understanding of menopausal stages and symptoms, enabling more informed self-identification

Out of the 1,187 respondents who completed the Qualtrics questionnaire and could be categorised, 151 were excluded for various reasons: 103 due to surgical menopause, 13 due to cancer treatment, three due to PCOS/POI, three due to unclassified menopause stage with HRT and endometriosis complications and 29 due to being postmenopausal but on HRT. Additionally, 57 respondents were excluded from the analysis due to failing attention and validity checks.

Measures

Each participant completed the online self-report questionnaire assessing a range of measures that are detailed in this section. These include assessments of executive function, menopause-related symptoms, menopause stage, caring responsibilities, health and lifestyle factors and socio-demographic characteristics. Table 2-1 presents a summary of the measures used in the questionnaire, with additional details provided in the sections that follow.

Table 2-1 Summary of questionnaire

Question number	**Information required / being asked**	**Description / Rationale**
[1] – [3]	Study information and consent for participation	• Consent is required for participation per the ethics approval
[4] and [5]	Demographic information	• Participants should be 40+ years old • Ethnic minority groups are particularly of interest in this study • Ethnicity options used are based on the options recommended by the ONS
[6]	Presence/occurrence/frequency of periods	• To establish menopause stage according to the STRAW +10 classification
[7]	Impact of menopause symptoms	• Self-reported symptoms • Based on the Greene Climacteric Scale
[8] – [11]	Career/job and educational background	• To build a socio-economic profile • Options for educational attainment is based on the options recommended by the Office of National Statistics (ONS)
[12] – [14]	Domestic responsibilities	• To determine the interplay between potential domestic responsibilities and menopause

Question number	Information required / being asked	Description / Rationale
[15] – [18]	Lifestyle related information	• Based on options used by GP surgeries to ascertain general state of patient health
[19]	Sleep quality information	• Rating of overall quality of sleep in the last 7 days • A modified version of the single-item sleep quality scale (SQS)
[20]	Executive dysfunction information	• 75-item self-report measure known as BRIEF-A

Socio-demographics

Sociodemographic measures included questions related to age, educational attainment, occupation, employment status, weekly work hours and ethnicity.

Caring responsibilities

Questions were asked to ascertain any duties or commitments that participants provide such as looking after children, elderly parents or relatives or looking after family with long term physical or mental health conditions or illnesses, or problems related to old age. Menopause literature lacks substantial evidence on the potential impact of these additional responsibilities, which disproportionately affect women.

Lifestyle factors

Smoking habit

Participants were asked how many times in a day they smoked cigarettes with a range of responses from ‘never’ to ‘31 or more’. This resulted in the identification of participants who never smoked to those who smoked regularly during the day.

Diet

In relation diet, participants were asked how many times in the past month that they consumed sweets, fruits, vegetables, fast food and skipped breakfast with options ranging from ‘never’ to ‘6 times or more/week’. Higher scores on the diet scale corresponded to poorer dietary habits.

Alcohol use

This measure was used to ascertain the drinking habit of participants by asking participants how often they had a drink during the week. Options ranged from ‘never’ to ‘4 or more times a week’. Higher scores on this measure reflected greater alcohol consumption.

Physical activity

Levels of physical activity were assessed using items from General Practice Physical Activity Questionnaire (GPPAQ) (Department of Health, 2009). Participants were asked how many hours were spent engaging in various physical activities during the week. Physical activities comprised of a wide range of activities such as swimming, cycling, gardening, housework and gym activities. Higher scores on this measure reflected a more active lifestyle.

Menopause stage

Menopause stage or reproductive stage of participants was based on participants responses to relevant questionnaire items on bleeding patterns. Bleeding patterns described were based on definitions from the terminology from the 2012 Stages of Reproductive Aging Workshop (STRAW+10) (Harlow et al., 2012). These were used as the primary mode of classification to categorise women into premenopause, perimenopause and postmenopause. Premenopause stage was defined as having regular monthly cycles that have not changed from how they have always been; Perimenopausal stage was defined as experiencing irregularities in the menstrual cycle and postmenopause stage was defined as not experiencing a menstrual cycle for 12 months or more. Based on responses from a piloted study of the questionnaire it was determined that the staging of menopause was not clear initially with no distinctions made between women on contraceptives and those on HRT. This was rectified to ensure that clear distinctions were made between these two groups. Some women who are on contraceptives do not experience periods and this is also the case when they begin using hormone replacement therapy (HRT). Some might also experience irregular bleeds as a result of using HRT whereas they might not have previously done so while on contraceptive drugs.

A woman might also be premenopausal but as she is on a contraceptive, it will be difficult to stage this woman based on her

bleeding cycle as she is not experiencing a monthly bleed and the Stages of Reproductive Aging workshop (STRAW+10) classifies a woman based on her bleeding cycle. In clinical practice, a combination of factors are taken into consideration before classifying women such as hormone levels, menstrual pattern, family history, age and menopausal symptoms (Recommendations | Menopause, 2015). As such, participants also had the option to self-classify their menopause stage acknowledging that bleeding patterns can be affected by contraception or hormone replacement therapy (HRT). This allowed for greater flexibility in categorisation beyond the predefined stages. Women who self-reported experiencing premature ovarian failure, polycystic ovarian syndrome, or primary ovarian insufficiency were excluded from the study. Women who reported having undergone surgical menopause or menopause because of cancer treatment were also excluded from the study.

Menopause symptoms

The Greene Climacteric scale (Greene, 1998) which consists of 21 symptoms was used to assess menopause symptoms and its severity in pre, peri and postmenopause women. The GCS is a validated tool that has widely been used in research, with numerous studies demonstrating its sound psychometric properties (Hunter & Rendall, 2007; Travers et al., 2005). Greene (1998) constructed the scale using factor analysis of the wide range of symptoms presented by women transitioning to menopause. Greene demonstrated that this measurement tool has acceptable test–retest reliability across subscales ranging from 0.83 to 0.87. A more recent work by Vallee et al. (2005) also confirmed its validity with GCS scores correlating strongly with other menopause symptom measures. Its psychometric properties have also been demonstrated and standardised in different population as reported by Seib et al. (2022) and many years of research demonstrating strong construct validity (Schneider, 2002).

Participants were asked to rate each symptom based on their current condition using a four-point Likert scale (0 = “not at all” to 3 = “extremely”). The symptoms are divided into four subcategories which measure psychological, somatic, vasomotor and sexual dysfunction. The psychological symptoms consist of (items 1-11), somatic (items 12-18), vasomotor (items 19-20) and loss of interest in sex (item 21). The psychological cluster is further broken down into two subclusters, anxiety (items 1-6) and depression (items 7-11). The total Greene Climacteric score (GCS) was calculated to measure the severity of menopause symptoms with higher scores indicating more pronounced symptoms. The total score is obtained by summing the individual symptom scores across all categories. Other commonly reported menopause symptoms in the literature but not included in the Greene Climacteric scale were included in the questionnaire but not analysed in this study.

Sleep Quality

A modified version of the single-item sleep quality scale by (Snyder et al., 2018) was used and asked participants to rate their overall sleep quality for the majority of nights from the last 7 days. Participants were asked to think about their quality of sleep overall, such as how many hours of sleep you got, how easily you fell asleep, how often you woke up during the night (except to go to the bathroom), how often you woke up earlier than you had to in the morning and how refreshing your sleep was. Ratings used were terrible, poor, fair, excellent and good with higher scores indicating better sleep quality

BRIEF-A

Individuals are best positioned to describe their EFs and how this is utilised in reacting to situations, monitoring their behaviour or in solving problems at home, work or in school (Gioia et al., 2000). In BRIEF-A, respondents are asked to self-report on 75 items related to their natural

settings or environment. In the daily life and everyday behaviour of adults, executive dysfunction can be observed. The assessment is made of nine scales which measure inhibit, shift, emotional control, self-monitor, initiate, working memory (WM), plan/organize, task monitor, and organization of materials and these shall be discussed shortly. Examples of the items related to some particular domains are 'I forget what I am doing in the middle of things' (WM), 'I have trouble accepting different ways to solve problems with work, friends, or tasks' (shift) and 'People say that I am easily distracted' (inhibit). A 3-point Likert scale, with the options 'never', 'sometimes' or 'always' are provided as options for participants to select which was applicable to them in their everyday behaviour. A Global Executive Composite (GEC) is a summary of all the nine subscales described above. The GEC is a composite of two index scores i.e. Behavioural Regulation Index, BRI, and the Metacognitive Index, MI and gives an overall measure of executive function. In this project, the BRI and MI indices were the primary executive function measures of interest, while GEC was examined in relation to the impact of lifestyle factors on overall executive function. The BRI consists of four subscales and the MI consists of five subscales (listed in Table 2-2).

Table 2-2 BRI and MI index scores and their corresponding subscales

Index scores	**Subscales**
BRI	Inhibit
	Shift
	Emotional control
	Self-monitor
MI	Initiate
	Working memory
	Plan / organise
	Task monitor
	Organisation of materials

The raw scores can be calculated for each of the scales as well as the indices and composite score. The T scores which can be obtained from

the raw scores are based on a comparison to a normative sample of 1500 self- and 1200 informant reports (Roth et al., 2005). T scores are used in the interpretation of EFs on self and informant reports. These scores have a mean of 50 and a standard deviation of 10 with T scores at or greater than 65 considered as clinically significant results and requiring further investigation. Thus, an individual's T scores provide information relative to scores received in the normative sample. T scores are used in the interpretation of executive dysfunction with higher scores indicative of greater difficulties with executive function in one's everyday life.

The BRIEF-A also has Negativity, Infrequency, and Inconsistency validity scales which detects if a respondent is answering questions in an unusual manner such as answering 'Often' to a question asking if you forget your name.

Brief-A subscales

Inhibit sub-scale is defined as the ability to suppress an inappropriate response at the right time or resist impulses. It consists of 8- items; e.g. "*I have problems waiting my turn"* and *"I make decisions that get me into trouble (legally, financially and socially)".* In adults who do not perform well in this subscale, they would tend to be disruptive in group activities, and this will be particularly evident on tasks requiring a delayed response.

Shift sub-scale assesses individuals' ability to transition between tasks, which can pose challenges for some. These skills are crucial for problem-solving and adapting to changing situations as they arise. This scale encompasses both behavioural responses to environmental changes and cognitive shifting, which is involved in flexible problem-solving. Disruptions to routine may lead some individuals to display anxious or emotional reactions, which are observed in the Emotional Control Subscale. Those facing challenges with cognition in terms of shifting, may exhibit rigid or inflexible thinking and struggle to generate new ideas. This sub-scale consists of 6-items, e.g., *"I have trouble*

thinking of a different way to solve a problem when stuck" and *"I am bothered by having to deal with changes".*

Emotional Control sub-scale assesses an adult's capacity to control or deal with emotional responses. Emotional explosives of outbursts is an example of an inability to control one's emotions. Crying unexpectedly or laughing hysterically in reaction to seemingly minor situations are examples of people who have poor emotional control. This sub-scale consists of 10-items; e.g., *"I react more emotionally to situations than my friends"* and *"I get upset quickly or easily over little things".*

Self-monitoring involves assessing one's capacity to observe the impact of their actions on themselves and others. Challenges with self-monitoring can manifest as a lack of recognition or awareness regarding one's behaviour within a social setting. It consists of 6-items; e.g., *"I don't think about consequences before doing something"* and "*I don't notice when I cause others to feel bad or get mad until it is too late*".

Initiate sub-scale assesses individuals' capacity to independently start tasks as well as activities, generate ideas, and formulate problem-solving strategies. Weak initiation skills often result in the desire to succeed in tasks but difficulty initiating them independently. Individuals with poor initiation abilities may require prompting to begin tasks. Additionally, those lacking organization skills can feel overwhelmed by large tasks, making it challenging for them to initiate tasks in the first place. It consists of 8-items; e.g., *"I need to be reminded to begin a task even when I am willing"* and "*I have trouble coming up with ideas for what to do with my free time*".

Working memory sub-scale assesses an individual's ability to hold information in one's mind while actively manipulating that information so that a task can be completed. It involves one's ability to take in and hold or store information that is essential for a variety of cognitive activities. Individuals who have poor working memory have trouble completing activities with multiple steps. Other examples include having problems remembering things like directions to a location or

instructions to complete a task even for a few minutes. In working memory, it is essential to have the ability to maintain consistent attention as well as performance on tasks over extended periods. It consists of 8-items; e.g., *“I have trouble with jobs or tasks that have more than one step”* and *“I have trouble remembering things even for a few minutes such as directions, phone numbers”.*

Plan and Organise encompass two aspects of executive function. Planning involves setting goals and devising suitable strategies to achieve them, while organisation involves imposing structure on information, actions, or materials to attain an objective. Together, these aspects enhance the ability to accomplish tasks in a timely manner. Individuals with low performance on this sub-scale tend to approach activities haphazardly, leading to overwhelmed feelings. Such individuals may struggle to effectively complete tasks, especially when necessary tools are not prepared in advance. It consists of 10-items e.g., *“I have good ideas but cannot get them on paper”* and “*I have trouble finishing a task on my own*”.

Task Monitor assesses one's capacity to monitor on-going activities and evaluate the adequacy of completed tasks. It evaluates problem-solving, task-oriented, and monitoring functions. Individuals experiencing difficulties with task monitoring lack awareness of their performance during problem-solving activities. It consists of 6-items; e.g., *“I misjudge how difficult or easy tasks will be”* and *“I make careless errors when completing tasks*”

Organisation of Materials sub-scale refers to being able to keep living spaces and materials in a tidy and organised manner. This includes orderliness at work, living spaces, and storage areas such as wardrobes, desks and bedrooms. Difficulties organising work and home spaces and cleaning up personal belongings are examples of difficulties exhibited with this scale. It consists of 8-items; e.g., *“I lose things (such as keys, money, wallet, homework, etc.)”* and “*I don't pick up after myself*”.

BRIEF-A Indices (BRI and MI)

Two indexes, the Behavioural Regulation Index (BRI) and the Metacognition Index (MI) are derived from the nine sub-scales described above. As mentioned previously, the BRI is made up of the Inhibit, Shift, Emotional Control, and Self-Monitor sub-scales. The BRI index refers to an individual's capacity to maintain appropriate control over one's behaviour as well as regulate one's emotional responses to situations. This includes monitoring one's actions, inhibiting thoughts and how we behave, thinking creatively when solving problems and regulation of emotions. The MI scale is made up of Initiate, Plan and Organise, Working memory, Task Monitor and the Organisation of Materials sub-scales. It also refers to an individual's capacity to methodically come up with solutions to problems by engaging in activities that involve planning and organisation. These planning and organisational activities must also be maintained in order to complete tasks even in different contexts. It involves maintaining attention and problem solving.

Assessing BRIEF-A validity

Inconsistency, infrequency and negativity validity scales on the BRIEF-A will be calculated as part of this research. Specific questions or BRIEF-A items are related to each validity scale and scored to get a total raw score.

Inconsistency scales

Scores on this scale refer to the manner in which an individual answers BRIEF-A items that are similar in a dissimilar manner in comparison to individuals in mixed healthy/clinical sample and individuals in the combined normative samples (Roth et al., 2005). For example, Item 46 ('I forget instructions easily') and Item 56 ('I have trouble remembering things, even for a few minutes (such as directions, phone numbers') are similar but if participants answer 'Never' and 'Often', then that is inconsistent. Scored greater than or equal to 8 are considered inconsistent.

Infrequency scales

This scale assesses the manner in which a participant's responses to BRIEF-A items deviate from typical answers provided. It measures five items that are answered in a typical manner by most people. Example, answering that one has trouble counting to three or that one never makes mistakes is highly unusual.

Negativity scales

The negativity scale assesses the degree to which an individuals' responses to BRIEF-A items reflect an atypically negative manner, (i.e. selecting 'Often'-3). Scores greater than 6 are considered unusually negative. Negativity scores were not used to exclude participants.

2.6 Statistical analysis

IBM SPSS Statistics 28 was used for data analysis and Microsoft Excel version 2509 and JASP 0.19.3 were used to visualise data and plot graphs. The following results will report findings from the main hypothesis and present them visually. Statistical analyses used in this research were based on the research questions and the types of data generated. Menopause groups included in analysis are premenopause, perimenopause (not on HRT) and postmenopause unless otherwise stated.

2.7 Results

Assumption testing

The dependent variables, that is BRI and MI indices, were checked for normality and extreme outliers (±3SD). The data was satisfied for equality of variance using Levene's Test for Equality of Variance (p > 0.05). The *'Test of Normality'* showed that BRI and MI scores were not normally distributed in premenopause and postmenopause women

(*Kolmogorov-Smirnov; p<0.001)*. This violated the assumption of normality. For Kurtosis and Skewness, standard errors for kurtosis and skewness are increased with larger samples and this was the case in some groups, but this is not uncommon in a large sample of 817 respondents. According to Tabachnick & Fidell. (2007) variables with statistically significant kurtosis and skewness do not deviate enough from normality to make a huge difference when analysing results. Fields, A. (2009) also recommends not using significance tests of kurtosis and skewness in large samples, such as in this current study, as they tend to yield produce significant results even with small deviations. The histograms and Q-Q plots were visually inspected and this showed that the extent of non-normality was not sufficient to transform data in this large sample size. As such, parametric tests were deemed suitable for data analysis. Assumption testing appropriate for tests were performed where appropriate and this included tests for homogeneity of regression slopes, variance, normality, and extreme outliers were performed on regression and ANCOVA analyses. Visual inspection of a normal probability plot of the residuals indicated that these were normally distributed.

Sample characteristics

Table 2-3 below for description of the study sample. Women were primarily Caucasian (75.89%), educated at degree level or above (68.64%) and in employment (81.82%). On average, age varied across the menopausal groups, with premenopausal women being the youngest, followed by perimenopausal women and then postmenopausal women being the oldest. Higher BRIEF-A scores reflect poorer executive function, and in this sample, overall scores remained within normal limits. Appendix 7 also shows the average scores of all the nine sub scales in premenopause, perimenopause and postmenopause women.

Participant characteristics

Table 2-3 Demographics of participants retained for analysis

Characteristic (n (%))		All	Premenopause	Perimenopause (not on HRT)	Perimenopause (on HRT)	Postmenopause
		n = 979	n = 257	n = 283	n = 161	n = 278
Ethnicity						
	White	743 (75.89)	169 (65.76)	218 (77.03)	145 (90.06)	211 (75.90)
	Black/African/Caribbean/Black British	106 (10.83)	42 (16.34)	29 (10.25)	5 (3.11)	30 (10.79)
	Asian/British Asian	74 (7.56)	36 (14.01)	20 (7.07)	2 (1.24)	16 (5.76)
	Mixed/Multiple ethnic group	17 (1.74)	3 (1.17)	6 (2.12)	4 (2.48)	4 (1.44)
	Other ethnic group	5 (0.51)	1 (0.39)	2 (0.71)		2 (0.72)
	prefer not to say	4 (0.41)	1 (0.39)	2 (0.71)		1 (0.36)
	missing responses	30 (3.06)	5 (1.95)	6 (2.12)	5 (3.11)	14 (5.04)
Caring responsibilities (elderly parents/relatives, family with long-term and age-related changes)						
	Yes	217 (22.17)	37 (14.40)	73 (25.80)	36 (22.36)	71 (25.54)
	No	760 (77.63)	220 (85.60)	210 (74.20)	124 (77.02)	206 (74.10)
	missing response	2 (0.20)			1 (0.62)	1 (0.36)
Parents						
	Yes	768 (78.45)	199 (77.43)	230 (81.27)	130 (80.75)	209 (75.18)
	No	211 (21.55)	58 (22.57)	53 (18.73)	31 (19.25)	69 (24.92)
Employment						

	Yes	801 (81.82)	226 (87.94)	240 (84.81)	144 (89.44)	191 (68.71)
	No	173 (17.67)	30 (11.67)	42 (14.84)	15 (9.32)	86 (30.94)
	Not stated	5 (0.51)	1 (0.39)	1 (0.35)	2 (1.24)	1 (0.36)
Education						
	Degree level or above	672(68.64)	203 (78.99)	189 (66.78)	114 (70.81)	166 (59.71)
	Non degree level	276 (28.19)	48 (18.68)	86 (30.39)	45 (27.95)	97 (34.89)
	No qualification	9 (0.92)	0	2 (0.71)	1 (0.62)	6 (2.16)
	Not stated	19 (1.94)	6 (2.33)	4 (1.41)	1 (0.62)	8 (2.88)
	Other	3 (0.31)	0	2 (0.71)		1 (0.36)
Characteristic (M (SD))						
Weekly employment hours		1.39 (0.88)	1.46 (0.85)	1.52 (0.84)	1.55 (0.87)	1.10 (0.93)
Caring responsibilities (elderly parents/relatives, family with long-term and age-related changes)		0.22 (0.42)	0.14 (0.35)	0.26 (0.44)	0.22 (0.42)	0.26 (0.44)
Diet Quality		6.13 (3.11)	6.29 (3.11)	6.53 (3.10)	6.17 (3.28)	5.56 (2.95)
Alcohol consumption		1.59 (1.22)	1.38 (1.17)	1.58 (1.18)	1.97 (1.16)	1.58 (1.30)
Physical activity		6.65 (2.49)	6.59 (2.51)	6.52 (2.42)	7.08 (2.46)	6.59 (2.55)
Sleep quality		1.80 (1.00)	2.14 (0.94)	1.66 (0.98)	1.45 (1.02)	1.82 (0.97)
Age (years)		49.04(6.41)	43.03 (3.08)	47.75 (4.30)	48.97 (3.99)	55.96 (5.02)
BRI		55.54(12.22)	51.82 (11.90)	56.89 (11.46)	59.50 (12.06)	55.31 (12.44)
MI		58.24(13.88)	53.37 (12.80)	60.28 (13.34)	63.06 (13.95)	57.86 (13.98)
Total Greene Climacteric score		22.97(11.02)	17.10 (10.15)	24.97 (10.26)	29.19 (8.63)	22.78 (11.17)

The influence of menopause stage on executive functions (Hypothesis 1)

An ANCOVA was used to examine the effect of menopause stage on executive function. Age was included as a covariate to understand the study's aim of examining whether menopausal stage impacts executive function independently of chronological ageing. According to Maki and Weber (2021), the most common covariate used in menopause studies is age because of its known association with cognitive performance. Thus, the inclusion of age was to align with existing menopause research that has included age as a covariate. According to Tabachnick and Fidell (2007), an ANCOVA as a form of the general linear model is deemed appropriate to adjust for differences in groups in non-experimental research where groups cannot be randomly assigned and are naturally occurring. Including age as a covariate statistically adjusts for age-related variance before examining the association between the independent variable, menopause stage and the dependent variable, executive function performance. This ensures that any group differences observed reflect menopause stage itself rather than differences in age. Tabachnick and Fidell note that ANCOVA functions as a descriptive model that clarifies the relationship between groups and an outcome variable after adjusting for the influence of a covariate. In this context, it allows a more accurate understanding of the association between menopause stage and executive function performance once age-related variance has been statistically controlled. Importantly, ANCOVA does not imply causality, which aligns with the aims of the present study, where the objective was to examine whether menopause stage was associated with executive function performance after adjusting group means for age. In ANCOVA, the model adjusts group means by statistically controlling for age, allowing comparisons between menopausal groups at equivalent levels of the covariate. This means the analysis does not assume that age influences all groups in the same way; instead, it estimates group differences in executive function performance after accounting for age-related variance. As such, the interpretation of results must consider

the role of the covariate rather than relying solely on the unadjusted overall effect of menopause stage on executive function performance. This ensures that any group differences observed reflect menopause stage itself rather than age-related variation in executive performance. Although a regression model could also have been used, an ANCOVA is more appropriate as it is essentially a regression model that includes a categorical predictor which are the menopause stages and the continuous variable which is age and is specifically designed for comparing group means after statistically adjusting for a covariate and this was primary the aim of this research.

To investigate differences between menopause groups in executive function, two analyses of covariance (ANCOVAs) were performed with group (premenopausal vs. perimenopausal (no HRT) vs. postmenopausal) as the between-subject factor. The dependent variables were the BRIEF-A indices, specifically the BRI and the MI T scores. Menopause stage was the categorical predictor or independent variable. Age was included as a covariate in both BRI and MI analyses to adjust for potential confounding. The assumption of homogeneity of variance was tested using Levene's test, which was non-significant ($p = 0.551$), indicating that the assumption of equal variances across groups was met. There was also homoscedasticity as assessed by visual inspection of the standardised residuals plotted against the predicted values for BRI and MI. The assumption of homogeneity of regression slopes was violated, as the interaction between the covariate (age) and menopause stage was statistically significant. However, since menopause stage is naturally occurring observational data rather than an experimentally manipulated variable, causal inferences cannot be drawn from the results. However, by controlling for biological age, a potential confounding factor influencing both menopause stage and cognitive scores any observed associations between menopause stage and cognitive performance are independent of age differences across groups.

BRI analysis

Adjusted means ± standard error are presented, unless otherwise stated. There was a significant main effect of menopause stage, F (2,814) =10.383, $p < 0.001$, $\eta p^2 = 0.025$. The covariate age was not significant, F (1,814) = 0.001 p = 0.979. As shown in Figure 2-1, post hoc analysis using Bonferroni corrected t-tests revealed that perimenopausal women (M = 56.89, SE = 0.721) reported significantly greater behavioural regulation difficulties in comparison to premenopausal women (M =51.83, SE = 0.954, p= 0.000026). There were no significant differences between perimenopausal and postmenopausal women (p = 0.654), nor between premenopausal and postmenopausal women (p = 0.106).

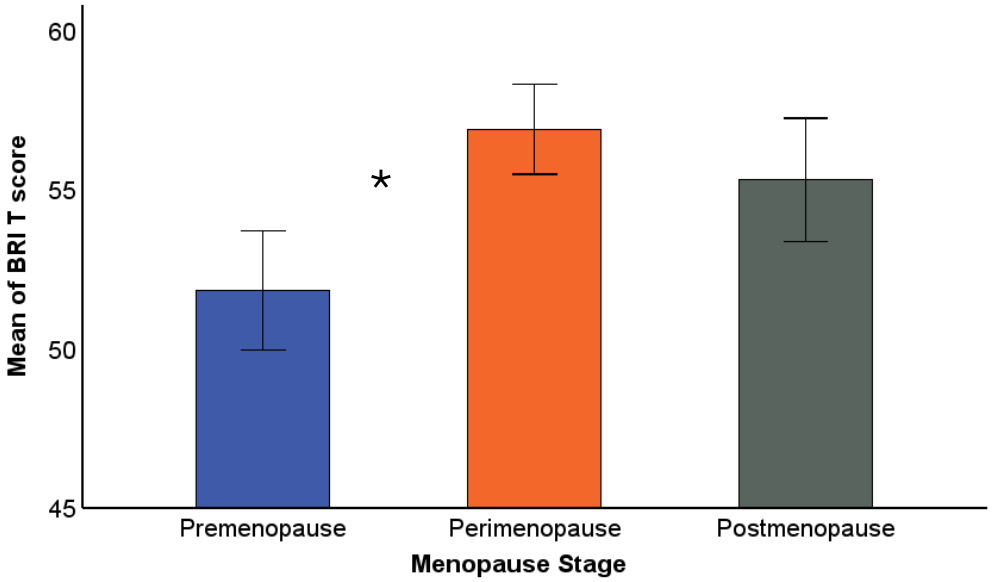

Figure 2-1 BRI score from the BRIEF-A in pre, peri and post menopause

Note: * Indicates the significant difference ($p < 0.05$). Error bars are 95% CI. Covariates appearing in the model are evaluated at the following values: Age = 49.06

Exploratory analysis of BRI subscales

The BRIEF-A subscales were analysed separately to examine differences in individual subscales between premenopausal, perimenopausal, and postmenopausal women. These are presented in Table 2-4. As the ANCOVA examining for group differences on

behavioural regulation and metacognitive skills were significant, group differences for each subscale were investigated. Post hoc comparisons using the stricter Bonferroni correction, adjusted for the nine BRIEF-A scales investigated ($p = 0.05/9 = 0.006$), revealed that only the Inhibit, Shift and Emotional Control subscales remain statistically significant under this more stringent criterion.

Table 2-4 BRIEF-A Informant report scores by menopause stage (BRI)

	Menopause Stage					
BRIEF-A scales	**Premenopause M (SE)**	**Perimenpause M (SE)**	**Postmenopause M (SE)**	***F***	**Partial η^2**	***P* value**
BRI	51.83 (0.95)	56.89 (0.72)	55.30 (0.99)	10.383*	0.025	0.000035
Inhibit	48.63 (0.78)	51.52 (0.59)	52.18 (0.81)	5.326*	0.013	0.005
Shift	55.50 (.99)	59.71 (0.75)	56.62 (1.03)	8.380*	0.020	0.000250
Emotional control	53.99(1.04)	59.82 (0.79)	57.83 (1.081)	11.68*	0.028	0.000010
Self-monitor	46.63(0.85)	49.22(0.64)	48.37(0.88)	3.467	0.008	0.032

Note: Age adjusted means for each group are presented above. BRIEF-A - Behaviour Rating Inventory of Executive Functions—Adult; BRI = Behavioural Regulation Index; n (premenopause) = 257; n (perimenopause) = 283; n (postmenopause) = 278. *p<.006 represents significant main effect of menopause stage.

MI analysis

There was a significant main effect of menopause stage, F (2,814) =14.360, $p < 0.001$, $\eta p^2 = 0.034$, as shown in Figure 2-2 below. The covariate age was not significant, F (1,814) = 1.223 $p = 0.259$. Post hoc analysis using Bonferroni corrected t-tests revealed that perimenopausal women (M = 60.44, SE = 0.809) reported significantly greater metacognitive difficulties in comparison to premenopausal women (M = 54.11, SE = 1.07, $p < 0.001$). There was no significant difference between perimenopausal and postmenopausal women (M = 57.01, SE = 1.11 $p = 0.055$). There was no significant difference between premenopausal and postmenopausal women ($p = 0.348$).

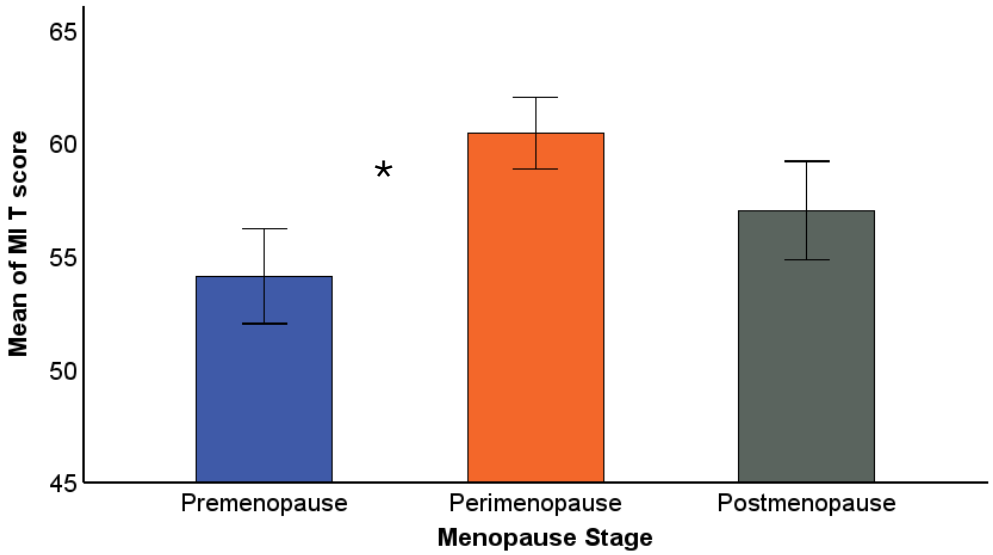

Figure 2-2 MI score from the BRIEF-A in pre, peri and postmenopause

Note: * Indicates the significant difference (p < 0.05). Error bars are 95% CI. Covariates appearing in the model are evaluated at the following values: Age = 49.06

Exploratory analysis of MI subscales

As the ANCOVA examining for group differences on metacognition was significant, group differences for each subscale were investigated. The MI BRIEF-A were also analysed to examine differences in executive function among premenopausal, perimenopausal, and postmenopausal women using a one-way ANCOVA, controlling for age. With the stricter

Bonferroni correction applied to account for the nine BRIEF-A scales investigated (p = 0.05/9 = 0.006), the Initiate, Working Memory, Plan/Organise, Organisation of Materials and Task Monitor subscales retained statistical significance.

Table 2-5 presents the mean scores on the MI BRIEF-A subscales and indices. BRIEF-A scores were all within normal limits except for the working memory score of 66.04 observed in perimenopausal women.

Table 2-5 BRIEF-A Self report scores by menopause stage (MI)

	Menopause Stage					
BRIEF-A scales	***Premenopause M (SE)***	***Perimenpause M (SE)***	***Postmenopause M (SE)***	***F***	***Partial η^2***	***P value***
MI	*54.11 (1.07)*	*60.44 (0.81)*	*57.01 (1.11)*	*14.360**	*0.034*	*< 0.001*
Initiate	*54.22 (1.08)*	*59.73(0.81)*	*56.46(1.12)*	*11.09*	*0.027*	*0.000018*
Working Memory	*57.23 (1.17)*	*66.04(0.88)*	*62.99(1.21)*	*21.242**	*0.050*	*< 0.001*
Task monitor	*53.74(0.99)*	*58.52(0.75)*	*55.90(1.02)*	*9.703**	*0.023*	*0.000068*
Plan/Organise	*53.20 (1.01)*	*58.02 (0.77)*	*53.85 (1.05)*	*11.747**	*0.028*	*0.000009*
Organisation of materials	*50.17(0.95)*	*53.75(0.72)*	*52.23(0.99)*	*5.472*	*0.013*	*0.004*

Note: Age adjusted means for each group are presented above are presented above. BRIEF-A - Behaviour Rating Inventory of Executive Functions—Adult; MI = Metacognition Index; n (premenopause) = 257; n (perimenopause) = 283; n (postmenopause) = 278. **p* < .006 represents significant main effect of menopause stage. Further exploration of pairwise group comparisons within each subscale of the BRI and MI index are in Appendix 4.

Another factor to consider is that the BRIEF-A provides age normalised T scores, which remove age related variance during scoring. Although the BRIEF A produces age normalised T scores, meaning that age-related variance is already removed during scoring, age was included as a covariate in the Chapter 2 analyses. This makes the age adjustment statistically redundant, but it does not bias the results. To confirm this, the analyses were repeated using raw BRIEF-A BRI and MI scores, which retain age-related variance. The same significant group differences were observed, with perimenopausal women reporting poorer executive function performance than premenopausal women.

In BRI analysis, there was a significant main effect of menopause stage, F (2,814) = 10.936, $p < 0.001$, $\eta p^2 = 0.026$. The covariate age was not significant, F (1,814) = 0.971 $p = 0.325$. Post hoc analysis using Bonferroni corrected t-tests revealed that perimenopausal women (M = 48.89, SE = 0.656) reported significantly greater behavioural regulation difficulties in comparison to premenopausal women (M =44.18, SE = 0.867, p= 0.0000156). There were no significant differences between perimenopausal and postmenopausal women (p = 0.581), nor between premenopausal and postmenopausal women (p = 0.100).

In MI analysis, there was a significant main effect of menopause stage, F (2,814) =15.332, $p < 0.001$, $\eta p^2 = 0.036$. The covariate age was not significant, F (1,814) = 0.027 $p = 0.869$. Post hoc analysis using Bonferroni corrected t-tests revealed that perimenopausal women (M = 69.255, SE = 0.977) reported significantly greater metacognition difficulties in comparison to premenopausal women (M = 61.359, SE = 1.292, $p < 0.001$) and postmenopausal women (M = 67.969, SE = 1.340, p = 0.044). There was no significant difference in EF performance between premenopausal and postmenopausal women (p = 0.315). The pattern of results was consistent when using T-scores, although the peri- versus postmenopausal comparison narrowly missed

significance (p = 0.055) compared with the significant result obtained when using raw scores (p = 0.044).

The influence of menopause symptoms on executive functions (Hypothesis 2)

Prior to investigating the influence of menopause symptoms on executive functions, I first compared symptoms severity across pre-, peri- and postmenopausal women.

Exploratory analysis of Total GCS scores across the three menopause groups, premenopause, perimenopause and postmenopause

To examine differences in menopause groups in Total GCS or menopause symptoms, an analysis of covariance (ANCOVA) was performed with group (premenopausal vs. perimenopausal (no HRT) vs. postmenopausal) as the between-subject factor. The dependent variable was the Total GCS scores from the Greene Climacteric scale. Menopause stage was the categorical predictor or independent variable. Age was included as a covariate in the analyses to adjust for potential confounding.

There was a significant main effect of menopause stage $F(2, 814) = 30.166$, $p < 0.001$, partial $\eta^2 = 0.069$. This indicates that menopause stage had a significant effect on menopause symptoms. There was no significant effect of age on menopause symptoms, $F(1, 814) = 0.625$, $p = 0.429$, partial $\eta^2 = 0.001$.

Post hoc analysis using Bonferroni corrected t-tests revealed that perimenopausal women (M = 25.06, SE = 0.64) reported significantly higher menopause symptoms in comparison to premenopausal women (M =17.51. SE = 0.84, $p < 0.001$) and postmenopausal women (M = 22.30, SE = 0.87, $p = 0.048$). Postmenopausal women (M = 22.30, SE = 0.87) reported significantly higher menopause symptoms in comparison to premenopausal women (M =17.51. SE = 0.84, $p = 0.003$).

Next, to investigate the severity of menopausal symptoms on executive function performance (BRI and MI, Hypothesis 2), two separate linear

regression analyses were conducted. All participants not taking HRT were included. Each analysis used either BRI or MI scores as the outcome variable and total symptom score on the Greene Climacteric scale (GCS) as the predictor variable. Age was included as a covariate in both regression models.

BRI Regression Analysis

A simple linear regression was conducted to evaluate the predictive value of Total Greene Climacteric score on executive function, BRI while controlling for age. To assess linearity, a scatterplot of BRI scores against Total GCS with superimposed regression line was plotted. A visual inspection of the plot showed a linear relationship between the two variables. There was slight heteroskedasticity and normality of the residuals. There was independence of residuals, as assessed by a Durbin-Watson statistic of 1.911. There were no extreme outliers in BRI and MI T scores.

Total GCS predicted BRI scores, F (2,815) = 265.07, p < 0.001 accounting for 39.4% of the variation in BRI scores with adjusted R^2 = 39.3%. However, age was not a significant covariate in the model, B = -0.036, t (815) = -0.731, p = 0.465, 95% CI (-0.13, 0.06). This indicates that age did not significantly contribute to the prediction of BRI scores. A summary of results from the regression can be seen in Table 2-6.

Table 2-6 Linear regression coefficient results for BRI

BRI	***B***	**95% CI for B**		**SE B**	**β**	**R^2**	**ΔR^2**
		LL	UL				
Model						.394	.393*
Constant	41.473*	36.71	45.24	2.42			
Age	-.036	-.132	.061	.049	-.020		
Total GCS	.692*	.632	.751	.030	.630*		

Note. Model = “Enter” method in SPSS statistics; *B* = unstandardised regression coefficient; CI = confidence interval; LL = lower limit, UL = upper limit; SE *B* = standard error of the coefficient; β = standardised

coefficient; GCS = Greene Climacteric scale; R^2 = coefficient of determination; ΔR^2 = adjusted R^2. *p < 0.001

MI Regression Analysis

A simple linear regression was conducted to evaluate the predictive value of Total Greene Climacteric score on executive function using MI scores while controlling for age. Total GCS predicted MI scores, F (2, 815) = 188.05, p < 0.001, accounting for 31.6% of the variation in MI scores with adjusted R^2 = 31.4%. Again, age was not a significant covariate in the model, B = 0.043, t (815) = 0.726, p = 0.468, 95% CI [-0.07, 0.16]. This indicates that age did not significantly contribute to the prediction of MI scores. The coefficients in Table 2-7 provide a summary of unstandardised coefficients (B), standardised coefficients (Beta), significance (p values) and confidence intervals for each predictor in the model.

Table 2-7 Linear regression coefficient results for MI

MI	***B***	**95% CI for B**		**SE B**	**β**	**R^2**	**ΔR^2**
		LL	UL				
Model						.316	.314*
Constant	40.123*	34.04	45.84	2.914			
AGE	.043	-.073	.159	.059	.021		
Total GCS	.693*	.612	.762	.036	.558*		

Note: Model = “Enter” method in SPSS statistics; *B* = unstandardised regression coefficient; CI = confidence interval; LL = lower limit, UL = upper limit; SE *B* = standard error of the coefficient; β = standardised coefficient; GCS = Greene Climacteric scale; R^2 = coefficient of determination; ΔR^2 = adjusted R^2. *p < 0.001

Sleep Quality and executive function (Hypothesis 3)

The impact of sleep disturbances on executive function on the menopause transition in premenopausal, perimenopausal and postmenopausal women was investigated. Sleep quality ratings, initially measured on a scale from 0 to 4 (0 = terrible, 1 = poor, 2 = fair, 3 = good, 4 = excellent), were recoded and centred for analysis. The recoding process transformed the scale to range from -2 to 2.

Prior to investigating the influence of sleep quality on executive functions, I first compared sleep quality across pre-, peri- and postmenopausal women.[1]

Exploratory analysis of sleep quality scores across the three menopause groups, premenopause, perimenopause and postmenopause

To examine differences in menopause groups in sleep quality, an analysis of covariance (ANCOVA) was performed with group (premenopausal vs. perimenopausal vs. postmenopausal) as the between-subject factor. The dependent variable, sleep quality was the mean-centred sleep scores. Menopause stage was the categorical predictor or independent variable. Age was included as a covariate in the analyses to adjust for potential confounding.

There was a significant main effect of menopause stage F (2, 814) = 12.319, $p < 0.001$, partial $\eta^2 = 0.029$. This indicates that menopause stage had a significant effect on sleep quality. There was no significant effect of age on sleep quality, F (1, 814) = 0.287, $p = 0.592$, partial $\eta^2 < 1$.

Post hoc analysis using Bonferroni corrected t-tests revealed that perimenopausal women (M = -0.33, SE = 0.06) reported significantly worse sleep quality in comparison to premenopausal women (M = 0.11, SE = 0.07), $p < 0.001$). There was no significant difference in sleep quality between premenopausal women and postmenopausal women (M = -0.15, SE = 0.*08, p* = 0.161) nor between perimenopausal and postmenopausal women ($p = 0.256$).

Next as per our pre-registered analysis, a Spearman's rank-order correlation was conducted to assess the relationship between mean-centred sleep quality scores and BRI and MI scores in premenopausal,

[1] See Appendix 5 for sleep quality examinations in perimenopausal and postmenopausal women

perimenopausal (no HRT) and postmenopausal women due to the ordinal nature of sleep quality variable. Separate visual inspection of plots of BRI and MI against sleep quality showed a linear relationship. Figures 2-3, 2-4 and 2-5 show correlations for the menopause groups.

For women in premenopause there was a significant negative correlation between sleep quality and BRI scores r_s (255) = -0.306, p < 0.001. There was also a significant negative correlation for the premenopause group between sleep quality and MI scores r_s (255) = -0.293, p < 0.001.

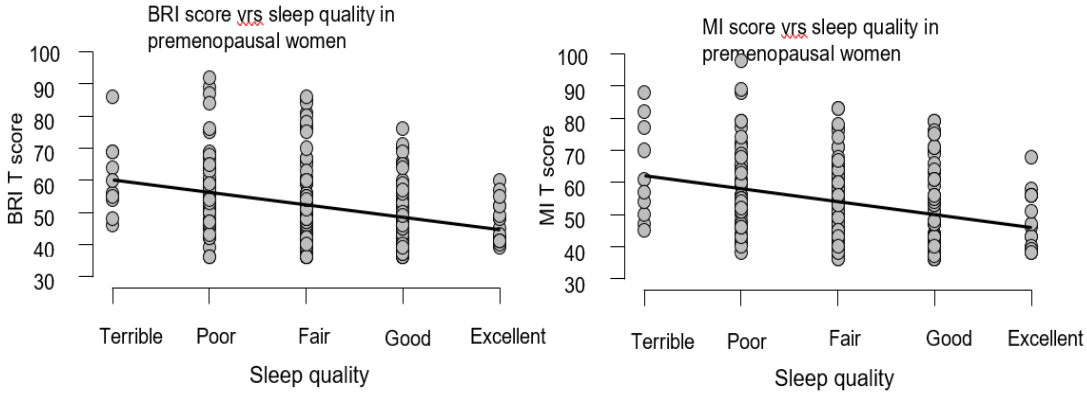

Figure 2-3 Correlation between sleep quality and BRI (left) and MI (right) scores in premenopausal women

For women in perimenopause (no HRT) there was a significant negative correlation between sleep quality and BRI scores r_s (281) = -0.193, p < 0.001. There was also a significant negative correlation for the perimenopause group between sleep quality and MI scores r_s (281) = -0.268, p < 0.001.

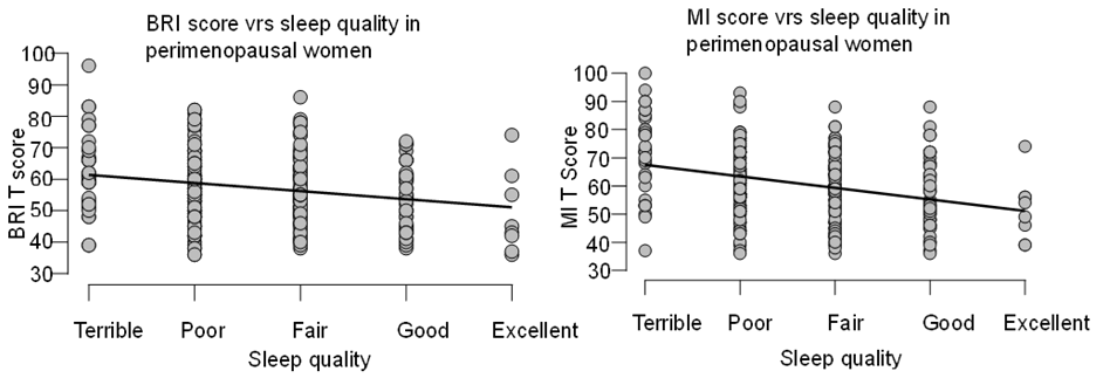

Figure 2-4 Correlation between sleep quality and BRI (left) and MI (right) scores in perimenopausal (no HRT).

For postmenopausal women there was a significant negative correlation between sleep quality and BRI scores ($r_s(276) = -0.248$, $p < 0.001$) and between sleep and MI scores ($r_s(276) = -0.256$, $p < 0.001$).

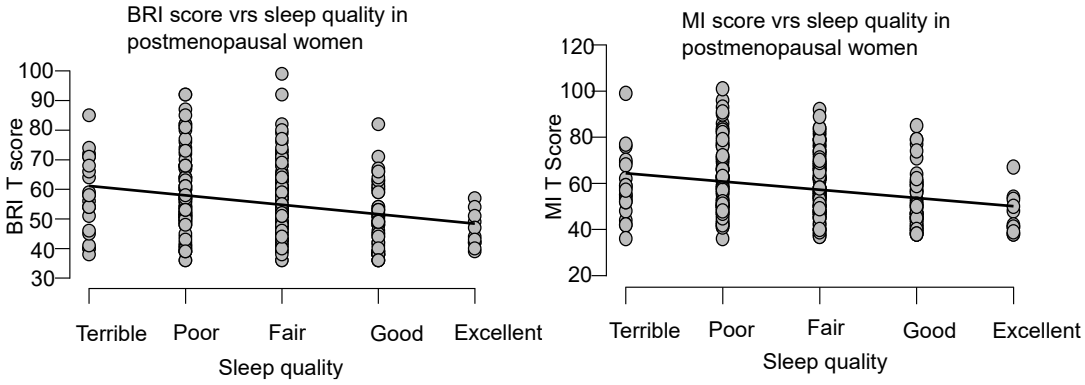

Figure 2-5 Correlation between sleep quality and BRI (left) and MI (right) scores in postmenopausal women

Note: The above results suggest that better sleep quality is associated with lower BRI and MI scores in both pre-, peri- and postmenopausal women.

BRI and sleep quality

An ANCOVA was performed using menopause stage as the independent variable and BRI as the dependent variable. Sleep and age were used as covariates.

There was a significant main effect of menopause stage, F (2, 811) = 5.835, $p = 0.003$, partial $\eta^2 = 0.014$ indicating differences in executive

function (BRI) in the groups. Sleep was also significantly related to BRI scores, F (1, 811) = 58.325, p < 0.001, partial η^2 = 0.067. There was no significant interaction between menopause stage and sleep quality, F (2,811) = 0.711, p = 0.491, partial η^2 = 0.002. Age was also not significantly related to BRI scores F (1, 811) = 0.020, *ns,* partial η^2 = < 1. Figure 2-6 shows BRI scores across sleep quality ratings across the menopause groups.

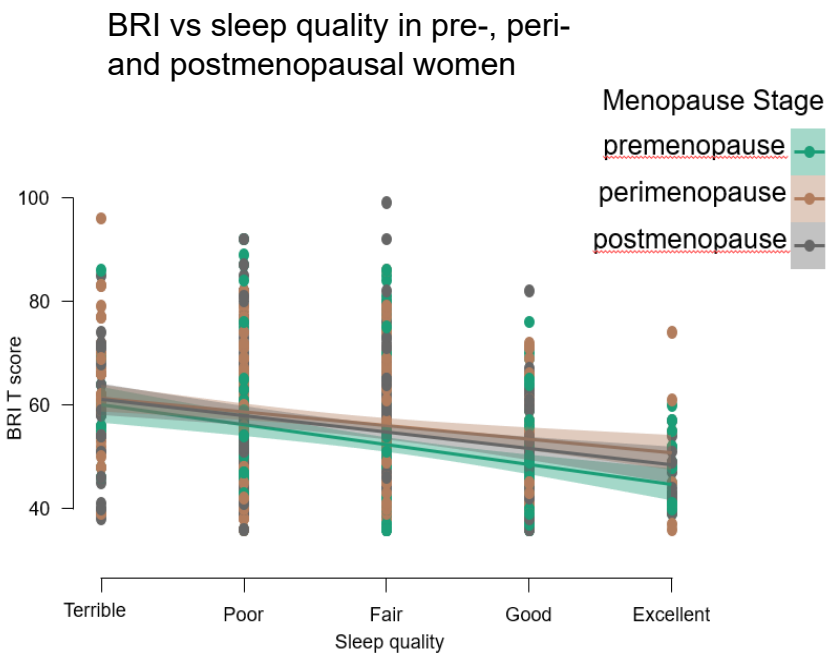

Figure 2-6 BRI scores across sleep quality ratings

Note: This showed that women with better sleep quality reported lower BRI scores. Error bars represent 95% CI.

MI and sleep quality

An ANCOVA was run to determine the effect of poor sleep on MI scores during premenopause, perimenopause and postmenopause stages. The process above was repeated but this time with MI as the dependent variable. It was also predicted that poor sleep will affect MI scores. There was a significant main effect of menopause stage, F (2,

811) = 7.765, p = 0.000457, partial η^2 = 0.019 indicating differences in executive function (MI) between groups. Sleep was also significantly related to MI scores, F (1, 811) = 67.932 p < 0.001, partial η^2 = 0.077, with poorer sleep quality linked to MI (metacognitive abilities). Age was not significantly related to MI scores, F (1, 811) = 0.917, p = 0.338, partial η^2 = 0.001. The interaction between sleep and menopause stage was also not significant, F (2, 811) = 0.078, p = 0.925, partial η^2 = 0.000193 suggesting sleep quality impacts MI similarly across all menopause stages. MI scores across sleep quality ratings during premenopause, perimenopause and postmenopause stages are plotted in Figure 2-7.

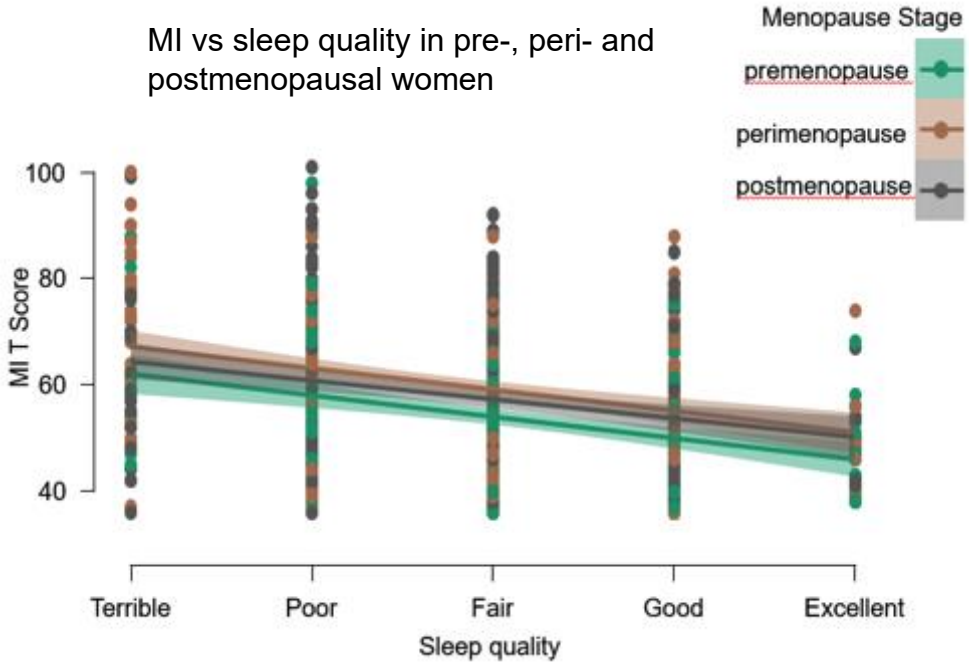

Figure 2-7 Mean MI scores plotted against sleep quality ratings

Note: Plot indicates better MI scores with improved sleep quality. Error bars represent 95% CI.

Exploratory analysis of socio-behavioural factors on GEC

A hierarchical multiple regression was conducted to assess whether the inclusion of age, menopause stage and various socio-behavioural factors improved the prediction of overall cognitive scores or executive function. The goal was to understand how a cluster of socio-

behavioural factors impact general cognitive health in a broader sense rather than specific domains. The global executive composite score (GEC) on the BRIEF-A was used to assess overall executive functioning across all domains for easier interpretability as specific targeted domains was not of interest in this analysis. This approach was chosen to enhance interpretability, as the focus of the study was on general executive performance rather than specific subdomains. Factors previously identified as associated with cognitive performance were examined. Lifestyle factors were categorised into demographic variables (weekly hours worked, caregiving responsibilities (not parents), educational level) and lifestyle factors (healthy diet, physical activity, alcohol consumption). Age was treated as a control variable, ensuring its effects were accounted for before examining additional predictors. The premenopause group served as the reference category for menopause stage, while women without caregiving responsibilities were the reference group for caregiving status. The full model of age, menopause stage (dummy variables for perimenopause and postmenopause created), demographic and lifestyle factors to predict GEC was statistically significant, $R^2 = 0.091$, $F(9, 806) = 9.010$, $p < 0.001$; adjusted $R^2 = 0.081$. In the first step, age significantly predicted GEC scores, $R^2 = .010$, $F(1, 814) = 8.194$, $p = 0.004$. The addition of menopause stage to the prediction of GEC scores (Model 2) led to a statistically significant increase in R^2 of .034, $F(3, 812) = 12.473$, $p < 0.001$. The addition of demographic variables (weekly hours worked, caregiving responsibilities, educational level) to the prediction of GEC (Model 3) also led to a statistically significant increase in R^2 of 0.015, $F(6, 809) = 8.402$, $p < 0.001$. The addition of lifestyle factors (healthy diet, physical activity, alcohol consumption) to the prediction of GEC (Model 4) also led to a statistically significant increase in R^2 of 0.032, $F(9, 806) = 8.927$, $p < 0.001$. In Model 4, perimenopausal women compared to premenopausal women, those with caregiving responsibilities compared to those without, individuals who consumed more alcohol, and those with less healthy diets self-reported significantly higher GEC scores, indicating overall poorer executive

function. Results of the hierarchical regression are displayed in Table 2-8.

Table 2-8 Hierarchical Multiple regression predicting GEC from age, menopause stage and socio-behavioural factors

	Predictors	B	Beta	P value	95% CI for LL	95% CI for UL
Model 1	(Constant)	47.121		<.001**	40.552	53.690
	AGE	.193	.100	.004*	.061	.326
Model 2	(Constant)	49.240		<.001**	40.061	58.419
	AGE	.083	.043	.440	-.127	.293
	perimenopause	6.261	.226	<.001**	3.864	8.658
	postmenopause	3.380	.121	.058	-.120	6.880
Model 3	(Constant)	53.401		<.001**	43.290	63.513
	AGE	.046	.024	.670	-.165	.257
	perimenopause	5.845	.211	<.001**	3.443	8.247
	postmenopause	3.159	.114	.075	-.323	6.642
	weekly hours worked	-.007	.000	.990	-1.026	1.013
	Education	-1.659	-.067	.056	-3.362	.044
	Caring responsibilities	3.336	.105	.002*	1.190	5.481
Model 4	(Constant)	45.500		<.001**	34.233	56.767
	AGE	.102	.053	.345	-.110	.315
	perimenopause	5.215	.189	<.001**	2.837	7.594
	postmenopause	2.622	.094	.135	-.818	9.062
	weekly hours	-.284	-.019	.581	-1.295	.727
	Educational level	-1.154	-.046	.182	-2.850	.542
	Caring responsibilities	3.706	.117	<.001**	1.595	5.828
	Alcohol consumption	1.232	.114	.001*	.494	1.969

	Diet	.646	.152	<.001**	.342	.950
	Physical activity	-.132	-.025	.485	-.505	.240

Note: Model = “Enter” method in statistics; *B* = unstandardised regression coefficient; CI = confidence interval; LL = lower limit, UL = upper limit, Beta (β) = standardised coefficient; *$p < 0.05$, **$p < 0.001$.

Exploratory analysis role of HRT on EF

Many perimenopausal women who responded to the questionnaire reported current use of HRT. As such exploratory analysis was conducted to investigate the potential influence of HRT on executive function while accounting for menopause symptoms.

For the Total Greene Climacteric score, a test of normality using Kolmogorov-Smirov showed data to be normally distributed. Visual inspection of the histograms and Q-Q plots showed that the extent of non-normality was not sufficient to transform data in this large sample size. As mentioned earlier when discussing BRI and MI, Fields, A., (2009) recommends not using significance tests of skew and kurtosis in large samples as they are likely to be significant, so this was not performed for Total Greene Climacteric score. The inspection of the boxplots revealed no outliers in the dataset.

Group Differences in Executive Function

An independent samples t-test was conducted to compare the BRI score between perimenopausal women not on HRT (M = 56.89, SD = 11.46) and perimenopausal women on HRT (M = 59.50, SD = 12.06). The assumption of equal variance was tested using Levene's Test and the results indicated no significant differences in variances between the groups, $F = 0.273$, $p = 0.602$. The t-test results showed that assuming equal variances, there was a significant difference in BRI scores between perimenopausal women not on HRT and perimenopausal women on HRT $t\ (442) = -2.27$, $p = 0.024$, 95% *CI* [-4.88, -.35]. Perimenopausal women on HRT (M= 59.60, SD= 12.06) reported higher BRI scores than perimenopausal women not on HRT (M = 56.89, SD = 11.46).

An independent sample t-test was conducted to compare the MI score between perimenopausal women not on HRT (M = 60.29, SD = 13.34) and perimenopausal women on HRT (M = 63.06, SD = 13.95). The assumption of equal variance was tested using Levene's Test and the results indicated no significant differences in variances between the groups, $F = 0.379$, $p = 0.538$. The t-test results showed that assuming

equal variances, there was a significant difference in MI scores between perimenopausal women not on HRT and perimenopausal women on HRT t (442) = -2.076, p = 0.039, 95% *CI* [-5.41, -0.15] with perimenopausal women on HRT reporting higher MI scores.

HRT and menopause symptoms

Given that there was a difference between those on and not on HRT in executive function in terms of the BRI and MI measures we investigated whether this was related to symptom level.

I first explored whether perimenopause women who are receiving Hormone Replacement Therapy (HRT) experience a lower severity of menopausal symptoms compared to women not receiving HRT. This is plausible since some women use HRT to manage menopause symptoms. An independent-samples t-test was run to determine if there were differences in menopause symptoms experienced by perimenopausal women on HRT and those not on HRT. Interestingly, perimenopausal women on HRT reported worse symptoms (M=29.19, SD = 8.63) than perimenopausal women not on HRT (M = 24.97, SD = 10.26), a statistically significant difference M = -4.224, 95% CI [-6.02, -2.43], t (381.17) = -4.625, p = 0.000005.

A multiple regression analysis was then conducted to examine the relationship between BRI scores, symptom severity, (mean-centred Total Greene Climacteric score) and HRT status among perimenopausal women as some women use HRT to manage symptoms. Interaction terms HRT status x mean-centred Total GCS were included to explore potential interactive effects between HRT status and symptoms as predictors for BRI score. Linearity was confirmed by partial regression plots and a plot of standardised residuals against the predicted values. There was slight heteroscedasticity, as assessed by visual inspection of a plot of studentised residuals versus unstandardised predicted values. There was no evidence of multicollinearity as assessed by tolerance values greater than 0.1. There were no studentised residuals greater than ±3 standard deviations, no leverage values greater than 0.2 and values for

Cook's distance above 1. The histogram and P-P plot of the standardized residuals indicated that the residuals were approximately normally distributed.

The multiple regression model statistically significantly predicted BRI scores, F (3,440) = 82.290, p < 0.001, adj. R^2 = 0.355. R^2 for the overall model was 0.359 which accounted for 35.90% of the variance in BRI scores. Regression coefficients and standard errors for these results can be found in Table 2-9. The severity of menopausal symptoms was a significant predictor of BRI scores, B = 0.643, t (440) = 11.761, p < 0.001, 95% CI [0.54, 0.75], with symptom severity associated with higher BRI scores. This positive relationship means that higher scores on the Total Greene Climacteric score (GCS) which indicate more severe menopausal symptoms, are associated with higher BRI scores, suggesting greater executive function difficulties. After controlling for menopause symptoms, HRT status was not a significant predictor of BRI scores, B = -0.701, t (440) = -0.729, p = 0.467, 95% CI [-2.59, 1.19]. This suggests that at average symptom severity, there was no significant difference in BRI scores between perimenopausal women on HRT and those not on HRT. The interaction term between HRT status and symptom score was also significant, B = 0.223, t (440) = 2.184, p = 0.029. Figure 2-8 shows the interaction plot of HRT status and menopause symptoms on BRI score. Pearson's correlations were run separately for perimenopausal women on HRT and perimenopausal women not on HRT on the relationship between menopause symptoms and BRI. Results revealed that both groups showed a positive and statistically significant correlation between symptoms and BRI. This was stronger in perimenopausal women on HRT, r = 0.620, p < 0.001 in comparison to perimenopausal women not on HRT, r = 0.576, p < 0.001. In summary, results suggest that among perimenopausal women on HRT severity of menopausal symptoms is associated with higher BRI scores, that is poorer executive functioning.

Table 2-9 Multiple coefficient regression results for BRI

BRI	*B*	95% CI for B		SE B	β	R^2	ΔR^2
		LL	UL				
Model						.359	.355*
Constant	40.832*	37.93	43.73	1.48			
HRT status	-0.701	-2.59	1.19	0.962	-.029		
Total GCS	0.643*	0.536	0.750	0.543	.632*		
HRT status*Total GCS	0.223	0.022	0.424	0.102	0.295**		

Note: Model = "Enter" method in statistics; *B* = unstandardised regression coefficient; CI = confidence interval; LL = lower limit, UL = upper limit; SE *B* = standard error of the coefficient; β = standardised coefficient; R^2 = coefficient of determination; ΔR^2 = adjusted R^2. *$p < 0.001$, **$p = 0.029$.

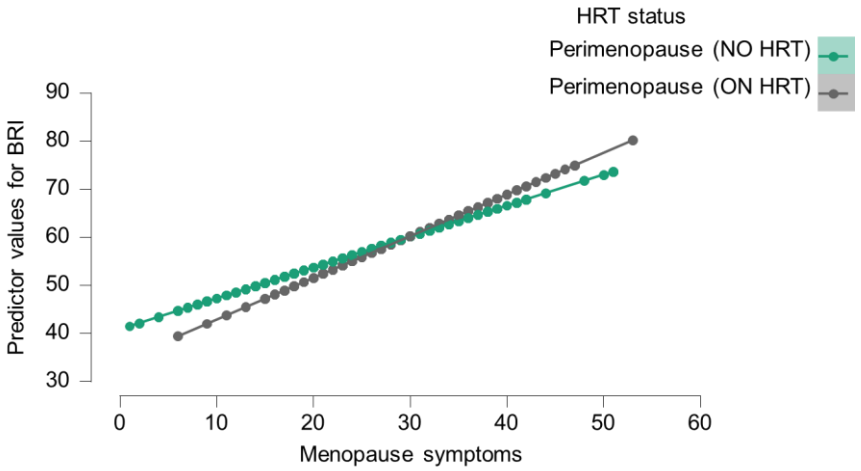

Figure 2-8 Interaction of HRT status and symptom severity of BRI scores

The same analysis as performed for BRI was performed for MI. The multiple regression model statistically significantly predicted MI scores, F (3,440) = 54.123, $p < 0.001$, adj. $R^2 = 0.265$. R^2 for the overall model was .270 which accounted for 27.0% of the variance in MI scores. The severity of menopausal symptoms was a significant predictor of MI scores, $B = 0.645$, t (440) = 9.512, $p < 0.001$, 95% CI [0.51, 0.78], with symptom severity associated with higher MI scores. This positive relationship means that higher scores on the Total Greene Climacteric score which indicate more severe menopausal symptoms, are associated with higher MI scores, suggesting greater executive

function difficulties. HRT status was not a significant predictor of MI scores, B = -.550, t (440) = -4.61, p = 0.645, 95% CI [-2.89, 1.79]. The interaction term was also not significant, B = 0.225, t (440) = 1.779, p = 0.076. Thus, only menopause symptoms predicted metacognitive skills.

2.8 Discussion

This study examined the influence of menopause stage, menopause-associated symptoms and sleep quality on executive functions. Additionally, exploratory analyses were also performed to understand the role of HRT and socio-behavioural factors on menopause. I next discuss the findings of these investigations.

Results showed that menopause stage significantly impacted executive functions independent of age with perimenopausal women reporting worse executive function in comparison to premenopausal women. Severity of menopausal symptoms also significantly influenced executive function with women who reported worse symptoms reporting poorer executive functions. Across the groups perimenopausal women reported significantly worse menopause symptom scores than premenopausal and postmenopausal women. Postmenopausal women also reported significantly worse menopause symptoms in comparison to premenopausal women.

Sleep quality also significantly impacted executive functions across all menopause groups. Sleep quality was the stronger predictor of executive function challenges with moderate effect sizes suggesting that poor sleep is associated with greater executive function challenges. The interaction between menopause stage and sleep quality was not significant suggesting that the effect of sleep quality on executive function across menopause groups is similar.

In exploratory analysis of the role of HRT in executive functioning, HRT status by itself did not significantly predict executive functions after controlling for menopause symptoms. In the BRI domain only, there was a significant interaction between HRT status and menopause symptom severity. The relationship between menopause symptoms and BRI was stronger in perimenopausal women on HRT. This suggests among perimenopausal women using HRT, those with more severe symptoms reported greater difficulties in executive function in comparison to perimenopausal not using HRT.

Exploratory analysis of behavioural factors showed that women with caring responsibilities, poorer diet quality and higher alcohol consumption reported significantly more difficulties with executive functions. The findings of this study demonstrate how different physiological and socio-behavioural factors contribute to executive function challenges. Next, I will discuss each finding and conclude with the strengths and limitations of this study.

Association between executive function and menopause stage

This study demonstrated that menopause stage significantly affects executive performance after controlling for the effect of age. In their everyday lives, perimenopausal women reported significantly higher scores in BRI, behavioural regulation (Inhibit, Shift, Emotional control) in comparison to premenopausal women. These higher scores reflect challenges with impulsivity, inappropriate emotional responses, difficulties with switching attention and changing focus from one topic to another. In addition, perimenopausal women reported statistically significant higher scores in MI, metacognitive abilities (Initiate, Working memory, Planning/Organisation, Task monitor, Organisation of materials) in comparison to premenopausal women. Some everyday challenges in the MI domain reported include difficulties with starting tasks and coming up with ideas on their own, remembering things, monitoring progress during tasks, retrieving instructions accurately and planning challenges and losing track of personal belongings such as keys, money, purses.

Additionally, the overall pattern of findings was consistent across both raw behaviour regulation and metacognition scores and age-normalised T scores, indicating that the observed group differences are robust and not dependent on the scoring method used. Although the peri- versus postmenopausal comparison reached significance when using raw scores ($p = 0.044$) but fell just above the threshold when using T-scores ($p = 0.055$), this discrepancy is very

small and does not change the overall interpretation of the results. The slight variation in *p*-values reflects the different ways raw and T-scores account for age, rather than a meaningful difference in the underlying effect. Importantly, both scoring approaches demonstrated the same directional pattern with women in the perimenopausal stage reporting greater executive function difficulties than premenopausal women, supporting the overall objective of this study. This suggests that the increased difficulties observed during the menopausal transition reflect genuine differences in self-reported executive functioning rather than being driven by age normalisation or analytic approach. Consequently, conducting the ANCOVA using raw scores while statistically controlling for age is as methodologically sound as using T-scores, and both approaches support the conclusion that perimenopause is associated with increased cognitive challenges. Future studies may wish to explore other approaches to further examine how raw and age-normalised scores behave in menopausal research studies, but in the present study both methods reach the same substantive conclusion, that is, a period of reported cognitive vulnerability during the menopause transition.

Furthermore, this finding supports our hypothesis that perimenopausal women would report higher (i.e. greater difficulty) scores on executive functioning in comparison to premenopausal women. This result is also consistent with findings by (Page et al., 2023) who used the Brown Attention Deficit Disorder scale (BADDS) to show that perimenopausal women had more difficulties with executive function compared with premenopausal women. This lends credence to the possibility that a decline in oestrogen during menopause may impact cognition. It has been postulated that the changing levels of oestrogen during menopause may negatively impact the prefrontal cortex region of the brain which may in turn contribute to declines in executive function (Keenan et al., 2001). These findings reinforce the broader theoretical framework that hormonal transitions during menopause, particularly

fluctuating oestrogen levels, may play a critical role in the challenging executive functions reported by many women.

Additionally in this study, the use of BRIEF-A offered an overall overview of the cognitive health of mid-life women, an area largely unexplored when relying on subjective reports. Most prior research has focused primarily on memory, overlooking the broader range of psychological symptoms associated with menopause. These cognitive symptoms extend beyond memory and include executive functions such as initiation, planning and organisation and task-monitoring. Although the results of this study are statistically significant, the scores obtained do not exceed clinical thresholds and remain within the normal range of executive functioning except for the working memory domain where perimenopausal women reported a mean score of 65.96 which marginally exceeds the clinical significance threshold of 65. This aligns with previous research showing that, despite the increased prevalence of self-reported cognitive complaints during the menopause transition, many women continue to exhibit normal cognitive functions (Fuh et al., 2006; Kok et al., 2006; Luetters et al., 2007). This suggests that, while some women may experience a perceived cognitive vulnerability during midlife, their performance still reflects typical functioning levels. This is reassuring, as it suggests that for most women, these cognitive shifts do not significantly impact their ability to manage daily activities.

Furthermore, the small effect size ($\eta p^2 = 0.025$) in this study, is consistent with similar effect size findings in a study by Kok et al., (2006) and Weber et al. (2014). This indicates a modest but meaningful association between menopausal stage and executive performance. Nevertheless, cognitive difficulties reported by some women during this transition should not be dismissed, as they can feel distressing and impact daily life. It is therefore important to acknowledge these concerns while also offering reassurance that such changes generally fall within the bounds of normal cognitive functioning.

Exploration of BRIEF-A Subscales

Following on from results above which highlighted the significant impact of menopause stage on BRI and MI, I next explored the impact of menopause stage on the subscales of BRI (inhibit, self-monitor, emotional control, shift) and MI (initiate, working memory, task-monitor, plan/organise, organisation of materials) for executive function challenges. Pairwise comparisons showed that perimenopausal women reported significantly higher scores than premenopausal women on all subscales except Inhibit and Organisation of Materials based on Bonferroni-corrected significance ($\alpha = 0.00185$).These findings suggest that perimenopausal women experienced greater difficulties with inflexible thinking, inappropriate emotional responses, beginning tasks, planning tasks or activities, keeping track of their work, remembering things even for a few minutes and maintaining order in their home or work environment. The fact that perimenopausal women experience executive function challenges during this period validates the concerns some women experience during the transition to menopause. The study also showed that aside shift and emotional control, which are in the BRI index, the other subscales are in the MI domain. This pattern suggests that the difficulties that perimenopausal women in this study experience are more related to the development of appropriate steps to achieve a task, beginning tasks and generating ideas, performance assessment and holding information in one's mind to complete a task. These neurocognitive difficulties can impact women's work performance as shown by (O'Neill et al., 2023).

Additionally, no significant differences were observed between perimenopausal and postmenopausal women in any of the subscales similar to findings by (Page et al., 2023) though postmenopausal scores did not reach premenopausal levels. The observed stability in executive function performance during postmenopause as indicated by these results suggest that women may have adapted to the significant fluctuations typically associated with the perimenopause stage or found ways of coping and this is worth exploring. It is plausible that

postmenopausal women could have adopted coping strategies, such as the use of calendars, diaries, and reminders, to mitigate memory lapses and maintain organisation for appointments and significant events. In interactions with women during recruitment efforts, many women indicated an increased reliance on reminders and technological tools to manage their daily activities. Supporting this observation, Greendale et al. (2009) found that cognitive function declines during perimenopause but subsequently improves in postmenopause. It would be valuable to quantify the extent to which women utilise external aids to remain organised in both professional and domestic contexts during and after the menopausal transition. Ledford (2023) discussed how the perimenopausal period is characterised by wide fluctuations in hormone levels, particularly oestrogen, which influences brain function. Once the transition to menopause is complete, neurons adapt to the absence of these hormones, and the brain compensates for the decline (Mosconi et al., 2021). It is also suggested that in the postmenopausal period, a ‘new normal’ is achieved, with improved performance and this could be a natural phase of neurobiological adjustment. Further investigation is needed to determine whether this improvement is due to physiological factors alone or a combination of physiological factors and external aids.

Association between executive function and menopause symptoms

During the transition to menopause, some women suffer from a barrage of symptoms This study found a significant and positive correlation between menopause symptoms and BRI (inhibit, self-monitor, emotional control, shift) and MI (initiate, working memory, task-monitor, plan/organise, organisation of materials). These menopause-associated symptoms significantly contributed to the prediction of the BRIEF-A subscales after controlling for aging. Over 30% of the variance in executive function skills were significantly predicted by menopause symptoms. Specifically, higher symptoms severity was associated with difficulties in behaviour such as

impulsivity, inflexibility in shifting, keeping track of one's behaviour, inappropriate emotional responses. Other executive functions impacted by greater symptom severity also included beginning tasks or needing reminders to begin a task, trouble remembering things, not planning for tasks and approaching tasks in haphazard way, not keeping track of one's problem-solving and lastly, problems with organising one's environment.

This finding of significant effects of symptoms on cognition is similar to findings in previous studies by Calle et al. (2024) and Crockford et al. (2025) that found associations between menopause symptoms and cognitive complaints using subjective measures. The cross-sectional, observational study conducted by Calle et al. (2024) in postmenopausal women found an association between menopausal symptoms and cognitive function, based on self-reported questionnaire data. As with the present study, the observational nature of their design limits causal inference. Nonetheless, the consistency in findings supports the relationship observed here. Similarly, Crockford et al. (2025) examined 896 postmenopausal women in a cross-sectional study and reported that greater menopausal symptom burden was associated with higher total scores on the Everyday Cognition (ECog-II), indicating more cognitive complaints. Calle et al. employed the Menopause Rating Scale and the Montreal Cognitive Assessment, while Crockford et al. used the Menopausal Symptom Burden Scale and ECog-II scale. Despite the use of differing assessment tools, all three studies including the current study reach the same conclusion that increased menopausal symptoms are associated with greater subjective cognitive concerns.

Supporting this relationship, Schaafsma et al. (2010) investigated subjective complaints of attention and memory in relation to menopausal stage and symptomatology and found that higher scores on menopausal symptom scales which consists of hormonal, physical and psychological symptoms were associated with an increased likelihood of reporting cognitive problems. Factors such as vasomotor

symptoms specifically and menopause-related symptoms emerged as significant predictors. One proposed explanation for this association is the neurobiological impact of hormonal fluctuations, particularly declining oestrogen levels during menopause (Santoro et al., 2015) which are known to influence cognition through their action on brain regions such as the prefrontal cortex (Iqbal et al., 2024). While it remains unclear why some women experience more pronounced menopausal symptoms than others (Crockford et al., 2025), it appears that for those with more severe symptomatology, cognitive complaints including those related to executive functioning are more likely to be reported. Furthermore, this significant menopause symptom finding on executive functions suggests that managing and treating the symptoms should be an important consideration for healthcare professionals.

Association between executive function and sleep quality

This study showed that there was a significant and negative correlation between sleep quality and BRI and MI in premenopausal, perimenopausal and postmenopausal when controlling for age. The significant linear trend demonstrates that, as sleep quality decreases, women experience worse executive function. Previous research has consistently shown that the prevalence of sleep disturbances is higher among perimenopausal, postmenopausal, and surgically menopausal women compared to their premenopausal counterparts (Xu & Lang, 2014). This increased prevalence has been demonstrated across multiple cross-sectional studies, even after controlling for age and other potential confounders, though the observed effects tend to be small in magnitude (Xu & Lang, 2014).

Evidence linking poor sleep to cognitive functioning is well established in the broader literature. For instance, Krause et al. (2017) demonstrated that sleep deprivation adversely affects several domains of executive function, including sustained attention and working memory. Similarly, Nebes et al. (2009) found that healthy older adults with better sleep quality outperformed poor sleepers on tasks

assessing working memory, attentional set shifting, and abstract reasoning or problem solving. Importantly, these associations remained significant when controlling for comorbid conditions such as depression and cerebrovascular disease. Regestein et al. (2004) also reported that postmenopausal women with lower self-reported sleep quality exhibited reduced cognitive performance. These findings collectively align with the current study's observed association between self-reported sleep quality and executive function. The association between sleep disturbances and cognitive performance during menopause has been linked to hormonal changes, particularly declines in oestrogen and progesterone, both of which play key roles in sleep regulation (Haufe & Leeners, 2023) Additionally, oestrogen has been implicated in supporting executive function, further highlighting its potential influence on cognitive health during this transitional period.

Given that sleep disruption is a common symptom during the menopause transition, and that poor sleep may impair cognitive processes such as planning, attention, and memory, it is imperative that sleep-related issues are addressed. Intervening in sleep difficulties may not only enhance overall wellbeing but also support the maintenance of cognitive functioning during this transitional life stage.

Influence of lifestyle factors on executive functioning

In addition to menopause stage particularly in the case of perimenopausal women, factors independently associated with worse executive functioning included alcohol consumption, caring responsibilities and quality of diet.

Executive functions can be influenced by a variety of demographic and lifestyle factors. In this study, no significant associations were found between age, physical activity, weekly hours worked, or educational attainment in relation to overall executive function. However, higher alcohol consumption was linked to poorer executive functioning, with women who consumed more alcohol reporting reduced cognitive performance. This finding aligns with the literature review by Day et al.

(2015), which identified an association between executive function difficulties and alcohol use, though those studies did not specifically focus on menopausal women. Regarding caregiving responsibilities (i.e. looking after or giving help or support to anyone because they have long term physical or mental health conditions or illnesses, or problems related to old age), an association was observed between women who provided care reporting poorer executive function compared to those without caregiving duties. This result is consistent with the findings of Lee et al. (2004), who identified a modest association between caregiving and cognitive function, as well as Bhattacharyya et al. (2024), who reported that caregiving was not associated with improved executive functioning. A poorer diet was also linked to worse executive functioning, a result similar to the study by Skoczek-Rubińska et al. (2021), which found an association between a less healthy diet and cognitive impairment.

While the measures used to assess these modifiable lifestyle factors were not standardised tools for evaluating executive function, the observed associations highlight the importance of considering these variables when assessing mid-life women transitioning into menopause. The interplay between these factors suggests that multiple underlying influences may contribute to self-reported executive function difficulties. Overall, these findings provide further characterisation of executive functioning while highlighting modifiable environmental and lifestyle factors that may influence cognitive outcomes in mid-life women. Identifying these factors offers potential opportunities for targeted interventions aimed at supporting executive function during the menopausal transition. Furthermore, more extensive research is warranted to examine these lifestyle factors in greater detail, as well as their impact on mid-life cognitive health.

Impact of HRT

In this study, several perimenopausal women (n=161) reported current HRT use so it was useful to explore how HRT moderates the

relationship between menopause symptoms severity and executive functions. Menopause symptom severity was significantly associated with behaviour regulation difficulties. Perimenopausal women reporting more severe menopause symptoms reported higher BRI scores indicating greater challenges in behaviour regulation. HRT status alone was not associated with BRI scores after controlling for menopause symptoms. This suggests there was no difference in executive function at average symptoms levels. Lastly and more importantly, there was a significant and positive interaction between menopause symptom severity and HRT status on BRI (Inhibit, Shift, emotional control and self-monitor). This suggests that the effect of symptoms severity on behaviour regulation difficulties is strongest in HRT women as indicated by the steeper rise in executive function difficulties with increasing symptom severity as seen in Figure 2-8. In MI index though, only menopause symptoms significantly influenced MI scores similar to trend observed in BRI. However, neither HRT status or the interaction between HRT status and menopause symptoms significantly predicted MI scores. This suggests that the metacognitive abilities of executive functioning are more influenced by symptom severity independent of whether HRT is being used or not. These findings are consistent with research by Crockford et al., (2025) showing that greater menopause symptom burden was associated with poorer cognitive functioning. Similarly, Maki & Thurston (2020) in a review, highlighted the role of menopause symptom in brain function and the need to consider female–specific risk factors such as menopause symptoms which includes vasomotor symptoms when examining cognitive decline in menopausal women.

Even though HRT was not shown to be beneficial in terms of cognition in this study, previous research has shown its effectiveness in treating menopause associated symptoms such as hot flushes, night sweats and sexual functioning. For example, a study by Welton et al., (2009) showed that HRT improved menopause-associated symptoms such as night sweats and hot flushes in menopausal women. This current study

depended on self-reported HRT use, without specific details about the duration, dosage, type, or method of administration. It is also possible that women on HRT in this sample had more severe or persistent symptoms which had prompted them to seek treatment which could explain the stronger association. These are important factors that could affect the outcomes.

Taken together, these findings in the research highlight the importance of considering menopause symptoms severity in predicting executive function difficulties with HRT playing a complex role in behaviour regulation than in metacognitive abilities Future research could explore whether individual symptom profiles and more detailed information on HRT use could shed light on its potential benefit on executive functioning or perhaps symptom management alone is the key.

2.9 Strengths and Limitations

A key strength of this study has been the large sample size and the inclusion of pre-, peri- and postmenopausal groups in this study. These groups provided an opportunity to compare perimenopausal women's subjective experience of executive functions with pre- and postmenopausal women. Some previous studies had not compared women's cognitive performance with women in all three stages of menopause (Huang et al., 2021; Epperson et al., 2011). The use of a premenopause group can serve as a control measure. The relatively balanced numbers of women in the various groups also enabled fair comparisons across the three groups. Another strength of this study is the use of validated measures to assess menopause symptoms and executive functions. The use of an ecologically valid questionnaire such as BRIEF-A is beneficial as it is less time consuming and less prone to practice effects sometimes observed in objective measures. BRIEF-A also included other executive function domains which have not yet been explored such as self and task monitoring, initiation and organisation of materials. Furthermore, these domains are difficult to

examine using objective measures, particularly when it comes to evaluating functions such as initiation and organisation of materials. The use of validated tools, such as the Greene Climacteric Scale and the BRIEF-A, facilitated a more comprehensive characterisation of menopausal symptoms and robust assessments of executive function performance, respectively. This will allow meaningful comparison to future studies that utilise the same measures to assess whether for example, treatment of menopause symptoms leads to fewer cognitive complaints.

This study is not without limitations. First, this study employed a cross-sectional design which allowed for us to recruit a large sample size including many women on HRT. However, this cross-sectional design does not allow causality of relationships to be inferred. Future research should adopt a longitudinal design whereby the same women are followed from premenopause, through to postmenopausal to assess executive function changes to validate the findings from this study. The second limitation of the study is that all measures employed in this study were self-reported. This is prone to participant information biases and future research should include objective measures to assess some of these cognitive domains. Besides using the self-report version of the BRIEF-A form, it is advisable to also utilise the informant version whenever possible. This allows knowledgeable and close individuals who have regular interactions with friends or family undergoing menopause to provide their assessment by completing the informant-report forms. This will lend credibility to answers provided as an objective opinion is also garnered.

Finally, despite much effort put into recruiting women from different communities and backgrounds, participants consisted mainly of White women (70.93%) with most women employed (79.47%) and well-educated at degree level or above (68.64%). Caution should be exercised when generalising the findings of this research to other groups. It is crucial to consider the role of women's beliefs, lifestyle, and cultural factors in their experience of the menopause transition. For

example, cross-cultural differences exist in hot flush reporting (Hunter & Rendall, 2007). Additionally, the significant impact of menopause symptoms on executive function has been demonstrated in this current study and other studies as mentioned earlier. Further work to explore role of individual menopause symptoms and how cultural differences influence this should be explored in a more diverse sample.

Furthermore, employing validated measures to assess alcohol consumption, physical activity, and dietary habits would have enhanced comparability across future studies, minimised recall bias, and strengthened statistical validity. However, it was also crucial to consider the practical constraints as such measures can often be time-intensive, potentially affecting participant engagement and questionnaire completion rates. Balancing methodological rigor with feasibility remains an important aspect of study design.

2.10 Conclusion

The findings from this study have shed light on the executive function challenges faced by perimenopausal women before the transition into menopause. Using the BRIEF-A in this study also pinpointed specific domains impacted during this midlife stage, offering both health professionals and women valuable insights into the subtle changes occurring in these areas. Some of these domains can prove challenging to assess using laboratory-based tasks on its own. This awareness of impacted domains can guide further research and encourage behaviours that may help mitigate or improve functioning in these domains. At the very least, subjective measures such as the BRIEF-A should be used alongside laboratory-based tasks or objective measures to assess executive functions. This study also revealed significant associations between menopause symptoms and executive function performance. Menopause symptoms, including sleeping difficulties, can adversely affect executive functions. Therefore, it is important to manage or treat these symptoms when addressing the

needs of menopausal women. Additional factors to consider include environmental and lifestyle influences, as well as the intricate relationship between menopause and its overall impact on executive function in mid-life women. The transition through menopause is multifaceted, shaped by both biological changes and external conditions. Further research is essential to fully understand these complexities and how they contribute to cognitive health during this stage of life. Future research should consider the utilisation of objective measures to assess EF, sleep quality and menopause symptoms where applicable.

3 Chapter 3 Laboratory-based assessment of cognition in menopausal women

3.1 Abstract

Some women report cognitive challenges during the menopause transition. Some studies have evaluated these cognitive complaints using subjective measures while others have also used laboratory-based measures. The main objective of this study was to determine whether there are any objective cognitive declines during this period beyond what would normally be expected as part of the cognitive ageing process. In addition, this study also examined the association between menopause symptoms and cognition. This was an in-person cross-sectional study for women aged 35-65 years. A total of 235 premenopausal, perimenopausal and postmenopausal women completed two questionnaires and took part in various laboratory-based measures of cognition. The main outcome measures were processing speed (Symbol Digit Modality Task (SDMT)), selective attention and inhibitory control (Flanker) and verbal working memory (Backward Digit Span (BDS)). Other outcomes measures included menopausal symptoms (Greene Climacteric Scale) and self-report executive functions as assessed by BRIEF-A. There was no significant influence of menopause stage observed between the groups on processing speed, selective attention and inhibitory control and verbal working memory. Processing speed was the only laboratory-based measure that was significantly associated with overall menopause symptoms ($p = 0.04$). There was also a significant correlation between menopause symptoms and self-report measures of executive functions ($p < .001$). Poor sleep was initially found to be negatively correlated with processing speed. However, when menopause symptoms and age were included in the regression model, this relationship was no longer significant. Instead, both menopause symptoms and age emerged as significant predictors of processing speed, with older age and more

severe symptoms associated with slower performance. In conclusion, severity of menopause symptoms and cognitive ageing are associated with cognitive performance in the processing speed domain. These findings suggest that the distinct and varied symptomatology experienced by menopausal women may increase vulnerability to cognitive decline, particularly when combined with the effects of cognitive ageing.

3.2 Introduction

In addition to self-report measures of cognitive performance, the research in this thesis also employed standardised laboratory-based tasks to assess cognitive functioning across menopause groups. The inclusion of this objective measure was to complement self-reported data and offer an additional means of understanding cognitive performance during the menopause transition. While self-report measures provide valuable insight into perceived everyday cognitive difficulties, they may not fully capture actual performance. Laboratory-based measures, on the other hand, offer standardised and objective data. Few studies in existing menopause literature have employed both approaches. Studies that have used both measures have also not examined cognitive performance across the distinct menopause stages (Epperson et al., 2015). By integrating both methods, this thesis offers a more comprehensive understanding of cognitive changes during menopause.

As mentioned earlier, the transition to menopause is a natural phase in reproductive ageing, which culminates in the end of a woman's fertility. However, impact of this reproductive ageing process extends beyond reproductive function. Increased forgetfulness and difficulty concentrating are some of the cognitive changes that some women report during this period (Unkenstein et al., 2016). Self-report measures have been used to validate these claims, but objective measures in the form of laboratory-based tasks can also be used to

examine cognitive change in menopausal women. Chapter 2 focused on subjective measures with a particular emphasis on executive functions. Aside reproductive ageing, studies by Singh-Manoux et al., (2012) and Davis et al., (2017) have shown that at midlife the onset of age-related declines in cognitive domains such as processing speed, verbal memory, fluency and reasoning are observed in both men and women. Thus, the main aim of this study was to examine how menopause stage impacts cognitive performance using objective measures assessing processing speed, verbal working memory and selective attention and inhibitory control.

As discussed in section 1.7, processing speed is a foundational cognitive skill that involves the ability to process information quickly and can impair performance across other cognitive domains and is sensitive to age (Lichtenberger & Kaufman, 2012; Salthouse & Ferrer-Caja, 2003; Salthouse, 1996). A review by Conde et al., (2021) also noted that processing speed deficits have been reported by menopausal women. Despite mixed findings in the literature (See Table 1-2), its inclusion gives a better understanding of broader cognitive functioning which is examined in this study. Another domain of interest, selective attention and inhibitory control, a core component of executive function, also remains underexplored in menopause research (see Table 2.2), despite reports from women of increased distractibility and difficulty concentrating as noted by Warga, (1999). Selective attention and inhibitory control reflect the ability to control one's attention focus and suppress irrelevant stimuli (Diamond, 2013) and these skills that may be compromised during the menopausal transition. Verbal working memory, a key component of executive function, was examined in this study due to its relevance to commonly reported menopausal symptoms such as poor memory and forgetfulness (Hayashi et al., 2022, Gold et al., 2000). Working memory cognitive complaints are documented in menopause research (Conde et al., 2021) and in the study presented in Chapter 2, women reported the highest average level of difficulty in the working memory domain

among all executive function subscales. Hampson (2018), in a review, highlighted that declines in working memory are closely linked to reductions in oestradiol levels, which may underlie the memory difficulties experienced by women during the menopausal transition as previously discussed in section 1.9. Thus, it was also important to also assess this domain.

However, it is also plausible that menopause and its associated hormonal changes and symptomology may also uniquely contribute to this decline among women (Gava et al., 2019). Studies have shown that menopause symptoms consistently change during the menopausal transition independent of ageing (Greendale et al., 2009). Cognitve decline is also reported while some women are experiencing several co-occurring symptoms (Maki & Weber, 2019). As such it is important to understand to what extent these reported cognitive symptoms are influenced by menopause symptoms as was examined earlier in chapter 2. While previous research has largely focused on individual or affective symptoms (as outlined in section 1.6), this study extended those findings by exploring how the broader experience of menopause symptoms influenced performance on laboratory-based cognitive tasks. Building on results from the previous chapter, this approach allowed for a more comprehensive understanding of how symptom severity may relate to objective cognitive outcomes across processing speed, verbal working memory and selective attention and inhibitory control domains.

Another factor of interest in this study was sleep quality. Its inclusion, as in the previous chapter, aimed to examine its independent contribution to cognitive performance, given its frequent disruption during the menopausal transition and its well-documented impact on cognition in existing literature. By accounting for sleep quality, the study sought to better understand how this common menopausal symptom may influence cognitive outcomes beyond menopause stage alone. The prevalence of sleep disturbances during menopause transition was discussed in section 1.6 along with impact on cognition in the wider literature. However, in existing menopause literature where

laboratory measures have been used to assess cognition, this prevalent symptom has also been underexplored. It could very well be that the independent effect of poor sleep contributes to the decline in cognitive performance reported by many midlife women. Furthermore, sleep is a modifiable lifestyle factor that can be improved through training to enhance sleep quality. As many as 40% to 56% of perimenopausal women report sleeping difficulties when compared to 31% in premenopausal women (Kravitz et al., 2003). Examining this issue could shed more light and provide a broader picture of other factors that potentially affect objective cognitive performance in midlife women.

By employing laboratory-based measures, this study aims to deepen understanding of cognitive performance across pre-, peri-, and postmenopausal women, building on self-report findings on executive functions from chapter 2. Given observed differences in executive function between these groups, an in-person assessment may offer more objective insights into cognitive changes in midlife women which is a dual approach that remains limited in existing research as mentioned earlier. Though laboratory-based studies have been employed to investigate cognitive changes during menopause, findings have been mixed, as discussed in section 1.11 and outlined in Table 1-2. These inconsistencies may be a result of variations in menopausal stage comparisons, differences in staging criteria, the cognitive measures used, and study design, particularly whether cross-sectional or longitudinal approaches were adopted. To ensure comparability with other studies, this study assessed cognition across all stages of the menopause by utilising computerised standardised cognitive tasks which allowed for more accurate and precise measurements as well as increased sensitivity to detect subtle changes.

3.3 Aims

The main aim of this study was to investigate whether menopausal stage is associated with objective cognitive performance across three groups of women: premenopausal, perimenopausal, and

postmenopausal. The aims and hypotheses of the study were preregistered (https://osf.io/fktve/?view_only=b1bf2c8fe8f346229910d494aa03a315).

Hypothesis 1: It was hypothesised that perimenopausal women would exhibit poorer performance on cognitive tasks assessing processing speed, selective attention and inhibitory control and verbal working memory, with age included as a covariate.

Another aim of the study was to investigate any associations between menopausal symptoms and cognitive performance.

Hypothesis 2: It was hypothesised that executive function performance would be affected by the severity of menopausal symptoms, as assessed by the Greene Climacteric Scale. Specifically, women with higher scores on the scale, indicative of more pronounced symptoms, were expected to exhibit poorer performance on working memory, processing speed and inhibitory control lab-based measures as well as self-report BRI and MI index, irrespective of menopause stage.

Exploratory analysis also examined the relationship between sleep quality and cognitive performance across the menopause groups as was done in Chapter 2. It was hypothesised that poorer sleep quality would be associated with lower cognitive performance.

3.4 Method

Study Design

This study was a mixed design study. The between-subjects factor was menopause stage with three levels, premenopause, perimenopause and postmenopause. The within-subjects factors relevant to the Flanker task was trial type with participants completing both congruent and incongruent trial conditions. The ratio of congruent to incongruent median reaction times was used as the dependent variable in the Flanker task. This study was part of larger study that included two other

PhD students. The effect size information from a closely aligned study in the field (Ferguson et al., 2021) which employed a similar series of executive function tasks and had a comparable participant profile to ours was used. The Stroop task data from female participants aged 34 years to 63 years was split by age group into 3 groups to approximately correspond to pre, peri and post menopause groups. Using congruent and incongruent reaction time data from pre, peri and post groups, I calculated interference ratios for the three groups using data from Fergusson and colleagues. The mean ratios for the three groups were then used to calculate a between group effect size of Cohen's *f* = 0.14, indicating a small, expected effect of menopause stage on interference ratio. A G power analysis was conducted for an ANCOVA (main effects) with three groups and one covariate (age). Using effect size *f* = 0.14, three groups, alpha criterion of 0.05 and a power of 0.80, this resulted in a minimum sample size requirement of 165 participants per group (495 in total) to detect a main effect of menopause stage on cognitive performance.

Due to time constraints, 256 participants took part in the study but out of these 235 participants were used in final analysis after exclusions which are detailed later in Section 3.5. This represents a limitation to statistical analyses and data interpretation has been done with caution.

A sensitivity power analysis was also conducted using *G* Power 3.1.9.7 to determine the minimum detectable effect size for the final sample of 235 participants. The analysis was based on a repeated-measures ANOVA with a between-subjects factor. The parameters used were power of 0.90 and alpha criterion of 0.05 and a combined measurement of 4 from the Flanker, verbal working memory and processing speed task. The analysis yielded a minimum detectable effect size of f = 0.185, (Cohen's *d* = 0.370). These results suggest that the study was adequately powered to detect a small to moderate effect size.

Participants

Women aged 35-65 years were recruited for this study. Fliers, postcards, magazine advertisements, blogs and social media channels were designed for the purpose of this study to be used for advertisements following ethical approval from the School of Psychology Ethics Committee. The research team, which consisted of two other PhD students as well as undergraduate and postgraduate student volunteers, advertised the study on social media channels, in local newspapers, across the university campus, and social spaces in the local community. It was also advertised in the business community and organisations with a large number of staff such as the University of Nottingham, NHS and Boots.

The research group shared their study at various events, both within and beyond the university. These included the Gender and Athena Swan event, Nottingham Wellbeing in the Workplace event, PauseTrack, the Festival of Science and Curiosity, as well as gatherings hosted by the BRE Group and Boots. Thus, women from different areas and communities were recruited to share their experience. Interested participants got in touch via email or by visiting the blog page or social media channels which were monitored on a regular basis. Participants that got in touch were sent the study information sheet and a pre-screening form which was used to assess eligibility for the study. Eligible participants were then booked in for a session with an available member of the research group.

Certain groups of women were excluded from the study. Specifically, individuals who reported being pregnant, breastfeeding, have a diagnosed neurodegenerative disease such as dementia, Alzheimer's, have undergone surgically induced menopause, those currently undergoing chemotherapy for critical illnesses, and participants who were assigned male at birth were not included in this study. Additionally, we excluded women currently undergoing hormone replacement therapy (HRT), individuals currently on hormone treatment

for gender transition and women diagnosed with a hormone-related condition (e.g., polycystic ovarian syndrome) who were experiencing irregular or absent menstrual periods for over a year, where each menstrual cycle is either less than 21 days or more than 45 days.

The STRAW + 10 (Harlow et al., 2012) allowed for the classification of women into the three main stages of menopause; premenopause, perimenopause and postmenopause. Based on self-identification or self-reported bleeding patterns, women were classed into three groups as described in Chapter 3. For women who provided information about their circumstances via free text rather than selecting an option, the Figure 3-1 flow chart below was used to determine their menopause stage when it could not be directly ascertained.

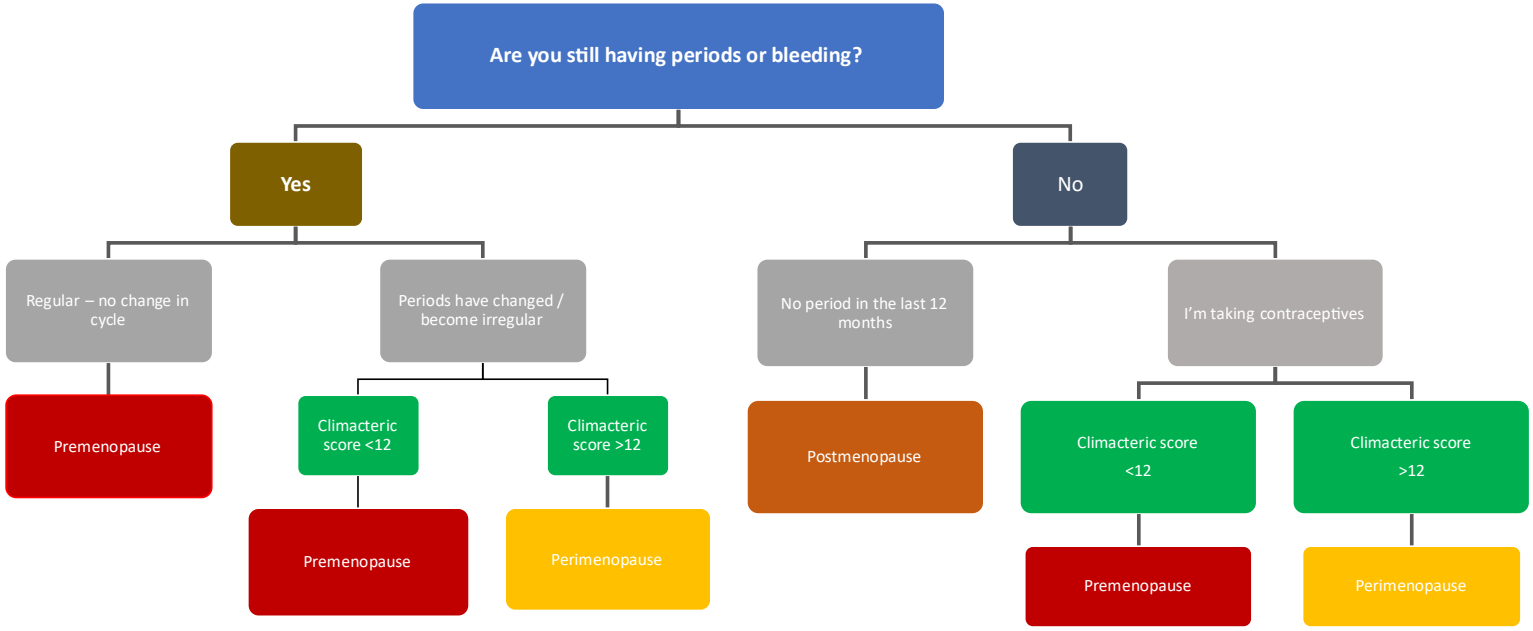

Figure 3-1 Menopause staging flowchart

Procedure

The entire procedure was conducted using a laboratory iMac Retina 4K (21.5-inch) computer, which was preloaded with the information sheet, consent forms, debrief materials, laboratory-based tasks, and links to Qualtrics-hosted questionnaires. Experiments took place in quiet, well-lit rooms, with participants seated comfortably approximately 70 cm from the screen. Participant responses were recorded using an Apple keyboard.

Participants were given the information sheet and consent form at the beginning of the experiment and also advised of taking breaks as and when needed. Each participant was given brief information about the study and experiments in accordance with the laboratory protocol designed by the research group. Participants took part in two questionnaires and six laboratory-based computerised tasks. These tasks and questionnaires were counterbalanced thereby minimising carryover effects and preserving the internal validity of the experiment. The questionnaire used in the study in Chapter 2 and already described was also used. The other questionnaire, *Perceived role overload* was also designed by another member of the research group. Two other PhD researchers in our group designed four of the tasks (visuospatial working memory, digit span, letter number sequence and task switching) and I designed and programmed the processing speed and Flanker tasks. The computerised tasks were designed and programmed using Psychopy-2023.2.3. All tasks took between 6-10 minutes to complete. All tasks were counterbalanced across each participant with one of two questionnaires completed at the end of every two computerised tasks. Feedback (correct, incorrect) was only provided during the practice test of the computerised tasks. At the end of the experiment, a debrief sheet was provided to participants and also paid an inconvenience allowance of £12. The study lasted approximately 1hr 15 minutes.

Measures

Processing Speed- computerised Symbol Digit Modalities Test (cSDMT)

A computerised version of the symbol digit modality task (SDMT) was used to assess processing speed based on previous versions by (Akbar et al., 2011; Bigi et al., 2017). On each trial, a panel of nine symbols, each matched to corresponding numbers 1 through 9, was visually presented on a computer screen (Figure 3-2). The symbol keys were randomised, with one symbol presented at a time. The symbol key measured 0.14° in width and 0.23° in height, positioned at the x-axis = 0 and y-axis = -0.2 on the screen. The panel of images measured 1.0° in width and 0.5° in height, positioned at the x-axis = 0 and y-axis = 0.2. The foreground colour in PsychoPy was set to grey (HEX-#808080) to ensure the symbols and numbers were clearly visible. Participants were asked to press the number that corresponded to the symbol shown below the reference key as in Figure 3-2. There was no time limit set for responses. Participants were instructed prior to the task to respond as quickly as they could.

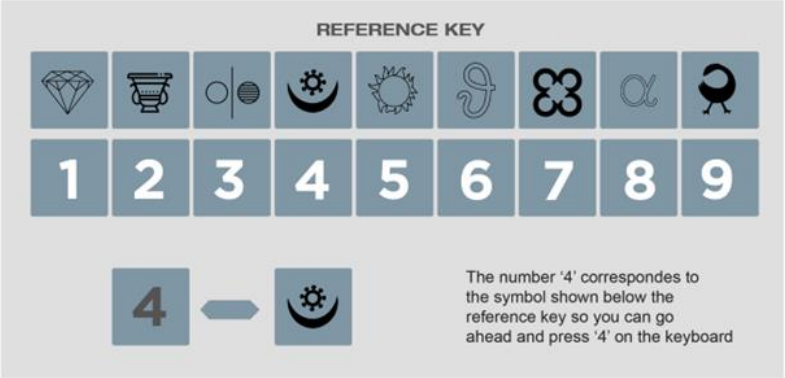

Figure 3-2 Processing speed instruction panel

Note: Provides further instructions for the task for participants after verbal instructions

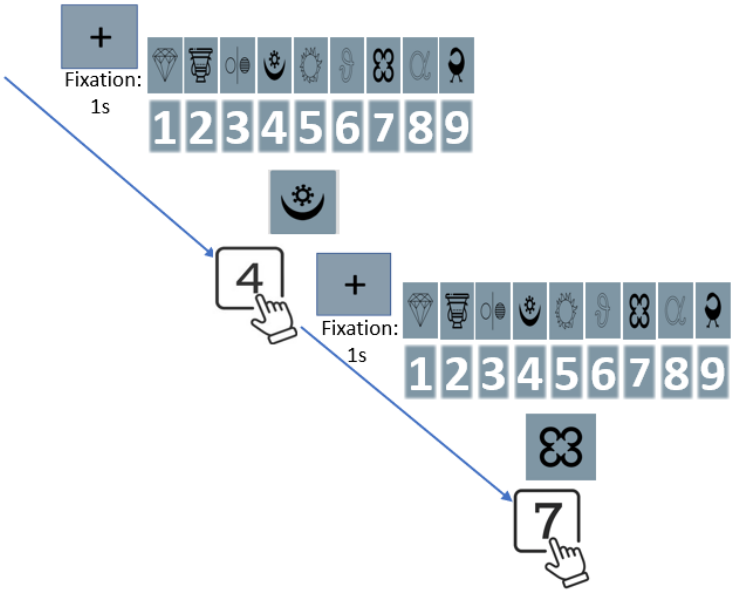

Figure 3-3 Reference key with response selection based on Symbol–Key association

Between each trial, a white fixation key, 0.05° in height and positioned at the x-axis = 0 and y-axis = -0.2, was presented for 1 second. The experiment consisted of six blocks of 18 trials each, totalling 108 trials. At the beginning of the experiment, participants completed a practice session with four trials to familiarise themselves with the test. If a participant made two or more inaccurate responses, the practice test was repeated, although this was not necessary for any study participants. During the practice test, feedback was provided on the correctness of responses and response times. Once the experimental trials began, no feedback was given, except after every 36 trials, when participants were given reassurances of their performance and reminded to respond as quickly as possible. This feedback remained on the screen until participants were ready to continue the experiment by pressing the space bar.

This task emphasises information processing speed through visual scanning, motor speed and the tracking (Strauss, 2006), with reaction times and accuracy of the trials. This domain is most susceptible to decline in normal aging and is fundamental

to all other cognitive processes. The dependent measures were the median reaction times of all correct responses.

Selective attention and inhibitory response - Flanker task

The Flanker task (Eriksen & Eriksen, 1974) is an objective measure used to assess inhibitory control (Diamond, 2013). As a measure of selective attention and inhibitory response according to Eriksen & Eriksen in 1974 participants are required to attend to a centrally presented stimulus or target while ignoring flanking stimuli surrounding the central target (Diamond, 2013). For congruent or compatible trials, the flanking stimuli require the same response as the central target and participants respond more quickly. The reverse is the case for incongruent trials or incompatible trials where flanking stimuli require an opposite response to the central target. Thus, participants are prone to error and tend to respond more slowly.

In this task, five arrows were visually presented on a computer screen. A trial consisted of one central target with arrow pointing to either the left or the right. This central target was flanked by two stimuli on the left and on the right. In the congruent condition, the central target faced the same direction as the surrounding stimuli and in the incongruent condition, the central target faced a different direction from the surrounding stimuli (Congruent condition: **<<<<<** or **>>>>>** incongruent condition: **<<><<** or **>><>>**). The arrows were centrally positioned on the screen at 0.5° in width and 0.5° in height with the foreground colour set to grey (HEX-#808080) in Psychopy. Participants were asked to focus on the central arrow and ignore surrounding stimuli and answer as quickly as they could. Participants were required to press the ‘Z’ key if the central arrow was facing the left and the ‘M’ key if the central arrow was facing right. See Figure 3-4 for the conditions presented to participants.

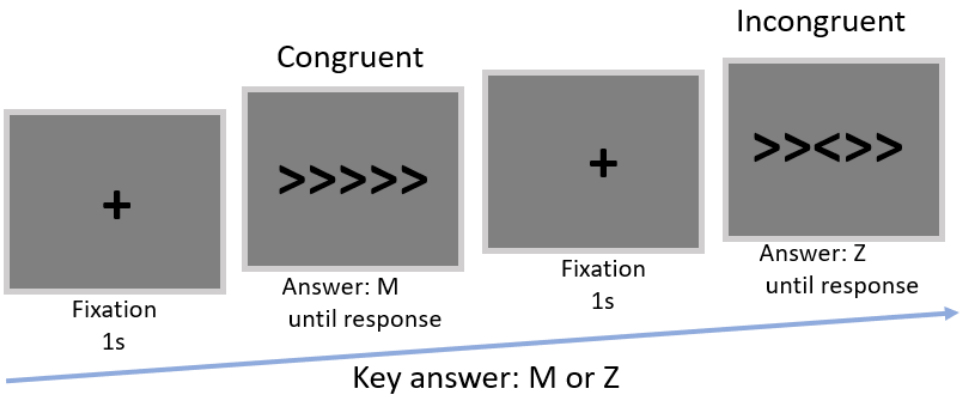

Figure 3-4 Diagram of Flanker experiment

Participants completed a total of 144 trials, with a break provided after every 18 trials. During each break, participants were encouraged to rest and reminded to respond as quickly as possible throughout the experiment. There was an equal number of congruent and incongruent trials.

The ratio of median reaction times for congruent to incongruent trials for correct responses was used as a dependent measure. Ratios were used to allow comparison across the different reaction times. Participants with lower ratios had smaller differences in their performance across the two trials. Accuracy was also included as a dependent measure calculated separately as the mean percentage of correct responses for congruent trials and for incongruent trials.

Digit Span Test:

The backward digit span task, adapted from the Wechsler Adult Intelligence Scale (WAIS-III) was used to assess working memory through an audio-based format. Before the experiment, participants were asked to look away from the computer screen in order to avoid getting feedback messages during the experiment.

Participants first listened to instructions read aloud, followed by a practice session with a 2-digit sequence to familiarise themselves with the task. During the experiment, they were presented with sequences of numbers, read out at 1-second intervals, and were asked to repeat them in reverse order. There was no time limit

for responses; once participants decided on their answer, the experimenter entered it and proceeded to the next audio sequence after a 1 second pause. The task began with shorter sequences (3-digit sequence lengths) and increased in complexity as participants progressed. Participants could take as long as they needed to respond. There were two trials at each list length. The experiment continued until a participant failed three sequences of the same length. Participants verbal working memory score was the total number of correct trials (total correct) (Unkenstein et al., 2016).

Other laboratory-based measures

This in-person study included additional tasks such as the visuospatial working memory test, letter number sequencing and task switching, though these were not included in the analysis. Due to time constraints, not all cognitive measures could be included in the study. The selected tasks focused on key domains: verbal working memory (assessed via the Backward Digit Span), processing speed, selective attention, and inhibitory control. While these measures have been examined in previous research, studies specifically targeting inhibitory control remain limited. Nonetheless, this combination of tasks offers valuable insight into women's cognitive performance and contributes to the existing literature by broadening the range of executive function domains assessed, while also allowing for comparability with relevant studies.

Self-report measures

Participants completed two questionnaires. The questionnaire used in the subjective study in Chapter 2 was used by participants who took part in this study. The other questionnaire, *Perceived role overload* was not used for analysis in this study.

3.5 Statistical analysis

IBM SPSS Statistics 28 was used for data analysis and Microsoft Excel, SPSS and JASP 0.19.3 was used to visualise data and plot graphs. The following results will report findings from the main hypothesis. Statistical analyses used in this research

were based on the research questions and the types of data generated. Descriptive statistics for the study sample used in analysis are presented in Table 3-1 as mean and standard deviation for continuous variables. For categorical variables, these are presented as frequencies and percentages.

Data screening and preparation

According to Tabachnick and Fidell (2007), missing data below 5% per item were deemed suitable for mean substitution. Peng et al. (2006) additionally support mean imputation provided that the proportion of missing data does not exceed a liberal threshold of 10–30%. Missing values analysis in this study indicated that most variables had less than 5% missing data except for the two verbal working memory tasks. Mahalanobis distance was used to identify multivariate outliers in all the six laboratory-based cognitive tasks. Missing values were addressed by using mean substitution of the respective task using the SPSS function. The distances were calculated using linear regression procedures with the p-value threshold set at 0.01. Since the overall project included nine independent variables for analysis by other students, the degrees of freedom for the chi-square distribution were nine. The critical cut off score was 27.877 at a significance level of $p < .001$(Tabachnick & Fidell, 2007). Cases exceeding this threshold were classified as outliers and subsequently excluded from further analysis.

256 women took part in the study. Of these, 9 were excluded due to specific criteria: use of hormone replacement therapy (n = 3), inability to determine menopausal stage (n = 2), cessation of periods due to cancer treatment (n = 2), hysterectomy (n = 1) and participation in pilot testing (n = 1). An additional 4 women did not complete the questionnaire required to determine menopausal stage, resulting in their exclusion while 3 more were excluded based on task performance criteria. A further 5 participants were excluded following Mahalanobis outlier detection.

In total, 21 participants were excluded, leaving 235 women in the final sample for analysis. The final sample consisted of premenopause (n=75), perimenopause (n=90) and postmenopause (n=70) women. This study focused on the cognitive

domains of processing speed, selective attention and inhibitory control and verbal working memory. These domains were examined in greater detail in subsequent analyses.

3.6 Results

Sample characteristics

See Table 3-1 for description of the study sample. The sample consisted mainly of white women (84.68%). Almost 86% of the participants were employed and 76.60% of the women were educated at degree level or above. 74.47% of women reported being parents. A one-way ANOVA was run with age as the dependent variable and menopause stage as the independent variable. Results from the analysis showed a significant main effect of menopause stage on age, F (2, 232) = 200.304, $p < 0.001$. Post hoc Bonferroni tests showed that participants in the premenopause group were younger than women in the perimenopause ($p < 0.001$) and postmenopause group ($p < 0.001$) and participants in the perimenopause group were younger than women in the postmenopause group ($p < 0.001$). A one-way ANOVA was also run with menopause symptoms as the dependent variable and menopause stage as the independent variable. Results from the analysis showed a significant effect of menopause stage on menopause symptoms, F (2, 232) = 4.308, $p = 0.015$. Post hoc Bonferroni tests showed that participants in the perimenopause group reported significantly higher menopause symptoms than women in the premenopause group ($p = 0.023$). There was no significant difference in menopause symptoms between perimenopausal and postmenopausal women ($p = 1.00$), nor between premenopausal and postmenopausal women ($p = 0.054$).

Participant characteristics

Table 3-1 Demographics of participants retained for analysis

Characteristic (n (%))		All n = 235	Premenopause n = 75	Perimenopause n = 90	Postmenopause n = 70
Ethnicity					
	White	199 (84.68)	62 (82.67)	77 (85.56)	60 (85.71)
	Black/African/Caribbean/Black British	12 (5.11)	3 (4.00)	6 (6.67)	3 (4.29)
	Asian/British Asian	13 (5.53)	7 (9.33)	1 (1.11)	5 (7.14)
	Mixed/Multiple ethnic group	8 (3.40)	3 (4.00)	3 (3.33)	2 (2.86)
	Other ethnic group	3 (1.28)		3 (3.33)	
Parents					
	Yes	175 (74.47)	59 (78.67)	65 (72.22)	51 (72.86)
	No	60 (25.53)	16 (21.33)	25 (27.78)	19 (27.14)
Caring responsibilities (elderly parents/relatives, family with long-term and age-related changes)					
	Yes	71 (30.21)	15 (20.00)	28 (31.11)	28 (40.00)
	No	164 (69.79)	60 (80.00)	62 (68.89)	42 (60.00)
Employment					
	Yes	201 (85.53)	72 (96.00)	78 (86.67)	51 (72.86)
	No	34 (14.47)	3 (4.00)	12 (13.33)	19 (27.14)

Education					
	Degree level or above	180 (76.60)	68 (90.67)	70 (77.78)	42 (60.00)
	Non degree level	51 (21.70)	7 (9.33)	19 (21.11)	25 (35.71)
	Not stated	1 (0.43)		1 (1.11)	
	Other	3 (1.28)			3 (4.29)
Characteristic (M (SD))					
Age (years)			42.12 (4.35)	46.93 (5.30)	57.24 (3.97)
Total Greene Climacteric score			17.21(9.84)	21.28 (8.77)	21.03 (10.47)
Sleep quality		1.93 (0.99)	2.17 (1.02)	1.91 (0.93)	1.69 (0.99)
Cognitive performance					
Processing speed median reaction times (secs)			1.51 (0.23)	1.52 (0.21)	1.73 (0.21)
Selective attention and inhibitory control (ratio)			0.87 (0.05)	0.87 (0.05)	0.85 (0.10)
Verbal working memory (Total correct)			5.60 (2.46)	5.21 (2.40)	5.08 (2.30)
BRI			52.92 (10.39)	55.39 (10.87)	54.34 (10.26)
MI			53.51 (10.84)	57.86 (13.31)	57.44 (11.90)

Assumption testing

Distributions of dependent variables were examined for normality and extreme outliers (±3SD) using histograms and boxplots and skewness ratios. There was a linear relationship between the covariate, age and dependent variables for each menopause group as assessed by visual inspection of a scatterplot. There was homogeneity of regression slopes as the interaction term between age and menopause stage was not statistically significant. Inspection of the *'Test of Normality'* demonstrated that processing speed median reaction times are not normally distributed in premenopausal women (*Kolmogorov-Smirnov; p<0.001)*. However, this was a fairly large sample. Fields (2009) recommends not using significance tests of skew and kurtosis in large samples as they are likely to be significant. Visual inspection of the histograms and Q-Q plots showed that the extent of non-normality was not sufficient to transform the data. Levy et al. (1980) found that when regression slopes are consistent across groups, ANCOVA remains robust against violations of normality even when group sizes are unequal. There was homoscedasticity, as assessed by visual inspection of the standardised residuals plotted against the predicted values. Tests for homogeneity of variance, normality, homoscedasticity and extreme outliers were performed on ANCOVA analyses. The data was satisfied for equality of variance using Levene's Test for Equality of Variance ($p > 0.05$). Descriptives and histograms on error residuals were examined to identify extreme outliers and non-normality.

Influence of menopause stage on cognitive performance (Hypothesis 1)

Similar to the study in Chapter 2, the overall aim of the study was to examine whether objective cognitive performance differed across menopause groups and whether any such differences were independent of chronological aging. An ANCOVA compares group means while statistically adjusting for a continuous covariate. As mentioned previously, age is a well-established predictor of cognitive performance and therefore an appropriate covariate to include when comparing naturally occurring groups that differ in age distribution. As

the primary aim was in comparing adjusted group means rather than estimating a full predictive model, ANCOVA provides a clear and interpretable test for addressing the research question. The ANCOVA yields unbiased adjusted means and valid tests of group differences especially as there were no interactions between age and menopause group.

A one-way ANCOVA was performed separately for each cognitive task. The dependent variables were processing speed median reaction times (SDMT), ratio of congruent to incongruent median reaction times (Flanker) and total correct score (BDS). The independent variable was menopause group (premenopause, perimenopause, postmenopause) and age were included as a covariate.

Processing speed task (SDMT)

A one-way ANCOVA was performed to examine whether processing speed median reaction times differed across menopausal stages (premenopausal, perimenopausal, postmenopausal), while controlling for age. The dependent variable was processing speed median reaction times; the independent variable was menopause stage and age was included as a covariate.

In the initial model, menopause group differences were not statistically significant, $F(2, 231) = 2.723$, $p = 0.068$, partial $\eta^2 = 0.023$. Age was a significant covariate, $p < 0.001$, partial $\eta^2 = 0.061$, indicating a moderate effect of age on processing speed. Pearson's correlation analysis showed a significant positive association between age and processing speed median reaction times ($r = 0.451$, $p < 0.001$) suggesting that older women were slower on the processing speed task.

These findings suggest that processing speed performance does not significantly vary by menopausal stage. However, age demonstrates a meaningful influence on processing speed.

Selective attention and inhibitory control (Flanker task)

Before the main analyses, an exploratory check was performed to assess whether expected interference effects were exhibited in the Flanker task thereby confirming its validity. Paired-samples t-tests were performed to compare participants' reaction times and accuracy in both the congruent and incongruent trial conditions to ensure that the task showed typical interference effects. With interference effects, it is expected that participants would have slower responses on incongruent trials compared to congruent ones. In terms of accuracy, it is expected that participants would be less accurate in incongruent trials compared to congruent trials.

A paired-samples t-test was used to determine whether there was a statistically significant mean difference in reaction times between congruent and incongruent trials. Unless otherwise specified, data from this test are mean ± standard deviation. No extreme outliers were detected as assessed by box plots. The assumption of normality was not violated as assessed by Kolmogorov-Smirnov; $p = 0.20$.

Participants were faster on congruent trials (M = 0.50, SD = 0.09) than on incongruent trials (M = 0.58, SD = 0.11), a statistically significant increase of 0.08 (95% CI, 0.07 to 0.09) seconds, t (234) = 17.59, $p < 0.001$.

Participants were also significantly more accurate on congruent trials (M = 0.99, SD = 0.01) than on incongruent trials (M = 0.97, SD = 0.05), a statistically significant decrease of 0.029 (95% CI, -0.04 to -0.02, t (234) = -8.48, $p < 0.001$.

A one-way ANCOVA was conducted to examine group differences in selective attention and inhibitory control with group (premenopause, perimenopause and postmenopause) as the independent variable and ratio of congruent to incongruent median reaction times as the dependent variable and age as a covariate.

Findings from the initial ANCOVA showed no significant differences in flanker interference across the menopause groups, F (2,231) = 0.345, p = 0.709, partial η^2 = 0.003, There was no significant effect of covariate, age, on flanker interference, F (1,231) = 1.594, p = 0.208, partial η^2 = 0.007. Similar to the findings on processing speed, flanker interference did not differ significantly across menopause groups. However, while age significantly influenced processing speed, it did not have a significant effect on flanker interference.

Verbal working memory (Backward digit span task)

Premenopause women scored higher on the task (46.70%) followed by perimenopause women (43.39%) and postmenopause women (42.34%). A one-way ANCOVA was conducted to examine group differences in verbal working memory with group (premenopause, perimenopause, postmenopause) as the independent variable, total correct scores as the dependent variable and age as a covariate. Results from the ANCOVA showed no significant difference in verbal working memory scores in the menopause groups, F(2, 231) = 0.299, p = 0.742, partial η^2 = 0.003. There was no significant effect of age on verbal working memory, F(1, 231) = 0.253, p = 0.615, partial η^2 = 0.001.

Associations between menopausal symptom severity on cognitive performance (Hypothesis 2)

Prior to investigating the associations between menopause symptoms and cognitive performance, I first compared symptoms severity across pre-, peri- and postmenopausal women.

Exploratory analysis of Total GCS scores across the three menopause groups, premenopause, perimenopause and postmenopause

To examine differences in menopause groups in Total GCS or menopause symptoms, an analysis of covariance (ANCOVA) was performed with group (premenopausal vs. perimenopausal (no HRT) vs. postmenopausal) as the between-subject factor. The dependent variable was the Total GCS scores from the Greene Climacteric scale.

Menopause stage was the categorical predictor or independent variable. Age was included as a covariate in the analyses to adjust for potential confounding.

There was a significant main effect of menopause stage F (2, 213) = 6.556, p = 0.002, partial η^2 = 0.054. This indicates that menopause stage had a significant effect on menopause symptoms. There was a significant effect of age on menopause symptoms, F (1, 231) = 4.466, p = 0.036, partial η^2 = .018.

Post hoc analysis using Bonferroni corrected t-tests revealed that perimenopausal women (M= 20.84.06, SE = 1.03) reported significantly higher menopause symptoms in comparison to premenopausal women (M=15.40. SE= 1.40, p = 0.003). There was no significant difference in reported menopause symptoms between perimenopausal women and postmenopausal women (M= 23.54, SE= 1.*65, p* = 0.578). Postmenopausal women reported significantly higher menopause symptoms in comparison to premenopausal women (p = 0.006). Given the findings above, I next investigated associations between menopause symptoms and cognitive performance.

Pearson's partial correlations as presented in Table 3-2 were conducted to investigate any associations between overall menopause symptoms and processing speed, working memory, selective attention and inhibitory control, behavioural regulation index (BRI) and metacognition index (MI) while controlling for age. The variables used were age, total menopause symptoms score, processing speed median reaction times, total correct scores (BDS), ratio of congruent to incongruent median reaction times (Flanker) and T scores from BRI and MI (BRIEF-A). To account for multiple comparisons across 5 correlations, the significance threshold was adjusted to $p < 0.01$.

Table 3-2 Partial Correlations Between Overall Menopausal Symptoms and Cognitive Measures

Cognitive Measure	Partial *r*	p-value
Processing speed	.189	.004*
Selective attention and inhibitory control	.033	.613
Verbal working memory	-.156	.017
BRIEF-A BRI	.627	<.001**
BRIEF-A MI	.576	<.001**

Note. All correlations control for age. Degrees of freedom (df) = 232. Significance (2-tailed), *$p < 0.01$, **$p < 0.001$. Behaviour Rating Inventory of Executive Function – Adult Version (BRIEF-A), Behaviour regulation index (BRI) and Metacognitive index (MI).

Results indicated that higher menopausal symptom severity was significantly associated with increased difficulties in behavioural regulation (BRI) ($r = 0.627$, $p < 0.001$) and metacognition (MI) ($r = 0.576$, $p < 0.001$), as measured by the BRIEF-A. Additionally, menopause symptoms was positively correlated with median reaction times on a processing speed task ($r(232) = 0.189$, $p = 0.004$) indicating slower performance with worse symptoms. No significant associations were found between overall menopause symptoms for verbal working memory ($r(232) = -0.156$, $p = 0.017$) and selective attention and inhibitory control ($r(232) = 0.033$, $p = 0.613$)

See Appendix 6 of exploratory analysis examining associations between menopause symptoms subclusters and cognitive performance.

An exploratory analysis examining how sleep quality influences cognitive performance (processing speed, selection attention and inhibitory control and verbal working memory)

Sleep quality ratings, initially measured on a scale from 0 to 4 (0 = terrible, 1 = poor, 2 = fair, 3 = good, 4 = excellent), were recoded and mean-centred for analysis. The recoding process transformed the scale to range from -2 to 2. Prior to investigating the influence of sleep quality

on cognitive performance, I first compared sleep quality across pre-, peri- and postmenopausal women.

Exploratory analysis of sleep quality scores across the three menopause groups, premenopause, perimenopause and postmenopause

To examine differences in menopause groups in sleep quality, an analysis of covariance (ANCOVA) was performed with group (premenopausal vs. perimenopausal vs. postmenopausal) as the between-subject factor. The dependent variable, sleep quality was the mean-centred sleep scores. Menopause stage was the categorical predictor or independent variable. Age was included as a covariate in the analyses to adjust for potential confounding.

Interestingly, there was no significant main effect of menopause stage on sleep quality, F (2, 231) = 0.993 p = 0.372, partial η^2 = 0.009. This indicates that there were no differences in sleep quality across the menopause stages. There was no significant effect of age on sleep quality, F (1, 814) = 0.287, p = 0.592, partial $\eta^2 < 1$.

I next investigated the relationship between sleep quality and cognitive performance.

Given the ordinal nature of sleep quality scores, a Spearman's rank order correlation test was used to examine the relationship between mean-centred sleep quality and cognitive performance. This preliminary analysis was performed prior to regression modelling to assess the strength and direction of associations between mean-centred sleep quality scores and each cognitive domain.

Mean-centred sleep quality scores were negatively correlated with processing speed (r = -0.194, p = 0.003), indicating that poorer sleep quality was associated with slower reaction times. No significant correlations were found between sleep quality and selective attention and inhibitory control (r = -0.001, p = 0.990) and working memory (r = 0.065, p = 0.324). As a result of this finding, a regression analysis was conducted on processing speed domain only.

Processing speed

Earlier findings in this study revealed no effect of menopause stage on cognitive performance while also identifying a significant and positive correlation between menopause symptoms and processing speed. The pre-registered analysis originally aimed to examine how sleep quality influences the relationship between menopausal stage and cognitive performance. However, due to the absence of significant effects related to menopausal stage, the analysis was adapted to include menopause symptoms instead.

A hierarchical multiple regression was conducted on processing speed (outcome variable) with age and menopausal symptoms as predictor variables (model 1) and sleep quality as predictor variable (model 2).

The full model of age, menopause symptoms and sleep quality to predict processing speed was statistically significant, $R^2 = 0.233$, F (3, 231) = 23.450, $p < 0.001$; adjusted $R^2 = 0.223$.
In the first step, both age ($\beta = 0.447$, $p < 0.001$) and menopause symptoms ($\beta = 0.169$, $p = 0.004$) significantly predicted processing speed median reaction times, $R^2 = 0.232$, F (2, 232) = 34.992, $p <$ 0.001. The addition of sleep quality to the prediction of processing speed median reaction times (Model 2) also led to a slight increase in R^2 of .233, F (3, 231) = 23.450, $p < 0.001$; *adjusted* $R^2 = 0.223$ and the full model also remained statistically significant. However, the addition of sleep quality did not significantly improve the model, $\Delta R^2 = 0.002$, F (1, 231) = 0.51, $p = 0.474$. The findings indicate that both age and menopause symptoms are significant predictors of processing speed, with older age and greater symptom severity associated with slower reaction times. Although the overall regression model including sleep quality was statistically significant, the addition of sleep quality did not significantly improve the model's predictive power. This suggests that sleep quality does not uniquely contribute to the prediction of

processing speed beyond the effects of age and menopause symptoms in this sample.

Exploratory analysis examining effect of menopause stage on self-report executive function performance

To investigate differences between menopause groups in self-report executive functions as described in Chapter 2, two analyses of covariance (ANCOVAs) were performed with group (premenopausal vs. perimenopausal vs. postmenopausal) as the between-subject factor. The dependent variables were the BRIEF-A indices, specifically the BRI and MI T scores. Menopause stage was the categorical predictor or independent variable. Age was included as a covariate in both BRI and MI analyses to adjust for potential confounding. BRI and MI means for the online and lab-based studies are shown in Table 2.3 and Table 3.1 respectively.

In BRI analysis, there was no significant main effect of menopause stage, F (2,231) =1.966, p = 0.142, ηp^2= 0.017. The covariate age was not significant, F (1,231) = 1.821 p = 0.179.

In MI analysis, there was also no significant main effect of menopause stage, F (2,231) =2.767, p = 0.065, ηp^2= 0.023. Age was also not significant, F (1,231) = 0.346 p = 0.557.

3.7 Discussion

This cross-sectional laboratory-based study complements the self-report study on executive functioning by integrating laboratory-based cognitive tasks. The use of laboratory-based tasks offers increased sensitivity and objectivity as it measures reaction times and accuracy more precisely and as such can detect subtle differences in performance. Although the current sample did not meet the target size, it nevertheless represents a relatively large number of women across menopausal stages when compared to existing studies in the literature (Fuh et al., 2006; Weber et al., 2013; Unkenstein et al., 2016; Martino et al., 2022). Additionally, sensitivity analysis demonstrated that the

sample was large enough to detect small to moderate effect sizes. However, non-significant results should still be interpreted with caution as the study may not have had enough power to detect subtle menopause group differences in cognitive. In a longitudinal study of 2.362 premenopausal, perimenopausal and postmenopausal women, Greendale et al. (2009) reported that challenges in cognitive performance during the menopausal transition were subtle and transient. Therefore, it is possible that a potentially larger sample may have detected subtle changes.

Though recruiting women in midlife for a large in-person research presents some logistical and demographic challenges, it remains critical for shedding light on the cognitive changes associated with menopause. The present study aimed to address this gap by integrating previously discussed subjective self-report measures with objective, computerised laboratory-based tasks, thereby providing a more comprehensive understanding of both perceived and measured cognitive changes across the menopausal transition.

This study found no significant effect of menopausal stage on processing speed, selective attention, inhibitory control, or verbal working memory. However, in the processing speed task specifically, age was significantly associated with performance, with older women demonstrating slower reaction times. Among all laboratory-based cognitive measures, only processing speed showed a significant positive association with overall menopause symptoms, suggesting that greater symptom severity is linked to slower processing speed, independent of age.

Interestingly, sleep quality did not differ significantly across the three menopausal groups. Although a statistically significant negative association was initially found between sleep quality and processing speed, this relationship did not hold when menopause symptoms were included in the regression model. Instead, only age and symptom

severity remained significant predictors with older age and greater symptom severity both associated with slower processing speed.

Lastly, consistent with findings reported in chapter 2, menopause symptoms were also significantly and positively associated with self-reported measures of executive function. These results highlight that while menopausal stage itself may not directly impact cognitive performance, symptom severity and age are meaningful predictors, particularly for processing speed. Next, I explore the findings from this study in more detail.

Influence of menopause stage on cognitive performance

This laboratory-based study investigated differences in cognitive performance across premenopausal, perimenopausal and postmenopausal women. After controlling for age, no significant differences were observed between menopause groups. Though these findings were contrary to my hypothesis, they align with outcomes reported in other cross-sectional studies assessing similar cognitive domains and introduced earlier. For example, Martino et al. (2022) reported no group differences in semantic and phonological verbal fluency, working memory, cognitive flexibility, inhibitory control and planning. A study by Luetters et al. (2007) also found no difference in working memory, processing speed and verbal episodic memory across menopausal stages. Studies by Schaafsma et al. (2010) and Jaff et al. (2020) also reported comparable processing speed across groups while Unkenstein et al. (2016) reported no significant differences in working memory, selective attention and inhibitory control, verbal fluency, episodic learning and memory. On the contrary, results from Weber et al. (2013) in working memory and Greendale et al. (2009) in processing speed showed a decline in performance during perimenopause when compared to premenopause.

Additionally, there was a significant effect of age on processing speed only with older participants having slower processing speed times in this study which aligns with existing literature (Zaninotto et al., 2018).

This indicates that cognitive slowing in this domain is more closely related to chronological ageing than menopause stage. Harada et al. (2013) documents processing speed as one of the domains affected by ageing with this domain beginning in early adulthood and extending into later life (Salthouse, 2010). Zaninotto et al. (2018) have shown that age-related cognitive decline is more pronounced in processing speed abilities with a marked decline as we age. Zaninotto et al in a 8-year longitudinal study of 10,626 participants with a mean age of 64.6 examined processing speed as one of its domains of interest and showed that increasing age was associated with decline in processing speed. Cognitive change as we age is a normal part of the ageing process with declines in cognitive abilities such as processing speed expected. Harada et al. (2013) suggests this may be as a result of structural and functional brain changes as we get older. The findings in this study suggest that while menopausal stage may not independently influence processing speed, age remains a critical factor in cognitive performance and should be accounted for when examining cognitive changes across the menopausal transition and this was considered as part of this research.

Another important consideration is the laboratory setting in which cognitive tasks were conducted. These findings suggest that the cognitive performance of women during the menopausal transition may not be significantly impaired, even when assessed using computerised measures with greater sensitivity. However, in this controlled environment, participants were provided with a quiet, distraction-free space to complete attention-demanding tasks which may very well lead to better performance. However, this context may not accurately reflect the real-life cognitive challenges faced by midlife women, who often navigate multiple roles and responsibilities. In this study for example, 20% of premenopausal, 31.11% of perimenopausal and 40% of postmenopausal women responded “yes” to having caregiving responsibilities for elderly relatives. Additionally, the highest proportion of employment was reported among perimenopausal women. These

findings suggest that women in midlife, particularly those transitioning through menopause, often navigate multiple roles simultaneously, including paid employment and caregiving which may contribute to increased cognitive load and reduced attentional capacity in everyday contexts but subtle enough such that they are not observed in laboratory-based tasks. Unkenstein et al. (2016), in their study of women attending a menopause clinic, similarly found no significant cognitive differences between premenopausal, perimenopausal, and postmenopausal groups. The authors proposed that during the menopausal transition, a period frequently characterised by competing demands and multiple roles, women may experience increased vulnerability in attentional functioning, particularly when faced with numerous simultaneous obligations. This underscores the potential disconnect between laboratory-based tasks and the lived cognitive experiences of midlife women. Given that sensitivity analysis confirmed the study was adequately powered to detect small to moderate effect sizes, the absence of significant differences across menopausal stages may reflect a genuine lack of effect rather than limitations in sample size. Weber et al. (2014) reviewed four cross-sectional studies that utilised seventeen different cognitive tests. These studies reported standardised effect sizes ranging from 0.018 to 0.333. These values are considered very small according to Cohen's guidelines, which were similarly reflected in this study.

Nonetheless, it remains possible that changes in cognition could occur during this transition, as reported by some longitudinal studies that have tracked women over a longer period. A longitudinal study by Greendale et al. (2009) showed worse performance during perimenopause. Perhaps more longitudinal studies are needed to better understand the cognitive changes associated with menopause. Nevertheless, in this sample of women, cognitive performance did not differ significantly across menopausal stages or age groups with the exception of the processing speed task, where older age was a significant predictor of slower reaction times. Given that some previous

studies have found significant associations between menopause stage and laboratory-based tasks, it is possible that other contributing factors such as socio-behavioural factors may be impacting cognitive performance. Due to time constraints, these external factors were not examined in the present study, but they warrant further exploration in future research.

Furthermore, although both in person and online studies used the same self-report measure of executive function, menopause stage differences emerged only in the online sample which was an interesting finding. This difference suggests that the self-report measures are potentially sensitive to the context in which they are completed. Existing research shows that individuals tend to disclose more cognitive and emotional difficulties in private or anonymous settings than in face-to-face environments, where social desirability, self-presentation pressures and fear of being judged are stronger (Joinson, 2001; Tourangeau & Yan, 2007). The results suggest for online environments, mid-life women were perhaps more open to reporting of perceived difficulties in comparison to in person settings where the more structured and formal environment where a researcher is present can make people more self-aware or more motivated to present themselves accurately or in a better light. This finding highlights the importance of considering the environment in which cognitive assessments are performed when interpreting self-reported executive function challenges in menopause research for example.

Associations between menopausal symptoms and cognitive performance

A contributing factor that may affect cognitive performance is menopause symptoms and this was examined in this laboratory-based study. The frequency and intensity of menopausal symptoms vary considerably among women, influenced by cultural background, social context, and individual factors, as evidenced by studies such as Lerner-Geva et al. (2010) and Fang et al. (2024). Although existing

research on the associations between menopausal symptoms and cognitive performance remains limited, some studies have demonstrated associations. In the present study, overall symptom scores severity was examined to assess their relationship with cognitive performance while adjusting for age. Processing speed was the only cognitive domain to show a significant association with menopause symptoms. Small but significant positive correlations indicated that women reporting more severe symptoms experienced slower reaction times on the processing speed task. Interestingly, although cognitive performance did not differ significantly across menopause stages, the finding suggest that menopause symptom burden rather than menopausal stage alone may serve as a more sensitive marker of cognitive change during the menopausal transition This is relevant given the menopause symptom variation that exists in women transitioning to menopause. This finding is consistent with prior research. Calle et al. (2024) investigated severe menopausal symptoms in 1287 postmenopausal women and found an association between severe menopause symptoms and cognitive impairment. Calle and colleagues examined memory, visuospatial skills, executive function, attention, language and orientation. Greendale et al. (2009) also found small but negative effect of menopause symptoms on processing speed in a study of 1,903 midlife women which included premenopause, perimenopause and postmenopausal women. While not all individuals in peri- or postmenopause experience severe symptoms, the presence and severity of symptoms may reflect underlying hormonal shifts, particularly declines in oestrogen, which have been linked to cognitive function. In this sample, peri- and postmenopausal women reported significantly higher symptom scores compared to premenopausal participants, reinforcing the relevance of symptom severity. Therefore, the absence of stage-related effects may reflect individual variability in symptom experience, while the observed associations with processing speed highlight the potential cognitive impact of menopause-associated symptoms.

In summary, aside the neuroprotective nature of oestrogen on cognitive brain functions, symptoms associated with menopause transition may also explain the poorer cognitive performance that some women experience. Weber et al. (2021) suggested that the cognitive declines during the transition to menopause might be secondary effects arising from menopause-associated symptoms such as vasomotor symptoms including elevated levels of anxiety, depression and sleep disturbance.

It is important that menopause-associated symptoms are integrated into both the management of menopause and future research, as they may play a role in supporting or enhancing cognitive performance.

Sleep quality and cognitive performance

As discussed earlier, sleep disturbances are common during the menopausal transition. In this sample of women, there was no significant difference in sleep quality across the menopause groups. Sleep quality was negatively correlated with processing speed suggesting that women who reported poorer sleep quality were slower on the processing speed task. No significant associations were found between sleep quality and cognitive domains of selective attention and inhibitory control and working memory. However, regression analysis identified age and menopause symptom severity as significant predictors of processing speed. While sleep quality initially showed a significant association with processing speed, this relationship did not remain once menopause symptoms and age were included in the regression model. This suggests that the influence of sleep quality may be accounted for by broader menopause symptoms. Additionally, the effect of age aligns with well-established findings that cognitive processing speed tends to decline with increasing age.

This significant association between menopause symptoms and cognitive impairment aligns with a review by Zhu et al. (2022) and findings by Jaff et al. (2020), and Greendale et al. (2010), who reported that symptom burden significantly predicted slower processing speed. These results support the view that menopause symptoms may

underlie the cognitive difficulties women often report during the transition. In this sample of midlife women, it appears that, overall symptom severity had a greater impact on cognitive performance than sleep quality alone, which was comparable across menopause groups. Moreover, the observed shared variance between sleep and other menopausal symptoms suggests that sleep may influence processing speed indirectly, as part of a broader symptom profile, rather than exerting an independent effect.

There was also a significant effect of age on processing speed as seen in earlier results when investigating effect of menopause stage on cognitive performance. This demonstrates that the declines in processing speed were also because of a factor such as chronological ageing and the changes associated with that process and not menopause symptoms alone. These results have demonstrated the need to consider other factors such as age and menopause symptoms and effects of various cognitive domains including processing speed. Result suggested that processing speed is also impacted by broader factors such as changes related to ageing and menopause symptoms than the quality of sleep experienced.

3.8 Strengths and limitations

This study has a relatively large sample size and involved women across the three stages of menopause; premenopause, perimenopause and postmenopause which is a key strength of the study. This is key to understanding the menopause transition as each stage presents its own unique hormonal profile and allows better comparison of cognitive changes. This has not been previously done in other studies. Weber et al. (2012) focused exclusively on perimenopausal women; Drogos et al. (2013) examined midlife women without specifying menopausal stage; and Lee et al. (2020) grouped participants simply as menopausal or non-menopausal, without further

categorisation. (Weber et al., 2012; Drogos et al., 2013; Lee et al., 2020).

Another key strength is that women attended the University or designated testing sites to take part in the study. This was performed under a controlled environment by adequately trained experimenters. This ensured uniformity in the data collection process.

Additionally, the use of computerised cognitive tasks offered greater sensitivity and precision in measuring reaction times compared to traditional paper-based methods, while also reducing manual data handling errors. Lastly, the employment of a validated menopause symptom questionnaire enhanced the reliability of symptom reporting and facilitates comparison with existing research as does the use of standardised laboratory-based cognitive tasks.

Due to the cross-sectional nature of this study, casual inferences cannot be made between variables. As previously mentioned, this study was also underpowered, and the sample size did not reach the target needed to draw firm conclusions. Previous studies have reported small effect sizes, and this study was powered to anticipate small to moderate effects but there was limited time to recruit participants. According to the participant demographics, 85.53% of women reported being employed which made it challenging in terms of scheduling appointments. It is possible that work commitments as well as other factors made it difficult for participants to find time to attend the in-person study thereby making it difficult to reach the target. However, findings from this study are relevant and could potentially guide future investigations and study design.

Another limitation of the study was the measurement of sleep quality. Sleep quality was assessed subjectively which could potentially introduce bias or inaccuracy in reports. Other objective methods such as polysomnography or wrist actigraphy could be used as these would offer more accurate assessments of women’s sleep quality when

evaluating sleep disturbances in mid-life women especially as this symptom is reported by menopausal women.

Lastly, the participant demographic was made up of predominantly White and highly educated participants despite intensive efforts to recruit from more diverse networks. Thus, the findings of this study are limited in terms of its generalisability to wider and diverse populations.

3.9 Conclusion

This cross-sectional study found no effect of menopause stage or reproductive ageing on processing speed, selective attention and inhibitory control and verbal working memory using laboratory-based tasks. However, severity of overall menopause symptoms was associated with poor performance on the processing speed suggesting symptoms a potential secondary impact on cognitive performance especially as it was perimenopausal and postmenopausal women who reported worse symptoms compared to premenopausal women. These broader associations should be considered when working with women to ensure that an awareness or if possible, treatments are initiated to address some of menopause symptoms. Given the presence of an ageing effect in this study, future research could adopt a longitudinal design by tracking changes in cognitive performance within the same women over time. This would capture the progression of cognitive ageing more accurately.

It was also interesting to note that in this laboratory-based study with a different sample of women, menopause symptoms were also strongly and significantly associated with self-reported behavioural regulation and metacognitive abilities as discussed in the study in chapter 2. While cognitive performance is often assessed through either self-report or laboratory-based measures or both, discrepancies between these approaches have been reported. The next chapter explores associations between laboratory-based measures and self-report measures of similarly named cognitive measures.

Nevertheless, the findings from two cohorts of women in both self-report and laboratory-based showing associations between menopause symptoms burden and executive function performance reinforces the validity of the findings in this research project. The associations also provides an opportunity to ‘normalise’ the experience for women and provide assurances that this is a unique but also shared experience by many women. In conclusion, during mid-life, it is important to consider to what extent menopause-associated symptoms impact selective cognitive domains and the broader role played by cognitive ageing.

4 Chapter 4 Association between self-report and laboratory-based measures of executive functions in menopausal women

4.1 Abstract

The aim of this brief exploratory study was to examine the associations between self-reported and laboratory-based measures of cognitive performance across premenopausal, perimenopausal, and postmenopausal women. This was a cross-sectional study that utilised data from laboratory-based study described in chapter 3. Women (n = 235) who took part in the in-person study completed the self-report BRIEF-A and also participated in flanker task and Backward Digit Span task. Specifically, the Inhibit and Working Memory subscales of the BRIEF-A were paired with the Flanker task and the Backward Digit Span task, which assess selective attention and inhibitory control, and working memory, respectively. Pearson's partial correlations revealed non-significant relationships between self-report and laboratory-based measures in both the working memory domain (p = 0.088) and the inhibitory control domain (p = 0.967). These findings suggest that, despite the use of similarly named cognitive constructs, there was no meaningful association between subjective reports and objective task performance. Future research should investigate other cognitive domains to determine whether this disconnect persists and explore whether self-reported cognitive complaints may serve as predictors of objective cognitive decline.

4.2 Introduction

In addition to the laboratory-based measures, executive functions (EF) were also assessed using the self-report BRIEF-A, as previously discussed in chapter 2. This measure captures participants' performance in real-life situations. The BRIEF-A measures provide a

crucial and complementary measure to laboratory-based measures with both having unique and distinct advantages. There are still crucial questions to answer in relation to whether any associations exist between BRIEF-A and laboratory-based measures. Executive functions (EF), particularly working memory and inhibitory control are essential for example remembering instructions and regulating behaviour respectively in everyday life. These domains were selected for the present study due to their relevance to real-world functioning and their prominence in cognitive ageing research. While working memory has been extensively studied using laboratory-based tasks, self-report measures have typically focused more broadly on general memory complaints rather than specific executive processes. Inhibitory control, meanwhile, remains comparatively underexplored in both self-report and lab-based contexts. The BRIEF-A questionnaire offers similarly named constructs that align with those assessed in experimental tasks, allowing for a direct comparison between subjective and objective measures of the same cognitive domains. However, previous research has rarely examined these two approaches side by side, and studies that do often focus on memory alone. This study addresses that gap by investigating whether self-reported and laboratory-based measures of working memory and inhibitory control are meaningfully associated, thereby evaluating the degree of convergence between perceived and actual cognitive performance.

Self-report measures of cognition are practical, efficient and useful measures that can be used to assess participants. Laboratory-based cognitive tasks on the other hand are conducted under controlled environment where one is shielded from distractions. Research examining associations between the two measures has produced somewhat mixed results. A study by Snyder at al. (2021) found weak correlation between self-report measure and laboratory-based tasks of executive functions. Snyder and colleagues sample consisted of youth aged 13–22 year-olds recruited from the community who took part in validated laboratory tasks and self-report questionnaires which

included the BRIEF. They also observed that there were more significant correlations between executive function laboratory-based measures and the BRIEF than other self-report questionnaires.

Another study by, Toplak et al. (2013) critically examined associations between laboratory-based tasks and self-report measures of executive function in 20 studies. The studies consisted of predominantly children's samples (n =13) and adult samples (n=7). Toplak and colleagues noted that 24% of the 286 correlations examined were statistically significant and the overall correlations were quite low (r = 0.19). They noted that a common assumption was made that self-report measures were assessing the same underlying cognitive processes in laboratory-based tasks. In contrast, Schmitter-Edgecombe at al., (2011) in a meta-analysis did not find any significant associations between laboratory-based and self-report measures of everyday functioning in healthy older adults who were aged 55-86 years and lived in the community. Similarly, a study by Meltzer et al. (2017) found no significant association between BRIEF-A and laboratory-based tasks assessing working memory, cognitive inhibition, planning and set-shifting. This study's sample consisted of 245 community-dwelling older adults aged 70 and above who did not have dementia. Consistent with these findings, Rabin et al. (2006) in a sample of 87 nondemented adults that included individuals with mild cognitive impairment and healthy controls also found no significant associations between BRIEF-A scores and executive function tests that included tests on working memory, memory, attention and spatial skills. This previous research suggests that laboratory-based tasks and self-report measures of cognition may not necessarily be measuring interchangeable psychological constructs (Gobel et al., 2022). Friedman and Gustavson (2022) reviewed evidence from the two measures and suggested different aspects that these two measures assess. According to Friedman and Gustavson (2022), self-report measures require individuals to reflect on behaviour over a period in different contexts including emotional situations and relies on an

individuals' sense of self-awareness. In contrast, laboratory-based tasks assess cognitive performance at a sitting under controlled environments where participants are monitored and given clear instructions on how to perform an emotionally neutral task. Taken together, these fundamental differences in what each method captures may be reason for inconsistency in results as also reported by Cyders & Coskunpinar (2012).

Despite the mixed findings between laboratory-based measures and self-report questionnaires, both provide crucial information which can indicate executive function challenges in participants and thus can be used to complement each other during this research. The BRIEF which is deemed to be more ecologically valid than laboratory-based measures (Gioia et al., 2000) has not been used in menopause research currently. The BRIEF is a useful tool for assessing cognition as it provides a picture of behaviour in a natural setting and provides unique information (Anderson, 2002). These measures could shed some insights to how particular executive function are affected during transition to menopause. These behavioural indicators of cognition in real-life situations are challenging to capture using laboratory-based measures only. On the other hand, laboratory-based tasks are performed in controlled environments and participants are provided with instructions and clearly defined goals. Thus, if performance is low in this setting, it may indicate challenges in processing information which could be exacerbated in real-world settings which are less structured (Toplak et al., 2013). Therefore, integrating both measures allows for a more comprehensive understanding of how cognition is impacted during the transition to menopause and is a key strength of this study as there are very limited studies that employ both measures.

4.3 Aims

Data collected for the in-person, laboratory-based study was used to explore potential associations between specific domains of the BRIEF-

A and performance on corresponding laboratory-based tasks. Specifically, the BRIEF-A Inhibit domain was paired with the Flanker task, which is widely used to assess selective attention and inhibitory control. Similarly, the BRIEF-A Working Memory domain was examined in relation to performance on the backward digit span measure which is also a well-established measure of working memory. These pairings were selected based on face validity, as both laboratory-based tasks are cognitively relevant to the domains represented in the BRIEF-A subscales. Previous research used these tasks to assess similar cognitive domains. For example, Diamond et al. (2013) discussed the use of the tasks such as Flanker and backward digit span to assess core executive functions which include selective attention and inhibitory control and working memory. Through this dual-method approach, the study aimed to enhance understanding of how subjective executive function reports align with laboratory-based tasks.

4.4 Method

The study sample and method were taken from laboratory-based study described in Chapter 3. The participants described in Section 3.6 were used for the data analysis.

4.5 Statistical analysis

IBM SPSS Statistics 28 was used for data analysis. The following results will report findings from the aim of the study. Statistical analyses used in this study was based on research question and the types of data generated. Pearsons' partial correlation was used to analyse data as the variables of interest were continuous variables. Age was controlled for in this analysis.

4.6 Results

Sample characteristics

Descriptive statistics for the study sample used in analysis were presented in Table 3-1. Self-report and laboratory-based cognitive performance on selective attention and inhibition and working memory tasks across premenopausal, perimenopausal and postmenopausal groups women are presented in Table 4-1. Self-report scores in the Inhibit domain were within the typical range across all three groups. However, in the working memory domain, perimenopausal and postmenopausal reported scores that slightly exceeded the BRIEF-A clinical significance threshold of 65, with average scores of M = 66.92, SD = 14.37 and M = 65.94, SD = 12.42 respectively.

A one-sample t-test was conducted to determine whether the mean BRIEF-A Working Memory score for perimenopausal women differed significantly from the clinical threshold of 65. The BRIEF-A Working Memory mean score (M = 66.92, SD = 14.37) was not significantly different from the threshold of 65, t (89) = 1.27, p = .208, 95% CI [-1.09, 4.93]. The effect size was small, d = 0.13, 95% CI [−0.07, 0.34].

A one-sample t-test was repeated for postmenopausal women to also determine whether the mean scores differed significantly from threshold of 65. The BRIEF-A Working Memory mean score (M = 65.94, SD = 12.42) was not significantly different from the threshold, t(69) = 0.64, p = .527, 95% CI [−2.02, 3.90]. The effect size was small, Cohen's d = 0.08, 95% CI [−0.16, 0.31].

Table 4-1 Cognitive performance of menopause groups

Cognitive performance M(SD)	**Premenopause (n = 75)**	**Perimenopause (n = 90)**	**Postmenopause (n = 70)**
BRIEF-A Inhibit	49.43 (9.48)	52.56 (10.53)	51.76 (9.42)
BRIEF-A Working memory	59.44 (12.98)	66.92 (14.37)	65.94 (12.42)
Selective attention and inhibitory control (ratio)	0.87 (0.05)	0.87 (0.05)	0.85 (0.10)

Verbal working memory (Total correct)	5.60 (2.46)	5.21 (2.40)	5.08 (2.30)

Note: Outcome measure for selective attention and inhibitory control - ratio of congruent to incongruent median reaction times in correct trials (ratio) and for the verbal working memory task - total number of correct trials (Total correct), BRIEF-A subscale - Inhibit T score, BRIEF-A subscale – Working memory T score

Assumption testing

Data was assessed for normality as outlined in section 3.6. Before conducting Pearson's partial correlations, scatter plots were used to assess linearity relationship between the continuous variables of interest. This included self-report scores from the BRIEF-A inhibit and BRIEF-A working memory subscale, as well as the laboratory-based tasks scores from the Backward Digit Span task (working memory) and the Flanker task (selective attention and inhibitory control). Histograms and Q-Q plots were used to visualise to assess the normality of the data, alongside box plots to identify outliers. One outlier was detected in the attention and inhibitory control variable. These were retained in the dataset to evaluate whether their inclusion had a substantial impact on the analysis results. This approach allowed for a comparison of outcomes with and without the outliers, helping to determine whether their presence significantly influenced the overall findings.

Assessing associations between self-report and laboratory-based measures of inhibitory control and working memory

Pearson's partial correlations were conducted to examine the relationship between BRIEF-A Inhibit scores and performance on the Flanker task, controlling for age. The measures used in the Flanker task was the ratio of congruent to incongruent median reaction times. Data from 235 participants who completed the in-person cognitive assessments were included in the analysis. All participants completed both the self-report measure and took part in the laboratory-based tasks. The mean age of the sample was M = 48.47 (SD = 7.63). Mean BRIEF-A Inhibit scores were M = 51.32 (SD = 9.93), and mean scores for selective attention and inhibitory control were M = 0.87 (SD = 0.07). The correlation analysis revealed a near-zero, negative, and non-

significant association between BRIEF-A Inhibit scores and laboratory-based selective attention and inhibitory control performance, r (232) = −0.003, p = 0.967. Results (outlier removed) still showed a non-significant association between the self-report measure and laboratory-based task, r (231) = 0.029, p = 0.661.

A second Pearson's partial correlation was conducted to assess the relationship between BRIEF-A Working Memory scores and performance on a laboratory-based verbal working memory task, again controlling for age. Mean BRIEF-A Working Memory scores were M = 64.24 (SD = 13.72) and mean verbal working memory total correct scores were M = 5.29 (SD = 2.38). The results indicated a weak, negative, and non-significant association between self-reported working memory difficulties and performance on the in-person working memory task, r (232) = −0.112, p = 0.088.

An important factor to consider was that the laboratory based cognitive tasks used in Chapter 4 are not age normalised, whereas the BRIEF-A provides age normalised T scores, which remove age related variance during scoring. As such, there is a potential mismatch in how age effects are represented across the two types of measures. To ensure that this difference in scaling did not influence the findings above, specifically the lack of significant correlations between the laboratory-based inhibition and working memory tasks and their corresponding BRIEF A scales, the analyses were repeated using the raw BRIEF A scores instead of the age normalised T scores.

The correlation analysis again revealed a near-zero, negative, and non-significant association between BRIEF-A Inhibit raw scores and laboratory-based selective attention and inhibitory control performance, r (232) = −0.001, p = 0.986.

For BRIEF-A Working Memory raw scores and performance on a laboratory-based verbal working memory task, results again indicated a weak, negative, and non-significant association between self-reported

working memory difficulties and performance on the in-person working memory task, r (232) = −0.114, p = 0.083.

The results remained unchanged such that BRIEF A inhibition and working memory raw scores showed no significant associations with laboratory-based inhibition or working memory performance, similar to the pattern obtained when using T scores. This consistency indicates that the absence of correlations between self-reported and performance based executive function is not a result of age normalisation but rather shows an actual dissociation between the two measurement approaches.

4.7 Discussion

This study examined associations between self-reported measures of cognition and laboratory-based measures of cognition in mid-life women. This is an interesting area to explore as there is a paucity of research that utilises self-report measures of cognition and laboratory-based assessments to assess cognition in menopause especially as subjective reports of cognitive complaints by women in research is rife but limited when using laboratory-based measures to assess cognition.

The BRIEF-A subscales correspond to specific aspects of executive function. Accordingly, this study examined whether any associations exist in the domains of working memory and inhibitory control. Results from Pearson's correlations adjusting for age showed non-significant relationships between the self-report and laboratory-based cognitive measures of working memory and selective attention and inhibitory control. These findings are consistent with previous research. A study by Mcauley, T., et al. (2010) of 97 clinical-referred and healthy youth aged 8 -15 years found no significant associations between BRIEF scores and laboratory-based measures of inhibition and working memory. Similarly in a much older sample, Meltzer et al., (2017) also found no significant correlations between BRIEF-A scores and working memory and inhibitory control. Additionally, Rabin et al., (2006) did not find any significant associations between BRIEF-A scores and working

memory. This consistent lack of associations between self-report and laboratory-based tasks suggests that these two measures may be assessing different constructs as suggested by Duckworth and Kem (2011) and supported by Toplak et al. (2013). Snyder et al. (2021) also noted that the self-report and laboratory-based measures though largely distinct, provide an opportunity to assess cognitive performance using two complementary approaches. Therefore, it appears that laboratory-based tasks are not related to similarly named cognitive domains on the BRIEF-A and should not be assumed to measure the same construct.

Snyder at al. (2021) and Mcauley et al. (2010) have noted that the two different approaches are measured under different circumstances. Laboratory-based tasks which are less ecologically valid are performed under conditions where the individual only has to focus on task with no distractions and is given clear instructions and support in order to perform the task. In contrast, though self-report measures are also prone to bias, they accurately reflect daily-life behaviours where distractions, emotional well-being and motivational levels may vary. Self-report measures are a reflection on situations that one faces several times instead of a laboratory-based tasks that assesses one at a single time point. Nonetheless, these two distinct approaches are worth exploring when assessing cognitive function in the context of menopause. They both uniquely provide crucial information about women's 'subjective perceptions of various cognitive domains that they believe are affected by the transition and also provides an opportunity to assess these cognitive domains objectively using laboratory-based measures. Together, they enrich our understanding of women's cognitive performance during the transition to menopause. Furthermore, the lack of correlation doesn't invalidate either measure taking into context the different aspects being measured. This apparent disconnect highlights the fact that subjective experiences of cognitive changes by menopausal women may not always be captured by laboratory-based measures.

4.8 Strengths and limitations

A key strength of this study is the use of two distinct approaches to assess cognitive performance in menopause research especially as this is currently lacking in the field. The number of women recruited to take part in this study who completed both the subjective and objective measures of cognition is fairly large in comparison to studies that have utilised both measures to examine correlations between the two approaches though these studies mostly used a youthful population. Additionally, two different cognitive domains were assessed, that is working memory and inhibitory control with tasks designed to enable comparison between these domains.

A key limitation of the study is its cross-sectional design, which prevents repeated assessments of cognitive domains over time. While the BRIEF-A captures self-reported executive functioning over the past month, the laboratory-based tasks reflect cognitive performance at a single time point, limiting the ability to examine fluctuations or changes in cognition across the menopausal transition. It would also have been useful to explore associations between various cognitive domains and its corresponding measure on the BRIEF-A and possibly design several tasks that measure a specific domain so an accurate measure of functioning in that domain is established and compared with self-report scores.

4.9 Conclusion

This study showed no association between self-report and laboratory-based measures in the cognitive domains of working memory and selective attention and inhibitory control despite the similar names used in both of these measures. Future research should incorporate the use of both measures to gain a broader understanding of the cognitive challenges that some women experience during the transition to menopause as they both provide an opportunity to understand and

observe women’s performance under different conditions. More research is needed to explore the reasons why these two measures do not correlate and expand the focus on other cognitive domains and in different contexts. It is possible that despite similar domain names on self-report and laboratory-based tasks, there might be other factors leading to null or low correlations between these two measures which warrants further investigation.

5 Chapter 5 General discussion and conclusions

This chapter provides a summary of key findings from the studies conducted as part of this research project. Women participated in this research project in two ways: one group completed an online questionnaire, while another group completed the questionnaire and also took part in laboratory-based tasks. The results obtained highlight the unique contribution of each study to the broader understanding of cognitive changes in the context of midlife transitioning to menopause. In addition to presenting the findings, this section explores the potential implications and interventions as well as strengths, limitations and future directions that have arisen from this research project.

5.1 Summary of research findings

This thesis aimed to examine the impact of menopause stage on cognitive performance in a sample of premenopause, perimenopause and postmenopausal women. Findings have shown that menopause stage, in particular the perimenopausal stage is vulnerable to cognitive changes as evidenced by the self-report measure, BRIEF-A that was used to assess executive function changes. In contrast, the use of laboratory-based tasks to assess objective cognitive performance revealed no impact of menopause stage on cognitive performance. The use of self-report and laboratory-based tasks to assess associations between similarly named cognitive domains revealed no significant associations. Additional investigations highlighted the influence of other contributing factors, including menopausal symptoms, sleep quality, and socio-behavioural factors such as alcohol consumption, diet quality, and caregiving responsibilities. This research adds to the existing literature by offering a better understanding of the multifaceted influences on cognitive function during the menopausal transition. An overview of the key findings from the studies conducted are presented below:

Menopause stage and cognitive performance

The overarching aim of this thesis was to examine the impact of menopausal stage on cognitive performance by employing both subjective and objective assessment methods. Firstly, executive functions were examined using BRIEF-A which is a self-report measure designed to shed light on an individual's everyday cognitive challenges. In addition, laboratory-based tasks were used to assess cognitive domains of processing speed, verbal working memory and selective attention and inhibitory control. Findings from the use of the BRIEF-A to assess executive functions showed that menopause stage negatively impacted executive functions with perimenopausal women in comparison to premenopausal women reporting worse or greater difficulties with executive functions regardless of cognitive ageing. These results suggest that during the perimenopause stage when women are experiencing wide fluctuations in their hormone levels, some women may experience executive function challenges as a result. The executive function skills that perimenopausal women highlighted included challenges with impulsivity; inappropriate emotional responses; difficulties with switching attention and changing focus from one topic to another; more pronounced difficulties with starting tasks and coming up with ideas on their own; remembering things; monitoring progress during tasks; retrieving instructions accurately; planning effectively for tasks; and organising their everyday environment such that they lose track of personal belongings such as keys, money, purses. These executive function skills described are served by the prefrontal cortex, a region of the brain that contains oestrogen receptors and therefore may be sensitive to oestrogen fluctuations and decline associated with menopause. This observed significant main effect of menopause stage on executive functioning is further supported by findings in a study by Page et al. 2023 who also reported significant executive function changes during the menopause transition period. However, unlike this study, Page and colleagues did

not use a comprehensive measure to assess executive functions, thus limiting the scope of measurement.

The objective assessment of cognitive performance assessed through laboratory-based tasks, revealed no significant main effect of menopause stage on cognitive performance in processing speed, verbal working memory and selective attention and inhibitory control. There was, however, a significant effect of age on processing speed times alone. This aligns with extensive research showing that cognitive processing speed declines with increasing age (Ebaid et al., 2017; Eckert, 2011).

Due to time constraints, the study did not achieve the intended sample size. However, it remained sufficiently powered to detect small to moderate effect sizes. Importantly, the findings were consistent with results observed in previous research, lending support to their validity despite the limited sample. Studies by Unkenstein et al. (2016) and Martino et al. (2022) did not find significant associations between menopause stage and working memory and selective attention and inhibitory control executive functions. Likewise, Schaafsma et al. (2010) and Luetters et al. (2007) did not find significant associations between menopause stage and processing speed. In contrast, a study by Weber et al. (2012) observed poorer verbal memory performance in perimenopausal women, although their sample was limited to that stage alone. Additionally, Greendale et al. (2010) in a longitudinal study found menopause stage had a negative effect on processing speed. Further investigation is warranted once the target sample size is achieved, to more thoroughly examine the potential influence of menopausal stage within a larger sample.

Overall, research examining executive function performance in the context of menopause remains limited, particularly studies that employ both subjective and objective measures. This study highlighted a discrepancy between self-reported executive difficulties and performance on laboratory-based cognitive tasks, revealing a gap in

how executive function is assessed across both approaches. Perimenopausal women reported greater difficulties with executive function performance on the subjective measure using BRIEF-A which is a reflection of their experience of daily activities over a month-long period. This validates the concerns of some women who find the transition challenging and also report a constellation of cognitive symptoms commonly referred to as ‘brain fog’. These perceived cognitive challenges they face may be contextual and emotionally influenced which are factors that are not exactly present in controlled environments where objective measures testing takes place. The laboratory-based tasks of objective performance which are assessed at a single time point found no significant group differences which is consistent with previous research as mentioned earlier. This divergence shows the importance of utilising both measures to capture the scope of cognitive challenges that is experienced by midlife women. It possibly provides an opportunity to understand how EF processes are applied in daily life in different settings where most women during the transition may have to carry on with their social, home and professional lives regardless of the cognitive challenges, Reassuringly, despite reported difficulties, scores on the BRIEF-A indices of were within normal limits for all participants including perimenopausal participants.

Menopause symptoms and cognitive performance

An aim of the study was to also understand the impact of overall menopause symptoms on cognitive performance. In both the online and in-person study, perimenopausal and postmenopausal women reported significantly worse symptoms in comparison to premenopausal women. Women who reported more severe menopause symptoms reported significantly greater difficulties with executive function as measured by BRIEF-A. Menopause symptoms accounted for a substantial proportion of the variance in executive function scores, ranging from 32% to 39%. Interestingly, women who took part in the laboratory-based tasks who reported more severe

menopause symptoms also reported poorer executive functioning as measured by BRIEF-A. Although menopause stage did not significantly influence cognitive performance in the in-person study, it is interesting that perimenopausal and postmenopausal women reported significantly higher menopause symptoms which was associated with cognitive performance. This suggests that the severity of menopause symptoms may have a greater impact on cognitive performance than menopausal stage alone. Some women experiencing multiple co-occurring menopause symptoms may report greater symptom severity, while others with only one or no symptoms will score much lower on the severity scale. This individual variability may help explain the significant impact of menopausal symptoms on specific cognitive domains, as well as the absence of a clear effect of menopause stage on overall cognitive performance in the in-person study as symptomology might differ amongst women transitioning to menopause. In the in-person study, menopause symptoms were associated with processing speed, but not with other cognitive domains, independent of age-related effects. Future research could benefit from profiling symptom patterns among menopausal women or examining cognitive performance after symptoms have subsided or diminished, to better understand these associations.

As mentioned earlier, processing speed was also significantly associated with overall menopause symptoms, with better task performance linked to fewer reported symptoms. The findings suggest that menopause-related symptoms impact cognitive performance, highlighting the need for further research to explore the mechanisms underpinning this relationship and whether other domains are also impacted. While menopause stage did not predict objective cognitive performance, symptom burden did, underscoring the variability in symptom presentation among women transitioning through menopause and the importance of assessing overall or perhaps individual symptom profiles. Furthermore, as these findings are from a cross-sectional study, it does not establish a causal relationship. Rather, it

substantiates the association between menopause symptoms and executive function performance in this sample of premenopausal, perimenopausal and postmenopausal women. These findings also contribute to existing literature by using validated measures of both menopause symptoms and executive function performance to shed light on how overall menopause symptom severity influences cognitive performance. By employing a comprehensive self-report measure, this study has provided a new perspective, and further studies are needed to explore other underexplored cognitive domains especially with regards to laboratory-based tasks.

Sleep quality and cognitive performance

The findings of the online study showed the significant role of sleep quality in executive function performance. Sleep quality was significantly associated with executive function performance with moderate effect sizes. Women reporting poorer sleep quality reported greater executive function challenges. Importantly, the benefits of sleep were consistent across premenopause, perimenopause and postmenopause stages, suggesting sleep exerts a beneficial effect on executive function performance. Although menopause stage showed a significant effect on executive functions, the interaction between sleep and menopause stage was not significant, this demonstrates that the benefits of good sleep are not moderated by menopause stage. It is important to consider how sleep, which is a potential modifiable lifestyle factor, can be managed during the transition to menopause especially as many women report sleeping difficulties during the period. In the in-person study, processing speed was the only domain affected by sleep quality with poor sleep associated with slower processing speed times. However, the effect of sleep quality on processing speed was lost after menopause symptoms were included in the analysis. This suggests that the cumulative effect of menopause symptoms plays a broader role in affecting cognitive performance.

Given that the transition to menopause is rife with fluctuating hormones with significant changes in oestrogen levels and progesterone which

play a role in regulating sleep, it is plausible that these changes may lead to sleep disruptions. This in turn, may impact certain cognitive domains such as processing speed. More research is needed to clarify whether other cognitive domains are similarly affected especially as this in-person study did not find an effect of sleep quality on processing speed once overall menopause symptoms were considered.

Lastly, there should be better evaluation of sleep complaints by midlife women as there could be other potential causes of the poor sleep reported. There could be other behavioural and psychosocial factors contributing to sleep disruption and worth exploring in future studies.

Menopause-associated factors and cognitive performance

Many perimenopausal women who took part in the online study indicated being on HRT. Some women use HRT to treat menopause-associated symptoms, and this has helped some women. The role of HRT on cognition is an underexplored area. Hamoda et al. (2020) in their recommendations for HRT, noted that some observational studies have reported an improvement in cognitive function among some women using HRT. This study aimed to explore the role of HRT use in perimenopausal women only, taking into consideration menopause symptom severity. The results showed a significant interaction between HRT status and menopause symptom severity in predicting executive functions related to behaviour regulation only such as Inhibit, shift, Emotional control and self-monitoring. There was no observed effect of HRT status on cognitive performance in this study, Specifically, findings indicated that perimenopause women on HRT reporting poorer executive functioning as symptom severity increased in comparison to perimenopausal women not on HRT. It is important to note that no information was gathered regarding the duration of use, nor the type or dosage of treatment all of which are known to influence therapeutic outcomes. Nevertheless, in this sample of women, HRT did not offer any cognitive benefits. Future research should explore whether certain symptom profiles and duration of HRT use or type or dosage also influence this relationship. These variables were not considered in the

online study, yet they may shape the outcome and also clarify the mechanisms that underpin this observation in this cross-sectional study.

For many women, the timing of menopause is also associated with psychosocial factors such as caregiving responsibilities. Other modifiable health and lifestyle factors such as eating habits (Jia et al., 2023), alcohol consumption (Cassidy et al.,2004) and physical activity (Yaffe et al., 2001) have been associated with cognitive function. The online study also examined how socio-behavioural factors such as age, educational attainment, caregiving responsibilities, weekly hours worked, alcohol consumption and diet influenced overall executive functions. Findings indicated that women who consumed more alcohol, had caregiving responsibilities and a poorer diet reported worse executive functions. These results have demonstrated a need to consider other underlying factors that potentially influences executive functions. While previous research has independently associated these factors with cognition, it is equally important to examine their role in the context of menopause. Some of these socio-behavioural factors are modifiable factors and may offer potential sources of intervention for women reporting executive function challenges.

Association between laboratory-based tasks and self-report measures of cognitive performance

The last study of this research aimed to explore any associations between self-report measures of cognitive performance and laboratory-based tasks. Associations were explored between similarly named cognitive domains on the BRIEF-A, that is Inhibit and Working memory to laboratory-based tasks of inhibitory control and working memory. No associations were found between these two measures. Previous research has suggested that the two measures assess two largely distinct constructs. Nevertheless, these two measures provide an opportunity to assess cognitive performance from two different perspectives. In literature, both measures in some studies have found cognitive impairment during the menopause transition in selective

domains while others have not. To date, no study to the best of my knowledge has explored cognitive performance in the context of the menopause using the two measures to assess similarly named domains. Unfortunately, the laboratory-based study was unable to recruit the required number of participants as planned. As a result, the study lacked sufficient power to detect small effects, and firm conclusions could not be drawn from the findings. However, in future studies, it would be insightful to include both self-report and laboratory-based measures, with self-report offering relevant everyday examples of the cognitive domains that can then be assessed objectively. This dual approach would allow us to gain a better understanding into how women perceive their own cognitive performance compared to how it manifests objectively. Moreover, examining these measures in different settings could provide us with more information as to how executive function skills are applied in controlled environments as opposed to everyday daily life when women have to deal with competing attentional demands at work, home and social challenges. It is important to also consider that laboratory-based tasks may lack the sensitivity to capture the subtle cognitive changes experienced by women transitioning to menopause. This is particularly relevant given that self-report measures in this study indicated cognitive functioning within normal limits, suggesting that subjective experiences of cognitive difficulty may not always be reflected in objective assessments in a cross-sectional laboratory setting.

5.2 Implications

For all women, menopause is a natural part of the reproductive ageing process. For most women, the transition to menopause is uneventful. However, for a small number of women, the transition can be fraught with bothersome symptoms including cognitive challenges commonly referred to as ‘brain fog’. With more women in the workplace and given that the typical age at which menopause occurs for most is between the ages of 45 and 55 years (Walker-Bone & Davis, 2025), it is

important to consider how menopause and its associated symptoms may affect work performance and the overall quality of life.

The findings of this thesis contribute to existing literature by shedding light on the perceived cognitive challenges of women as they transition to menopause. The results of this research that used both subjective and objective measures to examine executive function across menopausal stages indicate that executive function changes, when they do occur, are subtle, within normal limits, and influenced by a complex interplay of biological events which include menopause symptoms and socio-behavioural factors rather than just menopausal stage.

Menopause-associated symptoms are also associated with worse performance on cognitive measures (Crockford et al., 2025). As such, both menopause stage and severity of menopause symptoms appear to be associated with cognitive performance. Findings presented in this thesis have shown that perimenopausal women in comparison to premenopausal women self-reported greater challenges with executive function though results obtained were all within normal limits. This validates women's concerns and at the same time offers some assurance to menopausal women. As this thesis broadened the range of cognitive domains examined, it highlights opportunities for targeted interventions to support women affected in specific areas. For example, for women who start to observe changes in their cognition, advice and education on strategies to cope with this should be offered. Women should be encouraged to use reminders, calendars and write things down if working memory is an issue. Other coping strategies include encouraging reflection and feedback to reduce impulsivity, goal setting, regular progress checks and using to-do lists and timelines to plan and organise a task.

As menopause symptoms impacted cognitive performance as shown in this thesis, it is essential that these issues are addressed when women seek assistance from healthcare providers. The hormonal changes

women experience give rise to symptoms that vary widely in severity, and as outlined in Section 1.6, this thesis demonstrated that symptom burden is an important menopause-related factor influencing cognition. Additionally, existing literature by Calle et al. (2024), Crockford et al. (2025), and Maki et al. (2020), makes it more plausible that menopausal symptoms are linked to cognitive difficulties rather than the other way around. These studies showed that changes in oestrogen and the appearance of symptoms such as hot flushes, sleep problems, and mood changes are associated with differences in cognitive performance. This is supported by Brinton et al. (2015), who explain that many menopause-related symptoms arise because oestrogen helps regulate systems involved in thermoregulation, sleep, circadian rhythms and sensory processing. Thus, changes in oestrogen levels can disrupt these systems, and this disruption may show up as the physiological symptoms of menopause. Symptom severity often peaks during periods of hormonal fluctuation as evidenced in this study where coincidentally perimenopausal women reported worse symptoms in comparison to premenopausal women. These heightened symptoms may place additional strain on cognitive functioning, as reflected in the current study. Taken together, these findings suggest that the indirect impact of symptoms during the menopausal transition may contribute to the cognitive challenges observed, rather than cognitive changes driving symptom severity.

Consistent with this, findings presented in Sections 2.7 and 3.6 showed that more severe menopausal symptoms were associated with poorer performance on the BRIEF-A BRI and MI indices, as well as slower processing speed. As such, there is no single universal pattern of cognitive change in mid-life women as cognitive outcomes appear to differ depending on the severity of symptoms experienced. Symptom burden may therefore represent a key pathway through which oestrogen-related hormonal changes influence cognition. For example, this thesis showed that poorer sleep quality, a common menopausal symptom was linked to reduced cognitive performance, a finding also

reported by Regestein et al. (2004). As discussed in Section 1.6, other symptoms such as hot flushes and depressive symptoms have likewise been shown to negatively affect cognitive processes. Together, these findings highlight the importance of considering symptom severity and the impact of individual symptoms when examining cognitive functioning during the menopausal transition.

Perhaps addressing these symptoms could lead to overall cognitive benefit as part of the management of bothersome symptoms. This study did not show any benefit of HRT on cognitive performance and not enough data was collected about HRT usage. Currently, HRT is recommended as a treatment option for many women. It is essential healthcare professional consider the unique experience of each woman when considering HRT, as several factors such as dosage, timing of initiation of treatment, the specific type of therapy could influence effectiveness (Andy et al., 2024). Andy and colleagues' findings also suggested time-dependent effects of hormonal treatment on certain cognitive domains. Therefore, a personalised approach is recommended to ensure that treatment options align with women seeking management and treatment of their symptoms.

Consideration should also be given to socio-behavioural factors and its influence on cognitive performance. Healthy lifestyle choices should consistently be encouraged, particularly for women transitioning through menopause. Findings from the self-report study in chapter 2 revealed negative associations between certain socio-behavioural factors such as alcohol consumption, poor sleep, inadequate diet, and caregiving responsibilities and executive functions. While some of these factors are modifiable, others, like caregiving responsibilities may be more difficult to manage. It would be useful to explore these relationships in the laboratory-based study in future research once data collection is complete. Nonetheless, based on the self-report findings, perhaps women being given access to appropriate support may enhance their ability to manage cognitive demands. The addition of

other lifestyle modifications may also potentially lead to improved cognitive functioning.

Another important consideration in interpreting the findings from this research is the well-established distinction between subjective and objective measures of executive function. In the online survey, women reported executive-function difficulties on the BRIEF-A, but this pattern was not replicated in the laboratory sample, where no group differences emerged on either the BRIEF-A or the processing-speed, inhibition, and working memory tasks. The absence of correlations between self-report and laboratory measures further suggests that these approaches capture different aspects of cognition and everyday functioning or behaviour. This pattern is consistent with a substantial body of literature, including work by Meltzer et al., (2017) and Mcauley, T., et al. (2010), as discussed in section 4.7, showing that self-report and objective based executive function measures typically demonstrate low or negligible correlations. Together, these findings suggest that they capture different aspects of cognition and behaviour rather than the same underlying construct. In the context of menopause, this dissociation indicates that women's subjective experiences of cognitive change may not be detectable using standard laboratory tasks which lack ecological validity. In the context of menopause, this dissociation suggests that women's subjective experiences of cognitive difficulty may arise in everyday environments that place greater demands on cognitive processes than those captured by standard laboratory tasks, which typically lack ecological validity. Daily life involves competing demands, multitasking, distractions, emotional and physical symptoms, and the use of compensatory strategies that may become less effective during the menopausal transition. Although the lab-based measures did not validate these perceived difficulties in the present study, future research should examine a broader range of cognitive domains using both subjective and objective approaches to determine whether other aspects of cognition may show associations across measurement methods and may therefore be uniquely affected during the

menopausal transition. This thesis contributes to this existing literature by assessing executive functioning with both self-report and laboratory-based measures by examining core cognitive processes rather than focusing solely on memory which dominate much of the existing menopause literature.

Finally, this thesis cannot definitively identify the mechanisms driving any observed menopause group differences as the design does not allow for causal inference about the role of specific hormones which were also not assayed as part of this research. Given that the cross-sectional nature of the data limits the ability to distinguish menopause-related changes from broader midlife trajectories, these findings cannot directly link oestrogen decline whose modulation of prefrontal networks are involved in cognitive function. Future longitudinal, neuroimaging and biological studies will be essential for clarifying how these mechanisms unfold over time and for determining whether similar cognitive patterns are observed. Lastly, consideration should also be given to the assessment context, as the environment in which self-report measures are completed such as in online versus in-person setting and the ecological validity of the tasks themselves can potentially influence outcomes.

5.3 Strengths and Limitations

The studies presented in this research project has many strengths. One of the key strengths of this study is the inclusion of premenopause, perimenopause and postmenopausal women in the online study and laboratory-based study. This allowed for the comparison of cognition across the three key menopause stages,

Another key strength of the study lies in the relatively large sample size obtained for both the in-person and online study. Many of the women who participated were keen to contribute to menopause research and raise awareness about women's health which enhanced recruitment efforts. The large sample size strengthened the validity and reliability of

the findings. Although the in-person study did not meet the target sample size, the number of women who participated exceeded that of several comparable studies in the existing menopause literature, thereby adding further value to the research.

Many studies examining cognition and menopause have focused primarily on memory. However, the cognitive symptoms that women describe goes beyond just memory alone. By using the BRIEF-A, this research broadened the scope of cognitive domains to include a range of executive functions. This allowed for the identification of executive function challenges in behavioural regulation such as impulsivity and inappropriate emotional responses as well as metacognitive skills, including working memory, planning and organisational skills by perimenopausal women. Certain domains assessed by BRIEF-A such as Initiation and Organisation of materials are difficult to capture using laboratory-based measures. The use of this self-report assessment tool enriched the study by highlighting cognitive areas that warrant further exploration which may otherwise be overlooked in laboratory-based assessments.

Furthermore, the employment of both subjective and objective measures to assess cognition provided complementary insights and demonstrated that each approach showed two aspects of cognitive functioning. This dual approach highlights the value of incorporating both types of assessments in future research to advance the literature in the context of menopause. It highlighted the potential benefit of expanding the scope of self-report and objective areas of measurement.

In this thesis, cognitive performance and menopause symptoms were examined using valid and reliable measurements which will allow for comparisons with future studies. In addition, this research also explored the role of various socio-behavioural factors such as age, caring responsibilities, alcohol consumption and diet quality among others on cognitive performance. This offered a broader understanding

of the interplay between socio-behavioural factors and cognitive health during menopause.

The studies conducted as part of this study have limitations which have also been discussed in relevant chapters. An overview of the key limitations in this thesis is described subsequently.

Firstly, the design of this study was cross-sectional in nature and so causal relationships cannot be established. Longitudinal studies that track women from premenopause through perimenopause and into postmenopause would be particularly valuable as it will allow researchers to observe how cognition and menopause-related symptoms evolve over time. Such a design provides an insight into whether, and how, these changes occur across the stages of menopause.

The findings of the laboratory-based study were also interpreted with caution as the target sample size was not attained before conclusion of this research project. Sensitivity analysis indicated sufficient power to detect small to moderate effects; however, the reduced sample size may have limited the ability to detect smaller effects, and some associations may have gone undetected. Also, the smaller than expected sample size in the in-person study limits the generalisability of the findings from this research. Though great care was taken to recruit participants from various backgrounds and communities, both the online and in-person study samples were predominantly composed of Caucasian and highly educated participants, which may limit the generalisability of the findings to more diverse populations. Specifically, in the online study, 75.89% of participants identified as Caucasian and 68.64% held a degree-level qualification or higher. Similarly, in the in-person study, 84.68% of participants were Caucasian, with 76.60% possessing degree-level or above educational attainment. The results from this study may therefore not fully capture the experiences of women from different ethnic or educational backgrounds and so for future research, it is important to include these women especially as

findings from the SWAN study for example have shown different symptomology in women from Hispanic and Black background.

Self-reported data was collected from participants as part of this research project. This mode of collection lends itself to bias reporting from participants who can either under-report or exaggerate their responses. However, by recruiting from different communities, implementing shorter recall periods to questionnaire questions, incorporating attention and validity checks within the questionnaire, the study addressed these potential risks during the early stages of the study design. While these strategies would have helped to eliminate and minimise bias, thereby enhancing data reliability, they cannot be eliminated completely. Therefore, although the self-reported data provided a wide range of responses, where possible, objective measures should be considered where feasible as for example sleep quality can be measures objectively using actigraphy. Given the limitations discussed, the next section discusses recommendations to guide future research.

5.4 Future directions

To build on the findings in this research, further research is needed to examine association between menopause and cognitive performance while considering various factors such as menopause-related symptoms and demographic and lifestyle factors. It is also important to consider other cognitive domains and not just memory which has been the primary domain assessed in many studies. In both subjective and objective measures of cognition, future research should examine associations between self-report measures and other laboratory-based tasks not assessed in this study such as mental flexibility which is a one of the core executive function components. In addition, other cognitive domains that goes beyond the three cognitive domains of processing speed, verbal working memory and selective attention and inhibitory control assessed should be explored as this could reveal new

findings about potential problematic areas. For instance, spatial working memory is one area that in underexplored in menopause research.

Also, though the self-reported data offered a broad spectrum of responses, providing valuable insight into participants' perspectives. Nonetheless, where feasible, the inclusion of more objective measures should be considered to complement and strengthen the findings. For instance, the use of objective measures of sleep quality and some menopausal symptoms such as hot flushes would have allowed me to validate self-reported experiences and reduce risks such as recall bias and misreporting. Furthermore, in the context of menopause symptom management, additional research is needed to explore the impact of HRT for example on cognition considering detailed factors such as treatment type, dosage and duration of use,

Lastly, it will be useful for future research to employ a longitudinal study approach and assess cognitive changes over a longer period as this will be a more effective way to track cognitive changes.

5.5 Conclusions

Menopause is a normal part of the ageing process that all women will eventually experience. While this transition can bring a wide range of physiological and psychological changes largely influenced by changing hormonal milieu, it can also represent a period of acceptance, adaptation and empowerment particularly as public discourse around menopause more open and informed.

Investigating cognitive changes during the menopausal transition is inherently complex and requires a multifaceted approach, considering menopause-associated symptoms, modifiable lifestyle factors, and the potential role of exogenous therapies. Further research is warranted to deepen our understanding of this life stage. Reassuringly, the present study was able to validate the concerns of perimenopausal women who

reported cognitive changes, while also reassuringly finding that, on the self-report assessment, executive functioning indices of behaviour regulation and metacognitive skills remained within normal limits.

5.6 References

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6 Appendices

6.1 Appendix 1: Events

BRE Women's staff network – Invited to give oral presentation to staff network about PhD project.

Welsh government lunchtime staff meeting – As part of placement, I was invited to present my research project to the wider staff community.

Festival of Science and Curiosity – Organised science workshop for kids and included discussions about project to parents

Athena Swan women's stall event – Women attending event, visited the stall to discuss ongoing project

Menopause Café, Histon – Sharing menopause journey or experience workshop

UoN women's well-being webinar – Presented research project

Public Engagement The findings from the following chapters were discussed at these events:

Chapter 3: Meetings with MP Juliet Campbell and MP Lilian Greenwood

Notts Psych Pod Series 2 (**https://www.nottingham.ac.uk/psychology/outreach/notts-psych-pod.aspx**)

Chapter 2: UoN Athena Swan Webinar 2023, Welsh government, BRE organisation

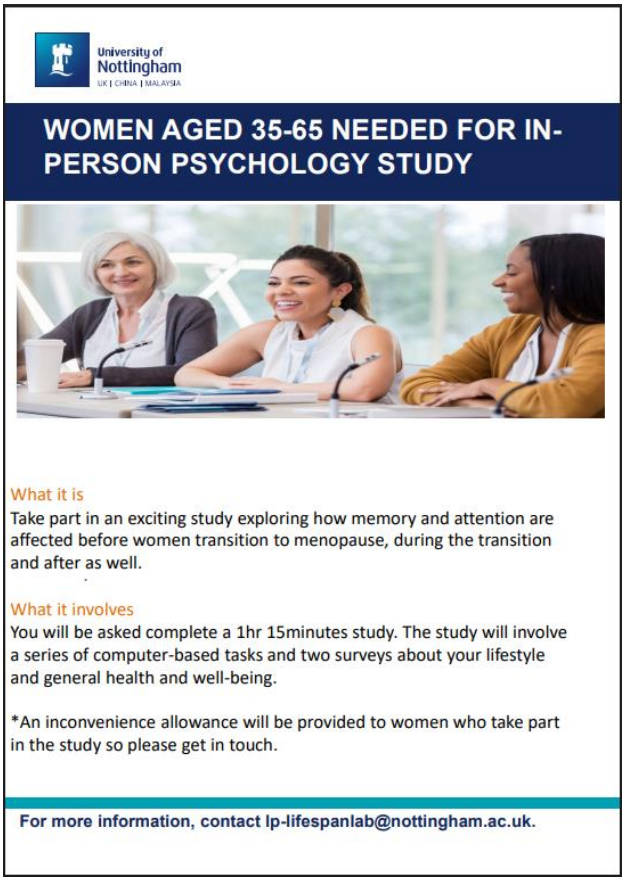
6.2 Appendix 2: Recruitment

General strategies for recruiting women were via the following:

- Fliers
- Social media
- Adverts
- Word of mouth
- Professional networks
- Community posters
- Prolific

A flier was designed for the purpose of this research to be used for advertisements. This was approved by the University of Nottingham School of Psychology Ethics Committee. The flier and advertisement describe a psychological study on attention and memory in women aged 40 years and above and does not specifically target women with attention and memory complaints. Fliers have been placed in hair salons, supermarkets, restaurants as well as churches. Some fliers were also distributed to members of the public who attended the Science in the Park Festival held in Nottingham, Athena Swan women's event and the Doctoral Training Partnership conferences and summer science festivals. Channels used to advertise the research include advertisements in the 'Menopause Matters' newsletter, mature students' network, social media posts on 'Menosupport' Facebook page, posters in hospitals, GP surgeries, community noticeboards, libraries, parent groups, cafes, BlackWomeninScience network, Black, African and Asian therapy network newsletter, National Education Opportunities Network (NEON) conference, Building Research Establishment (BRE) women's seminar and recruitment via school WhatsApp groups. Anonymous links, single-use links and QR codes were generated from Qualtrics and assisted in the distribution of the questionnaire. A link to the questionnaire has also been shared with acquaintances to distribute to their personal and professional networks and create a snowball effect. A Google search is also being used to identify internet communities/groups for midlife women who meet the age criteria. These groups are not necessarily menopause support groups but community or neighbourhood groups. A research blog page, www.menocog.wordpress.com has also been created to

advertise the study to recruit participants. By recruiting women from different areas, the study is not restricted to just menopause support groups but all women in the community who fit the criteria and are therefore representative of the general population. An example of a poster used for recruitment is shown below.



6.3 Appendix 3: Questionnaire

Prolific Attention and Memory - Prolific Diverse link

Start of Block: Information sheet

University of Nottingham School of Psychology Information Sheet

Title of project: Attention and Memory in Menopause.

Researcher: Karen Barnor

Supervisors: Professor Harriet Allen, Professor Lucy Cragg

Contact details: Karen.Barnor@nottingham.ac.uk, Lucy.Cragg@nottingham.ac.uk, H.A.Allen@nottingham.ac.uk

Menopause is a fresh beginning that can be lived richly, fully and in good overall health by a majority of women. This is a women-centred research study on the effects of menopause on attention, memory, self-control and mental flexibility. The study is open to women 40 years and above. It aims to understand the experiences of women before they transition to menopause, during and after the menopause transition.

Before you decide if you wish to take part, it is important for you to understand why the research is being done and what it involves. Please take time to read the following information carefully.

Menopause occurs at a time when there could be other stressors in life. This study aims to understand how different experiences affect performance.

If you participate, you will be asked questions about yourself, lifestyle, general health and well-being. There will also be self-assessment questions to assist us in understanding psychological functions such as memory, attention and self-control.

Some questions simply ask you to choose a particular option, please follow these instructions. These questions are to check the questionnaire is working correctly.

All data collected will be anonymised, confidential and used for research purposes only. In accordance with the new General Data Protection Regulations (GDPR) Article 6(1e), the University processes your data as it allows us to conduct research in the public's interest. Further details on how your information is processed and how to find out when it will be disposed of can be found at https://tinyurl.com/researchprivacynotice. Details on how to contact the University's Data Protection Officer and your rights towards your data can be found at: https://www.nottingham.ac.uk/utilities/privacy/privacy.aspx.

This online questionnaire will last approximately 15 minutes.

Participation in this study is totally voluntary and you are under no obligation to take part. You are free to withdraw at any point before or during the study. This study is open to any adult who wishes to take part but is aimed at people who have experienced periods.

As an online participant in this research, we are obliged to make you aware that there is always a potential risk of intrusion by outside agents, for example through hacking, and therefore the possibility of being identified.

If you have any questions or concerns please don’t hesitate to ask now. We can also be contacted after your participation at the above address for a summary of your results. If you have any complaints about the study, please contact: Stephen Jackson (Chair of University of Nottingham School of Psychology Ethics Committee) stephen.jackson@nottingham.ac.uk

Page
Break

University of Nottingham School of Psychology Consent Form

Title of project: Attention and Memory in Menopause
Researcher: Karen Barnor
Supervisors: Professor Harriet Allen and Professor Lucy Cragg
Contact details: Karen.Barnor@nottingham.ac.uk, Lucy.Cragg@nottingham.ac.uk, H.A.Allen@nottingham.ac.uk

The participant should answer these questions independently:

Q1: Have you read and understood the information sheet?

- ○ Yes
- ○ No

Page
Break



Q2: Questions regarding consent

	YES	NO
Have all your questions been answered satisfactorily if applicable?	○	○
Do you understand that you are free to withdraw from the study at any time without giving reason?	○	○
I give permission for my data from this study to be shared with other researchers provided that my anonymity is completely protected.	○	○

End of Block: Information sheet

Start of Block: Introduction



Q3: Do you agree to take part in the study?

By clicking the button below I indicate that the study has been explained to me to my satisfaction, and I agree to take part. I understand that I am free to withdraw at any time.

- ○ Yes
- ○ No

End of Block: Introduction

Start of Block: Prolific ID



Q3a: What is your Prolific ID? Please note that this response should auto-fill with the correct ID

_____

End of Block: Prolific ID

Start of Block: About you, Country, Age and Ethnicity

Q3b: Which country do you reside in?

_____

Demographics

The questions below relate to your age and ethnicity.

Q4: What is your age?

_____
_____

Q5: Which of the options below best describes you?

- ○ African
- ○ Caribbean
- ○ Any other Black, African or Caribbean background
  _____
- ○ Indian
- ○ Pakistani
- ○ Bangladeshi
- ○ Chinese
- ○ Any other Asian background
  _____

- ○ English, Welsh, Scottish, Northern Irish or British
- ○ Irish
- ○ Gypsy or Irish traveller
- ○ Any other white background

  _____

- ○ White and Black Caribbean
- ○ White and Black African
- ○ White and Asian
- ○ Any other Mixed or Multiple Ethnic background

  _____

- ○ Arab
- ○ Any other ethnic group

  _____

- ○ I prefer not to say

The next few questions are about your periods and bleeding patterns. Q6: Do you still have periods or are you bleeding?

- ○ Yes
- ○ No

If you answered YES to still having periods or bleeding, please select the option which best suits you.

- ○ Yes - I have skipped cycles for 60 days or more
- ○ Yes - My periods have not changed from how they have always been – regular monthly cycles
- ○ Yes - In consecutive months, my periods have been delayed by 7 days or more
- ○ Yes - but my periods have changed or become irregular. I have had a period within the last 12 months
- ○ Yes - I am taking contraceptives and I am premenopause (not started menopause)
- ○ Yes - I am taking HRT and I am perimenopause (currently going through menopause)
- ○ Yes - I am taking HRT and I am postmenopause
- ○ Yes - I am taking contraceptives and I am perimenopause (currently going through menopause)
- ○ None of the above - please describe below

  _____

If you answered NO to still having periods or bleeding, please state the option which best suits you.

- ○ No - I have not had a period in 12months
- ○ No - I am taking HRT and I am postmenopause
- ○ No - I have had a surgical operation e.g. hysterectomy, removal of ovaries etc
- ○ No - My periods stopped after cancer treatment
- ○ No - I am taking contraceptives and I am premenopause (not started menopause)
- ○ No - I am taking HRT and I am perimenopause (currently going through menopause)
- ○ No - I am taking contraceptives and I am perimenopause (currently going through menopause)
- ○ None of the above - please describe below

  _____

End of Block: About you, Country, Age and Ethnicity

Start of Block: Brief description of Menopause Symptoms using Greene Climacteric Scale.

A brief description of symptoms using Greene Climacteric Scale and other commonly reported symptoms.

Q7: Please select to what extent you have been bothered over the past 6 months by the symptoms below

	Not at all (0)	A little (1)	Quite a bit (2)	Extremely (3)
Heart beating quickly or strongly	○	○	○	○
Feeling tense or nervous	○	○	○	○
Sleeping difficulties	○	○	○	○
Excitable	○	○	○	○
Panic or anxiety attacks	○	○	○	○
Loss of interest in most things	○	○	○	○
Tiredness or a lack of energy	○	○	○	○
Please select option, 'Quite a bit (2)' in the third column.	○	○	○	○
Poor concentration	○	○	○	○
Crying spells	○	○	○	○

Feeling unhappy or depressed	○	○	○	○
Irritability	○	○	○	○
Numb feeling in parts of the body	○	○	○	○
Headaches	○	○	○	○
Pressure or tightness in head	○	○	○	○

Page
Break

Q7 cntd: Please select to what extent you have been bothered over the past 6 months by the symptoms below

	Not at all (0)	A little (1)	Quite a bit (2)	Extremely (3)
Muscle and joint aches	○	○	○	○
Loss of feeling in hands and feet	○	○	○	○
Feeling dizzy or faint	○	○	○	○
Breathing difficulty	○	○	○	○
Hot flushes	○	○	○	○
Night sweats	○	○	○	○
Loss of interest in sex	○	○	○	○
Mood swings	○	○	○	○
Changes in skin/dryness	○	○	○	○
Clumsiness	○	○	○	○

Frequent visits to the toilet	○	○	○	○
Weight gain	○	○	○	○
Please select option. 'Extremely (3)' in the fourth column	○	○	○	○
Heavy periods/flooding	○	○	○	○
Lowered confidence	○	○	○	○
Vaginal dryness	○	○	○	○
Poor memory	○	○	○	○

Page Break

End of Block: Brief description of Menopause Symptoms using Greene Climacteric Scale.

Start of Block: Employment

This section relates to your current employment or any paid role you have had in the last 6 months.

Q8: Are you currently employed?

- ○ Yes
- ○ No

Q9: Please select from below how many hours you usually work in a week.

- ○ 0-15
- ○ 16-30
- ○ 31-48
- ○ 49 or more

Q10: Please state your job role.

_____

_____

End of Block: Employment

Start of Block: Education

This question is about your level of qualifications.

Q11: Please select the highest level of education you have completed.

- ○ No qualification
- ○ Primary school
- ○ O level/GCSE's or equivalent
- ○ AS, A levels or equivalent
- ○ Apprenticeship
- ○ NVQ or equivalent
- ○ Degree level or above e.g. HND, HNC, NVQ level 4 and above
- ○ Prefer not to say
- ○ Other qualification or equivalent. Please state below

  _____

End of Block: Education

Start of Block: Caring & lifestyle

Section below relates to caring responsibilities.

Q12: Are you a parent?

- Yes
- No

Q13: Do you have any children aged 0-17 living with you at home or who you have regular responsibility for?

- Yes
- No

Q14: Do you look after, or give help or support to anyone because they have long term physical or mental health conditions or illnesses, or problems related to old age?

- No
- Yes, 9 hours a week or less
- Yes, 10-19 hours a week
- Yes, 20-34 hours a week

- ○ Yes, 35-49 hours a week
- ○ Yes, 50 or more hours a week

Lifestyle questions will be asked in this section. Questions will be about how much you exercise, eating habits, drinking and smoking habits.

Q15: How often do you have a drink containing alcohol?

- ○ Never
- ○ Monthly or less
- ○ 2-4 times a month
- ○ 2-3 times a week
- ○ 4 or more times a week

Q16: How many cigarettes would you say you smoke in a day?

- ○ None
- ○ 10 or fewer
- ○ 11-20

- ○ 21-30
- ○ 31 or more

Q17: During the last week, how many hours did you spend on each of the following activities?

	None	Some but less than 1 hour	1 hour but less than 3 hours	3 hours or more
Physical exercise such as swimming, tennis, football, jogging, aerobics, gym workout etc	○	○	○	○
Cycling, including cycling to work and during leisure time	○	○	○	○
Walking, including walking to work,	○	○	○	○

shopping, for pleasure etc					
Housework or childcare	○	○	○	○	
Gardening or DIY	○	○	○	○	

Q18: The questions below are about your eating habits from the past month.

	Never	Occasionally	1-2 times/week	3-5 times/week	6 times or more/week
How frequently do you skip breakfast?	○	○	○	○	○
How often do you eat fruits?	○	○	○	○	○
How often do you eat vegetables?	○	○	○	○	○

How often do you eat fast food?	○	○	○	○	○
How often do you eat sweets?	○	○	○	○	○

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The following question relates to your overall sleep quality for the majority of nights in the past 7 days only. Please think about your quality of sleep **overall**, such as how many hours of sleep you got, how easily you fell asleep, how often you woke up during the night (except to go to the bathroom), how often you woke up earlier than you had to in the morning and how refreshing your sleep was.

Q19: During the past 7 days, how will you rate your sleep quality overall?
Please select ONE choice.

- ○ Terrible
- ○ Poor
- ○ Fair
- ○ Good
- ○ Excellent

End of Block: Caring & lifestyle

Start of Block: Brief QNS

During the past month, how often has each of the behaviours been a problem?

	Never	Sometimes	Often

Q1 I have angry outbursts	○	○	○
Q2 I make careless errors when completing tasks	○	○	○
Q3 I am disorganized	○	○	○
Q4 I have trouble concentrating on tasks (such as chores, reading or work)	○	○	○
Q5 I tap my fingers or bounce my legs	○	○	○
Q6 I need to be reminded to begin a task even when I am willing	○	○	○
Q7 I have a messy closet (wardrobe/cupboard)	○	○	○
Q8 I have trouble changing from one activity or task to another	○	○	○
Q9 I get overwhelmed by large tasks	○	○	○

Q10 I forget my name	○	○	○
Q11 I have trouble with jobs or tasks that have more than one step	○	○	○
Q12 I overreact emotionally	○	○	○
Q13 I do not notice when I cause others to feel bad or get mad until it is too late	○	○	○
Q14. I have trouble getting ready for the day	○	○	○
Q15 I have trouble prioritizing activities	○	○	○
Q16. I have trouble sitting still	○	○	○
Q17 I forget what I am doing in the middle of things	○	○	○
Q18 I do not check my work for mistakes	○	○	○
Q19 I have emotional outbursts for no reason	○	○	○

Q20 I lie around the house a lot	○	○	○
Q21 I start tasks (such as cooking, projects) without the right materials	○	○	○
Q22 I have trouble accepting different ways to solve problems with work, friends or tasks	○	○	○
Q23 I talk at the wrong time	○	○	○
Q24 I misjudge how difficult or easy tasks will be	○	○	○
Q25 I have problems getting started on my own	○	○	○
Please select option, 'Never' in the first column.	○	○	○

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Break

During the past month, how often has each of the following behaviours been a problem?

	Never	Sometimes	Often
Q26 I have trouble staying on the same topic when talking	○	○	○
Q27 I get tired	○	○	○
Q28 I react more emotionally to situations than my friends	○	○	○
Q29 I have problems waiting my turn	○	○	○
Q30 People say that I am disorganized	○	○	○
Q31 I lose things (such as keys, money, wallet, homework etc)	○	○	○
Q32 I have trouble thinking of a different way to solve a	○	○	○

problem when stuck			
Q33 I overreact to small problems			
Q34 I do not plan ahead for future activities			
Q35 I have a short attention span			
Q36 I make inappropriate sexual comments			
Q37 When people seem upset with me, I do not understand why			
Q38 I have trouble counting to three			
Q39 I have unrealistic goals			
Q40 I leave the bathroom a mess			
Please select option, 'Sometimes' in			

the second column.			
Q41 I make careless mistakes			
Q42 I get emotionally upset easily			
Q43 I make decisions that get me into trouble (legally, socially, financially)			
Q44 I am bothered having to deal with changes			
Q45 I have difficulty getting excited about things			
Q46 I forget instructions easily			
Q47 I have good ideas but cannot get them on paper			

Q48 I make mistakes	○	○	○
Q49 I have trouble getting started on tasks	○	○	○
Q50 I say things things without thinking	○	○	○

Page
Break

During the past month, how often has each of the following behaviours been a problem?

	Never	Sometimes	Often
Q51 My anger is intense but ends quickly	○	○	○
Q52 I have trouble finishing tasks (such as chores, work)	○	○	○
Q53 I start things at the last minute (such as assignments, chores, tasks)	○	○	○
Q54 I have difficulty finishing a task on my own	○	○	○
Q55 People say that I am easily distracted	○	○	○
Q56 I have trouble remembering things, even for a few minutes (such as phone numbers, directions)	○	○	○

Q57 People say that I am too emotional	○	○	○
Q58 I rush through things	○	○	○
Q59 I get annoyed	○	○	○
Q60 I leave my room or home a mess	○	○	○
Q61 I get disturbed by unexpected changes in my daily routine	○	○	○
Q62 I have trouble coming up with ideas for what to do with my free time	○	○	○
Q63 I do not plan ahead for tasks	○	○	○
Q64 People say that I do not think before acting	○	○	○
Q65 I have trouble finding things in my room, closet, or desk	○	○	○

Q66 I have problems organizing activities			
Q67 After having a problem, I don't get over it easily			
Q68 I have trouble doing more than one thing at a time			
Q69 My mood changes frequently			
Please select option, 'Never' in the first column.			
Q70 I don't think about consequences before doing something			
Q71 I have trouble organizing work			
Q72 I get upset quickly or easily over little things			
Q73 I am impulsive			

Q74 I do not pick up after myself	○	○	○
Q75 I have trouble completing my work	○	○	○

End of Block: Brief QNS

Start of Block: Comments

Please feel free to add any comments about study in the text box below and click next to move on to end of questionnaire where your responses will be submitted.

_____

Please visit URL below to complete the study: https://app.prolific.com/submissions/complete?cc=CJGBD701 to

_____

End of Block: Comments

6.4 Appendix 4: Pairwise comparisons

For pairwise comparisons within each subscale presented in Table 7, an additional Bonferroni correction was applied to control for the three comparisons (premenopausal vs. perimenopausal, premenopausal vs. postmenopausal, and perimenopausal vs. postmenopausal). This resulted in a final significance threshold of p = 0.00185. Compared to premenopausal women, perimenopausal women had significantly higher scores on Shift, Emotional control, Initiate, Task monitor, Plan/Organise and Working memory subscales. No significant differences were observed between perimenopausal women and postmenopausal women and also between postmenopausal women and premenopausal women.

Table 6-1 Pairwise comparisons of subscales between the menopause groups

Comparison ⟹	*Peri-pre*		*Post-pre*		*Peri-post*	
Outcome ⇓	*Mean difference (95%CI)*	*P value*	*Mean difference (95%CI)*	*P value*	*Mean difference (95%CI)*	*P value*
BRI	*5.06 (2.35,-7.77)*	*0.000026*	*-3.46 (0.49, -7.40)*	*0.143*	*1.60 (4.70, -1.51)*	*0.65*
Inhibit	*2.99 (-0.70, -5.01)*	*0.005*	*-3.59 (-0.34,-6.76)*	*0.025*	*-0.66 (-3.19, 1.97)*	*1.00*
Shift	*-4.21(-1.38,-7.03)*	*0.001**	*-1.12 (2.99, -5.22)*	*1.00*	*3.09(6.32,-.14)*	*0.06*
Emotional Control	*-5.84(-2.87,-8.80)*	*0.000008**	*-3.94(0.47, -8.15)*	*0.098*	*1.98 (5.39, -1.39)*	*0.48*
Self-Monitor	*-2.60(-.194,-5.01)*	*0.03*	*-1.75 (1.76, -5.25)*	*0.70*	*0.85 (3.61,-1.91)*	*1.00*
MI	*-6.33(-3.29,-9.37)*	*0.000002*	*-2.90(1.52, -7.32)*	*0.35*	*3.43(6.91, -0.053)*	*0.06*
Initiate	*-5.50(-2.45,-8.57)*	*0.000053**	*-2.23(2.21, -6.68)*	*0.69*	*3.27 (6.77,-0.23)*	*0.08*
Task monitor	*-4.79(-1.99,-7.59)*	*0.000137**	*-2.16(1.92, -6.24)*	*0.61*	*2.62 (5.83,-0.59)*	*0.15*
Working memory	*-8.82(-5.50,-12.14)*	*9.4464E-10**	*-5.77(-0.94,-10.60)*	*0.013*	*3.04(6.85,-0.76)*	*0.17*
Plan/Organise	*-4.82(-1.94,-7.69)*	*0.000190**	*-0.65(3.54,-4.83)*	*1.00*	*4.17(7.46, 0.88)*	*0.007*
Organisation of Materials	*-3.58(-0.88,-6.28)*	*0.005*	*-2.05(1.87,-5.98)*	*0.63*	*1.53(4.62,-1.57)*	*0.712*

Differences were calculated based on estimated marginal means controlling for age. Bonferroni calculated p = 0.00185.

6.5 Appendix 5: Sleep quality in perimenopause and postmenopause women

I next investigated the impact of sleep disturbances on executive function on the menopause transition in perimenopausal and postmenopausal women as these groups report sleeping difficulties during the transition to menopause. Sleep quality ratings, initially measured on a scale from 0 to 4 (0 = terrible, 1 = poor, 2 = fair, 3 = good, 4 = excellent), were recoded and centred for analysis. The recoding process transformed the scale to range from -2 to 2.

BRI and sleep quality

An ANCOVA was performed using menopause stage (perimenopause (not on HRT) and postmenopause) as the independent variable and BRI as the dependent variable. Sleep and age were used as covariates.

It was predicted that poor sleep would affect BRI scores regardless of menopause stage. There was no significant main effect of menopause stage, F (1, 557) = 0.127, *ns.* partial η^2 = 0.000229. However, sleep was significantly related to BRI scores, F (3, 557) = 32.662*,* $p < 0.001$, partial η^2 = 0.055. Polynomial contrasts were employed to test for linear, quadratic, and cubic trends across five levels of sleep (terrible, poor, fair, good and excellent).

Age was also not significantly related to BRI scores F (1, 557) = 0.634, *ns,* partial η^2 = 0.001. Figure 6-1 illustrates BRI scores across sleep quality ratings during perimenopause and postmenopause. This showed that women with better sleep quality reported lower BRI scores.

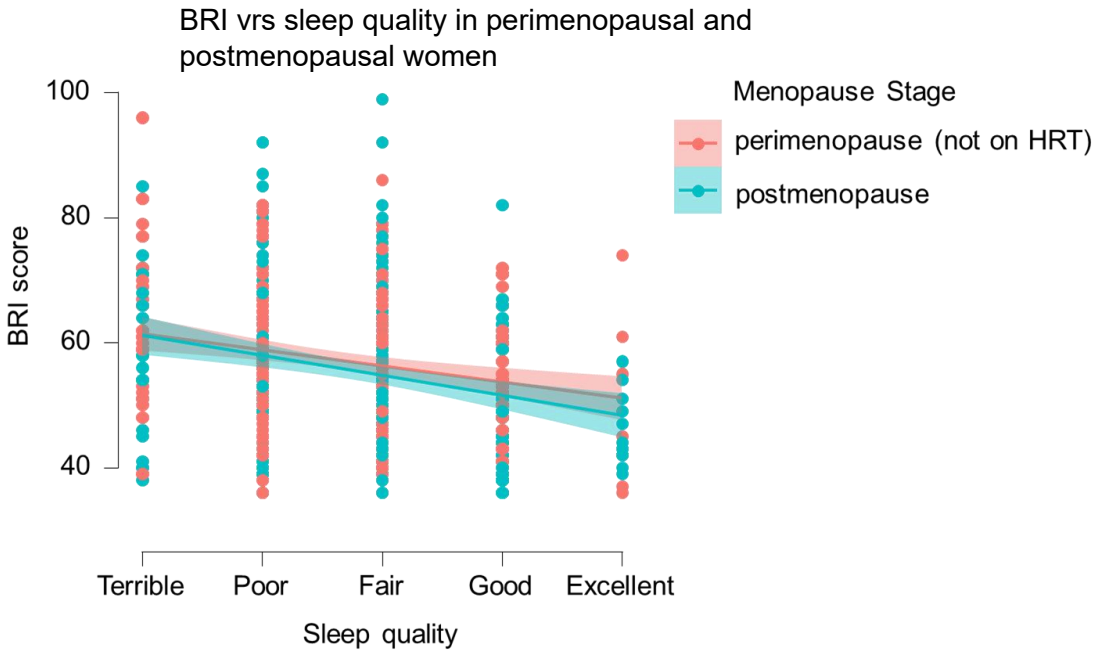

Figure 6-1 Mean BRI scores plotted against sleep quality ratings.

Note: Error bands are 95% CI.

MI and sleep quality

An ANCOVA was run to determine the effect of poor sleep on MI scores during perimenopause and postmenopause stages. The process above was repeated but this time with MI as the dependent variable. It was also predicted that poor sleep will affect MI scores regardless of menopause stage. There was no significant main effect of menopause stage, F (1, 557) = 2.327, p = 0.128. partial η^2 = 0.004. Age was not significantly related to MI scores F (1, 557) < 1, *ns,* partial η^2 < .001. Sleep was significantly related to MI scores, F (3, 557) = 44.925 p < 001, partial η^2 = 0.072. There was a significant linear trend of MI across levels of sleep quality, F (4, 530) = 10.265, p < 0.001, partial η^2 = 0.072. MI scores across sleep quality ratings during perimenopause and postmenopause are plotted in Figure 6-2.

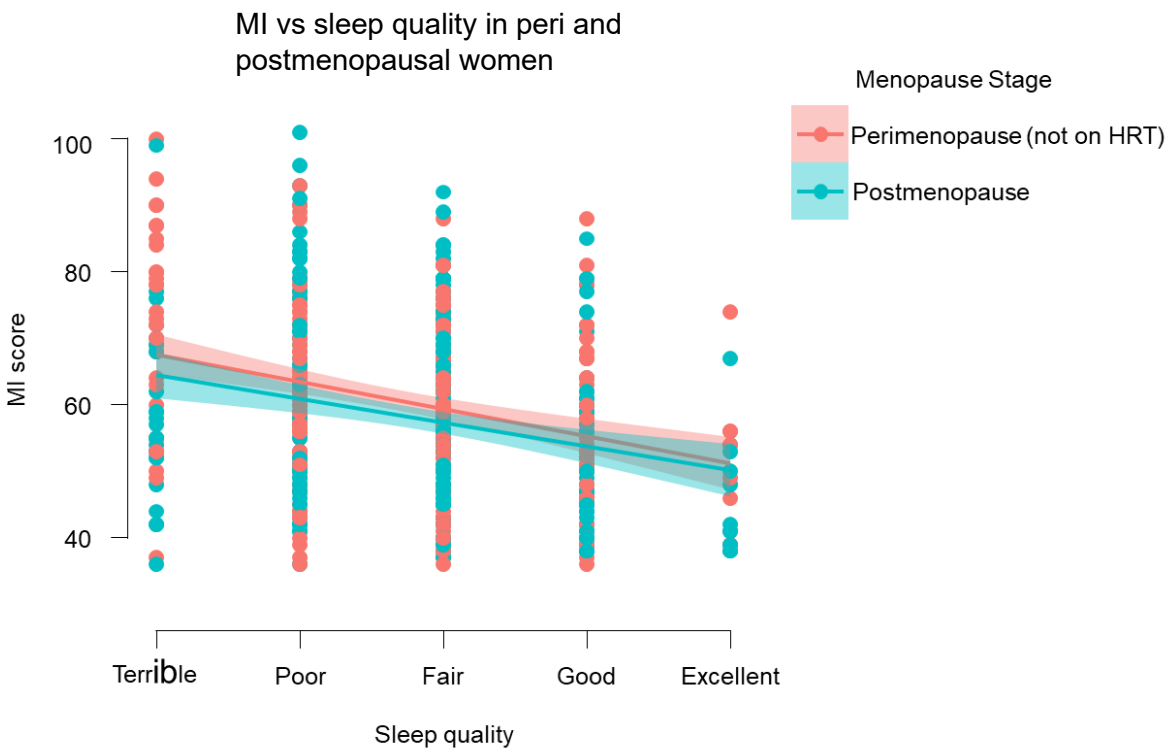

Figure 6-2 Mean MI scores plotted against sleep quality rating

Note: Error bars represent the 95% CI.

6.6 Appendix 6 Exploratory analysis of menopause symptom subclusters and cognitive performance

Menopause symptoms were measured using the Greene Climacteric scale. This scale consists of subclusters further broken down into psychological, physical, vasomotor and sexual symptoms. Pearson's partial correlations were run to assess the relationship between menopause symptoms subclusters and cognitive performance while adjusting for age (df = 232) and are shown in Table 6-2. To account for multiple comparisons across 12 correlations, the significance threshold was adjusted to $p < 0.004$. There were no significant associations between menopause symptoms subcluster and processing speed, selective attention and inhibitory control and verbal working memory cognitive performances ($p > 0.004$).

Table 6-2 Pearson's partial correlations on associations between menopausal symptoms subclusters and cognitive performance

Cognitive measure	Psychological	Physical	Vasomotor	Sexual
Processing Speed Median RT (secs)	.148	.158	.050	.160
Selective Attention & Inhibitory Control (ratio)	.028	.080	−.059	−.027
Verbal Working Memory (Total correct)	−.186	−.084	.027	−.103

Note. Correlations adjusted for age, $p < 0.004$, The Greene Climacteric Scale subclusters are divided into psychological (including anxiety and depression), physical, vasomotor, and sexual symptoms, reflecting distinct aspects of menopausal experiences. *r* = correlation, *df* = degrees of freedom, RT = reaction times

6.7 Appendix 7 Raw Mean Scores for BRIEF-A subscales

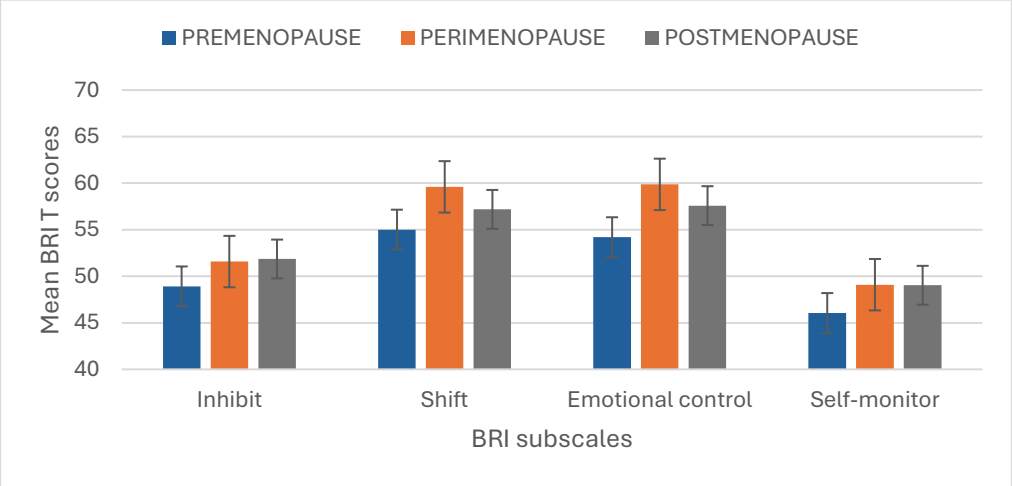

Figure 6-3 Raw mean scores for the BRI subscales of the BRIEF-A

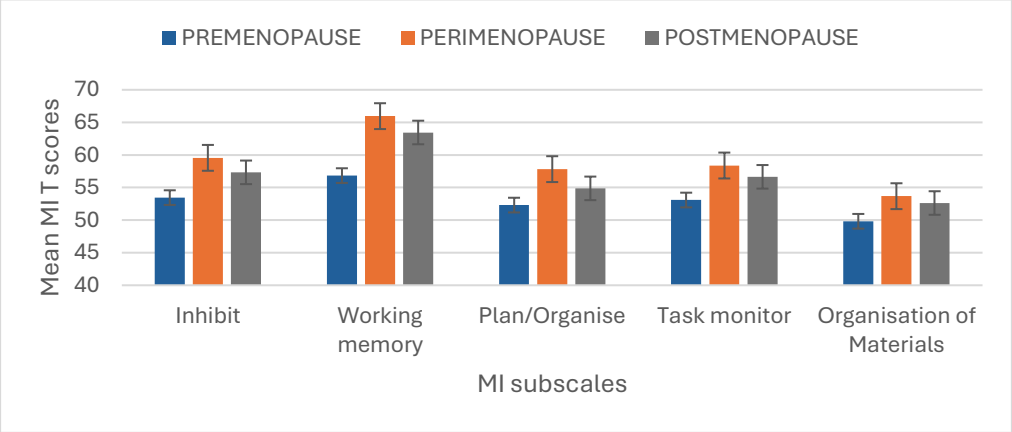

Figure 6-4 Raw mean scores for the MI subscales of the BRIEF-A

6.8 Appendix 8 Exploring age, menopause stage and menopause symptom as predictors of processing speed

A hierarchical multiple regression analysis was conducted to examine whether age, menopause stage, and menopause symptom severity predicted processing speed, as measured by median reaction time. processing speed. Age was entered as a control variable in the first step. Menopause stage was dummy coded with the premenopausal group serving as the reference category. The outcome variable was median reaction time on a processing speed task, with higher scores indicating slower performance. In Model 1, age significantly predicted processing speed, $R^2 = .203$, F (1, 233) = 59.40, $p < .001$. with older age associated with slower reaction times, $B = .451$, t (233) = 7.71, $p < .001$, 95% CI [0.010, 0.017]. In Model 2, menopause stage (dummy variables for perimenopause and postmenopause) was added. This led to a small, non-significant increase in explained variance, adjusted $R^2 = .018$, F (2, 231) = 2.72, $p = .068$. Neither perimenopausal ($B = -.096$, t (231) = -1.30, $p = .194$) nor postmenopausal stage $B = .083$, t (231) = 0.76, $p = .451$) significantly predicted processing speed. In Model 3, menopause symptom severity was added and significantly improved the model, $R^2 = .032$, F (1, 230) = 9.99, $p = .002$. The full model was statistically significant, $R^2 = .254$, F (4, 230) = 19.57, $p < .001$, adjusted $R^2 = .241$. In the final model, age remained a significant predictor ($B = .414$, $t = 4.36$, $p < .001$) and menopause symptom severity was also a significant predictor ($B = .185$, $t = 3.16$, $p = .002$.). Perimenopausal stage was not significant ($B = -.146$, $t = -1.98$, $p = .050$) while postmenopausal stage remained non-significant ($B = .013$, $t = 0.12$, $p = .909$).

6.9 Appendix 9 PIPS Placement

PIPS Reflective Statement

Note to examiners:

This statement is included as an appendix to the thesis in order that the thesis accurately captures the PhD training experienced by the candidate as a BBSRC Doctoral Training Partnership student.

The Professional Internship for PhD Students is a compulsory 3-month placement which must be undertaken by DTP students. It is usually centred on a specific project and this reflective statement is designed to capture the skills development which has taken place during the student's placement and the impact on their career plans it has had.

PIPS Reflective Statement:

My 3-month placement was with the Water Branch team in the Welsh government. I worked on a project that involved the assessment of drinking water quality standards in Wales in the context of recent WHO recommendations and the revised parameters at EU level. My project also investigated desalination technologies and the efficient removal of Boron from desalinated water. This involved me utilising my research skills to conduct a literature review examining desalination technologies around the world. At the end of the project, I presented my findings to the team and also prepared a report for the team that identified evidence gaps and highlighted emerging technologies.

My next project involved looking at private water supplies in Wales. There were several opportunities to engage with other departments such as the Department of Environmental, Food and Rural Affairs. My engagement with internal and external stakeholders improved my communication skills and assisted me in my research as I was able to draw on the knowledge and skills of different teams.

Reflecting on the placement, I realise this was an excellent opportunity as I gained an understanding of how policies are developed to manage

water systems sustainably as well as the different roles played by members of the team. This has given me an insight into various careers in the civil service and how my current skills and knowledge can be applied in different roles and context.