

Research Article

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Cognitive Well-being in Midlife: Counseling Approaches to Menopause-Associated Brain Fog

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Abstract

Cognitive changes during the menopausal transition are common among women, and they frequently cause concern regarding underlying cognitive disorders. Health-care providers have an important role in providing guidance, reassurance, and normalization of these experiences. This International Menopause Society White Paper presents an evidence-based approach to clinical decision-making and counseling. It describes the particular cognitive changes of menopause, their magnitude and duration, and the effects of estrogen and menopausal symptoms. It also provides highlight points for hormone therapy discussion, its cognitive consequences, and risk of dementia, including absolute risk considerations. Finally, it summarizes modifiable risk factors for age-associated cognitive impairment and dementia, along with pragmatic tips for maximizing brain health in midlife and beyond.

1. Introduction

Cognitive difficulties are common among many midlife women that can impact daily functioning and health. These difficulties have been adequately documented during the menopause transition (MT) with evidence on the role of estradiol (E2) in cognitive function. Further, menopausal symptoms like vasomotor symptoms (VMS), sleep disturbances, and mood changes also contribute to cognitive difficulties. However, the important questions are:

- Do these changes indicate a risk of dementia?
- Does menopausal hormone therapy (MHT) prevent cognitive decline, or might it increase the risk of late-onset dementia?

The 2022 World Menopause Day theme, Cognition and Mood, mirrors the urgency of these questions. To answer them, this International Menopause Society-commissioned White Paper gives an overview of the current literature and a framework for clinicians to effectively counsel and support menopausal patients. This article addresses important questions commonly faced in clinical practice, such as:

- What is cognitive function, and how does brain fog during menopause relate to it?
- How does cognitive function during menopause change?
- Which menopausal factors affect cognition?
- What is the role of MHT in cognitive health?

- What other modifiable risk factors impact cognition at midlife?
- What are the widely accepted recommendations for maximizing brain health that clinicians can recommend to patients?

1.1. Defining Cognition and Menopause Brain Fog

Cognition is engaging in all the processes of thinking and knowing, including everything from perception, memory, reasoning, to the solution of problems, and decision making. A lot of women who go through menopause have cognitive complaints for example, difficulty remembering words or numbers jogging their memory, due to the above problem the subject can't concentrate, an inability to continue with the line of thought, and forgetting the appointment or occasion. In some instances, these cognitive disturbances may present as attention deficit hyperactivity disorder (ADHD). These symptoms are referred to as "brain fog" when taken collectively. The severity of the symptoms varies from person to person, but most of the women go through only the mildest symptoms.

There is evidence that appears in some studies of basic scientific research, showing that menopause-related cognitive impairment might be the result of long-lasting brain changes that go into the late stages of life and could eventually be responsible for dementia. The question, however, is whether the menopause itself becomes the cause of it. Is it the fact that each woman going through menopause ultimately undergoes an unstoppable cognitive decline? The actual picture here is that all women do pass through menopause, but only a few will get dementia. In the U.S., the lifetime risk for Alzheimer's disease (AD) in women is approximately 19.5% at age 45 and it slightly increases to 21.1% by the age of 65. The prevalence of AD varies according to biological sex, and the location of the disease-most women suffer from AD, and cases are more common in Europe and North America than they are in Asia, Africa, and South America. With these figures in mind, the probability of getting midlife dementia turns out to be very low- unless the family tree shows a history of early-onset AD. The worldwide incidence of midlife dementia is only 293.1 per 100,000 women.

1.2. Clinical Counseling and Decision-Making Key Takeaways

Menopause brain fog is the cognitive symptoms many women feel during menopause, which primarily target memory and attention. Menopause-related cognitive changes differ from dementia, since dementia prior to age 64 is uncommon. Even though some studies indicate a link between menopause-related cognitive change and later-life dementia, the cognitive changes associated with menopause are widespread, and the majority of women will not develop dementia even after undergoing menopause.

1.3.Cognitive Domains Affected by Menopause

Clarifying the impact of menopause on cognition is needed, requiring neuropsychological testing done over time, prospectively, through follow-up from premenopause to postmenopause. Most reliable studies have consistently indicated that the cognitive functions most significantly affected throughout the MT are verbal memory and learning, with somewhat smaller or less stable effects for psychomotor speed and working memory/attention.

Working memory is the capacity to store and process information temporarily, for example, recalling an e-mail address while writing a message. Verbal learning and memory constitute encoding and retrieving words, word pairs, short paragraphs, or other verbal information. Research repeatedly finds that women do better than men on verbal memory and learning tasks throughout their life. The majority of middle-aged women are forgetful and research supports complaints that correlate the severity of symptoms with performance at verbal memory test. There are also changes found in long-term studies wherein higher-order capacities such as the executive functions of planning and strategizing remain steady during menopause.

1.4.Cognitive Changes and Risk Factors

In spite of evidence that menopause-associated cognitive changes do occur, mean cognitive performance is within normal ranges. The only longitudinal study of new-onset cognitive impairment during menopause was in low-income women of color, half of whom were HIV infected. The study determined that 11–13% of the participants developed cognitive impairment, with rates being comparable between HIV-infected and HIV-uninfected women. It's not yet known why some women are more prone to mental decline during menopause. Education, occupation, hobbies, genetic risk, physical and mental health, and stress in life can all be potential contributors. Those who have had fewer cognitively challenging experiences have low cognitive reserve, and that may put them at increased risk. Also, chronic menopausal symptoms, particularly sleep disruptions, could play a role in this mental vulnerability.

1.1.Do These Cognitive Changes Reverse?

A fundamental clinical question is whether cognitive changes continue after menopause. From the Study of Women Across the Nation(SWAN), any appreciable alterations in cognitive performance seem to be restricted to perimenopause. Conversely, results of the Penn Ovarian Aging Study indicate verbal learning impairment continuing after menopause, while issues of verbal memory typically reverse. Yet these studies did not observe participants far enough into post menopause to ascertain the complete degree of cognitive recovery. Changes in verbal learning, memory, and attention/working memory continued post menopause in research involving low-income women of color. These observations show that, although memory challenges do resolve over time in most women, a few remain to have difficulty with verbal learning after menopause.

1.6.Reassurance for Women

These results are reassuring that cognitive problems during menopause are not signs of the development of dementia, including Alzheimer's disease (AD). Cognitive changes usually appear perimenopause and usually return to normal after postmenopause. The overall trend is that cognitive change during menopause is related to changes in sex steroid hormones and menopausal symptoms and not an early stage of a degenerative brain disorder.

1.7.Key Takeaways for Clinical Counseling and Decision-Making

According to a study, it has been confirmed that the difficulty that menopausal women complain about with respect to their cognitive abilities is real. Word recall and learning problems are the two cognitive domains that are most affected. Such problems often start in perimenopause when menstrual cycles are irregular and periods are being skipped. Even if the mentioned illnesses can be rather uncomfortable, in most cases, women experience normal cognitive function, and only a small proportion of 11–13% develop clinically significant impairment. The timing of the alterations indicates that they are caused by hormonal fluctuations and the symptoms of menopause and not Alzheimer's disease which, however, is rare at this stage.

1.8.Menopause-Related Factors That Affect Cognition

Estrogen receptors are to be found in the locations of the brain which are responsible for memory and other cognitive processes that is to say the hippocampus and prefrontal cortex. It has been shown that estrogen (E2) plays a major role in cognitive decline which is related to menopause. While the ovary extraction or the inhibition of E2 production by pituitary analogs have been associated with a decline in verbal learning and memory, this decline of intellectual faculties can be significantly alleviated by replacing the estrogen, which implies that the E2 loss is a cause of the cognitive decline and apathy that were made undisputable in the longitudinal studies.

The more important consequence of the called 'wearable technology' menopausal symptoms is that it affects the cognitive functioning of a person and makes it worsen. The piece of evidence argues that the frequency of vasomotor symptoms (VMS) that are habitual is an important factor for memory loss, not just that, even after the other reasons such as self-reported sleep disturbances were controlled and sleep quality was measured objectively. The study says also that brain images of VMS women show surreptitious alterations of both brain structure and function.

Apart from these, the sleep and mood arena are very important. The two have been observed to play a significant part in contributing to cognitive troubles during the menopausal period. As far as sleep and menopause-related cognitive impairment are concerned, a direct causal relationship has not been established so far, but the findings of the sleep deprivation studies clearly show that cognitive functions are impaired by sleep disturbances as well as by verbal learning and memory. Furthermore, the research data evidence links of mood issues (such as depression and anxiety) with the cognitive decline of menopause. Nevertheless, the relationship between the treatment of mood disorders and memory improvement remains uncertain. Cognitive impairment in midlife is affected by fluctuations in estrogen (E2), vasomotor symptoms (VMS), sleep disturbances, and mood changes. Treatment of these symptoms can potentially enhance cognitive function.

2.What Role Does MHT Play in Cognition? 2.1.MHT and Cognitive Function

According to current research, menopausal hormone therapy (MHT) may be of benefit for cognitive performance in perimenopause when symptoms first emerge and in women with bothersome VMS. There are no randomized trials addressing the effects of MHT or oral contraceptives on cognition in perimenopausal women, and no trials assessing the effect of MHT on cognition in women with moderate-to-severe VMS. The majority of studies have been aimed at the effect of MHT on cognitive function in early and late postmenopausal women. Results of four large-scale clinical trials suggest that MHT has no effects on cognition in early postmenopausal women, irrespective of the regimen—oral E2, transdermal E2, conjugated equine estrogens (CEE) with medroxyprogesterone acetate (MPA), or CEE alone.

In the case of late postmenopausal women, the results differ depending on the regimen employed:

CEE/MPA seems to have adverse cognitive effects in women 65 years and older. Oral E2 with vaginal progesterone has neutral cognitive effects in women greater than 10 years after natural or surgical menopause. Small studies in surgically menopausal women indicate estrogen therapy (ET) can benefit memory function.ET tends to have neutral effects on cognition in older women.

2.2.MHT and Dementia Risk

Numerous women are concerned that if they took MHT, they would be at a higher risk for dementia. Evidence from the Women's Health Initiative (WHI) indicates that CEE/MPA is linked to a doubling of all-cause dementia in five years. CEE, by itself, seems to have no impact on dementia risk.

2.3.Contradictory Evidence on Dementia Risk with MHT

Long-term results of the Women's Health Initiative (WHI) have reported conflicting evidence regarding menopausal hormone therapy (MHT) and Alzheimer's disease (AD). Although a 5-year assessment associated CEE/MPA with doubling the risk of dementia, the 18-year follow-up indicated CEE resulted in a 26% lower AD death rate, and CEE/MPA was not associated with AD mortality. The reasons behind such conflicting results are unknown. If both results are correct, they might signal an initial hazard of hormone therapy (HT) on dementia in susceptible women, for example, with poor baseline cognitive function or diabetes, followed by possible long-term dividends.

To date, no large trials exist to clarify which MHT regimens are most promising for cognitive health. Rather, investigators must depend on large population-based studies, with the result that the findings usually conflict:

AFinnish case-control study (84,000+ women) reported that systemic MHT (ET alone or estrogen plus progestin therapy - EPT) was associated with increased risk of AD, irrespective of formulation—even CEE was linked with increased AD risk. Conversely, a UK-based nested case-control study (118,501 women, aged 55+ years) reported no overall increased or decreased dementia risk with MHT.

ET for >10 years was associated with reduced risk of dementia, whereas MHT use for 5–9 years raised dementia risk by 10%, and use for >10 years raised risk by 20%. E2 use for 1–5 years (but not >) was related to reduced AD risk. Progesterone preparations had minimal effect on risk of dementia, though dydrogesterone seemed to have a slightly reduced risk compared with other progestogens. Based on these conflicting results, no conclusions can be made about which estrogen preparations are safest or most effective in reducing dementia risk.

2.4.Considerations for Oophorectomized Women

In women who have undergone oophorectomy, estrogen therapy (ET) through the usual age of menopause can be recommended. Studies have shown that women who had not had ET after surgery were at an increased risk of cognitive impairment or dementia 30 years later than women who started ET soon after surgery and continued until the age of 50, when spontaneous menopause would have set in. This is a reminder that caution is exercised in planning bilateral oophorectomy, keeping its advantage on one side in contrast with a possible long-term adverse effect. Appropriate monitoring and treatment measures should be in place for women who are undergoing the procedure.

2.5.Counseling Patients on MHT and Dementia: Risk vs. 2.8 Potential Benefit Mi

When counseling patients about MHT and risk of dementia, it's useful to place findings in context using absolute risk numbers from the Women's Health Initiative Memory Study (WHIMS):

According to WHIMS data, the number of women needed to treat with CEE/MPA to cause one additional case of all-cause dementia is 436.For women using MHT to manage vasomotor symptoms (VMS), these numbers may offer reassurance.Some women may inquire about MHT for dementia prevention—it's important for clinicians to clarify perceived benefits.Employing the 18-year follow-up WHI results, which estimated a 26% lower risk of death from dementia with CEE, an estimated number needed to treat 2004 women to prevent a single AD-related death. This would translate to a best-case situation in which only 1 woman out of every 2004 on MHT would see her AD-related mortality decrease. Such data serve to illustrate that MHT will not have a major impact on a single woman's personal risk of dementia. Other evidencebased treatments must instead take priority in minimizing AD risk.

2.6. Key Points for Clinical Practice and Decision-Making

Current practice guidelines advise against MHT at any time for treating menopausal cognitive symptoms or for prevention of cognitive impairment and dementia.

There are two large knowledge gaps in the scientific literature:

- Whether MHT has an effect on cognition in women with moderate-to-severe VMS.
- Whether MHT or oral contraceptives improve cognitive function during perimenopause.

The use of MHT early in post menopause seems to be safe for cognitive function.

Estrogen therapy (ET) in women with early menopause could help preserve cognitive health and lower the risk of dementia. ET is still safe for cognitive function even when used later in post menopause.

2.7. Modifiable Risk Factors for Dementia

Most women with cognitive issues during menopause are concerned about their risk of developing dementia later in life. One of the messages to be communicated to patients is that dementia may be delayed or prevented in many cases by taking care of certain health factors. Although certain risk factors, like age and gender, cannot be modified, studies indicate that approximately 40% of dementia in the world is attributable to modifiable risk factors.

World Health Organization (WHO) guidelines and the 2020 Lancet Commission recognize main modifiable risk factors as:

- Physical inactivity
- Cognitive engagement (e.g., learning new skills)
- Social interaction
- Obesity
- Hypertension
- Diabetes
- Hearing impairment
- Depression

2.8.Midlife: A Critical Time to Act

Midlife is an excellent time to intervene, as research indicates five factors substantially boost dementia risk by 41–78%:

- Obesity
- Diabetes mellitus
- Smoking
- High cholesterol
- Borderline hypertension

Moreover, another review detected that psychological stress, excessive drinking, and elevated homocysteine levels were associated with increased dementia risk

2.9.A Multi-Faceted Approach to Risk Reduction

Risk reduction for dementia means that multiple factors must be addressed, as studies indicate the cumulative effect of risk factors:

- One risk factor doubles dementia risk (20% increase)
- Two risk factors triple dementia risk (65% increase)
- Three risk factors quadruple dementia risk (200% increase) [59]

A major clinical trial demonstrated that a multidomain lifestyle intervention, such as diet, exercise, cognitive training, and vascular risk factor monitoring, significantly enhanced cognition in those at risk for dementia.

2.10.Hypertension and Risk of Dementia

Blood pressure control is especially crucial for preventing dementia in midlife. Evidence suggests:

Reducing systolic blood pressure (SBP) to 120 mmHg decreases the risk of mild cognitive impairment, a prodrome to dementia. SBP \geq 130 mmHg raises the risk of cognitive impairment and dementia by 34%. The relationship between diastolic blood pressure (DBP) and dementia risk is U-shaped, with DBP between 90–100 mmHg conferring a decreased risk of AD.

2.11. Exercise, Weight Control, and Social Engagement

Promoting exercise and weight control is important for cognitive well-being. Research indicates that:

Women at midlife are especially encouraged to decrease dementia risk via exercise. A longitudinal study on women at midlife discovered that greater cardiovascular fitness was associated with lower dementia risk.

The WHO encourages older adults to have either:

150 minutes per week of moderate-intensity aerobic physical activity OR 75 minutes per week of vigorous-intensity aerobic physical activity OR Both combined.

2.11. Social Engagement and Cognitive Health

Having strong social relationships is crucial for long-term cognitive well-being. Studies show that social isolation, loneliness, low social engagement, and social isolation raise the risk of cognitive impairment and dementia in older people.

3. Conclusion

Menopausal cognitive complaints are prevalent and tend to cause anxiety, with most women worrying that these symptoms portend the development of dementia in the future. Menopause practitioners have a significant role to play in demystifying these fears and offering evidence-based advice to enable patients to preserve cognitive function. Menopause most notably affects learning and remembering verbal information, with working memory and attention less affected. While these changes happen, most women have normal cognition during menopause. Although problems with memory are usually resolved postmenopause, some women, particularly those of lower education, social disadvantage, or other risks, may develop ongoing cognitive impairments.

Decreasing levels of estrogen (E2) and menopause symptoms i.e., vasomotor symptoms (VMS), sleep disturbance, and mood disturbances—affect cognition in women during midlife. Treatment of these symptoms is likely to enhance cognitive function, although clinical trial data are as yet unavailable to establish this course of action. Notably, memory problems during menopause must not be confused with dementia since dementia prior to age 64 is uncommon. Cognitive difficulties in perimenopause may be associated with an increased risk of dementia in later life, according to some research, but this work is preliminary.

Menopausal hormone therapy (MHT) is not currently advised at any age to treat cognitive symptoms or to prevent cognitive decline or dementia. WHIMS results show that CEE/MPA raises the risk of dementia, with an estimated number needed to treat (NNT) of 436 women for one additional case of dementia. Long-term follow-up results from the WHI, however, reverse previous reports and imply that CEE decreases the risk of Alzheimer's disease death. Even in this optimal scenario, the NNT for the prevention of death from AD is 2004 women, rendering MHT an untrustworthy approach to dementia prevention [1-45].

In light of the absence of consistent evidence between MHT formulation and duration, clinical counseling would thus concentrate on a multi-faceted approach to decreasing the risk of dementia through modifiable factors, such as:

- Obesity
- Hypertension
- Diabetes
- Physical activity
- Smoking cessation
- Cognitive engagement
- Social interaction
- Hearing health
- Mental well-being

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