EDITORIAL

What do we think about cognition and menopause?

The recent reappraisal of the effects of hormone therapy in the wake of the publication of the Women’s Health Initiative study has included consideration of the effect of hormone therapy on cognitive function.1,2 This aspect of the Women’s Health Initiative came via the Women’s Health Initiative Memory Study, which included only women aged 65 to 79 years. The negative effects that were demonstrated in this older group stimulated discussion about whether hormone therapy use in the early menopause might have a different effect. The argument is that exposure to estrogen in the early postmenopausal years is likely to have a more positive effect on cognitive function and later dementia that cannot be tested in the Women’s Health Initiative Memory Study design.

There are a number of reports about the effect of hormone therapy on aspects of cognition, and the results are inconsistent and conflicting. The article by Kok et al3 published in this issue of Menopause adds to the data on this question, reporting no effect detected, but that is not the main point of the study. The particular importance of this study is the contribution it makes to our understanding of the even more fundamental question of the effect of menopause itself on cognitive function.

Menopause is well known to be associated with a range of effects, some of which seriously reduce the quality of life of affected women. Some symptoms are relatively unique to menopause so that the symptom can easily be followed through its course, and appropriate advice can be given and management can be offered. The hot flash is the classic example of this. Urogenital atrophy works on a different time scale, but the same principles apply. With the psychological disturbance that some women experience at menopause, matters are more difficult because the symptoms, including depressed mood, are multifactorial in origin. For any postmenopausal woman reporting psychological symptoms, the clinician may have difficulty assessing the extent to which the symptoms are due to the menopausal transition and the extent to which other issues are contributing. Questions around the effect of menopause on cognitive function merge into this area. Clinicians hear from some women at menopause that their mental functioning has deteriorated with the onset of menopause and, as with psychological symptoms, it is difficult to know whether this is a menopausal effect. When one hears such statements from women year in, year out in the menopause clinic, it is natural to assume that menopause does involve a reduction in cognitive function for some women, and for years, I have assumed that this is the case.

In my early career, I was influenced in this view by the work of Bungay et al.4 They studied the nature of menopausal syndrome by means of a postal questionnaire in a community survey spanning a wide age range in approximately 500 men and 1,100 women in which the respondents did not know that the focus of the study was menopause. They mapped the prevalence of symptoms in 5-year age bands from well before to well after menopause. The most obvious association with the years of the menopausal transition was a peak prevalence of flushes and sweats. In addition, there was also self-reporting of impaired concentration and poor memory in women in the years leading into the transition but not in men.

In general, the literature on cognitive function in postmenopausal women has been inconsistent, and this may not be surprising in a context where there are many different measurement instruments for the aspects of cognition and where individuals have very different levels of cognitive performance as they enter menopause. For this reason, it is valuable to have longitudinally collected data across the menopausal transition. With the report in the current issue of this journal, we now have at least three studies that contribute longitudinal information in this area, and the new study provides by far the longest perspective because it provides assessments of cognition at 8, 43, and 53 years in the same women.5,6 Overall, these longitudinal studies do not suggest a major effect of menopause.5,6

As part of the important longitudinal Melbourne Women’s Midlife Health Project, Henderson et al5 assessed a group of 326 women in a word list memory task as an assessment of verbal memory.5 They did not detect an effect of menopause on episodic verbal
memory in the group, which ranged from 52 to 63 years of age. In a longitudinal study from Chicago over a period of nearly 6 years, approximately 800 women were selected at random from their communities by Meyer et al., who examined cognitive function with yearly follow-up. The women were eligible for the study if they were in the age range 42 to 52 years and were not yet postmenopausal and had not undergone hysterectomy. The cognitive functions assessed were working memory and perceptual speed. The authors tested the hypothesis that these functions would decline as women passed into menopause, but this was not confirmed. They observed small improvements with time in the measures tested and could not confirm their hypothesis.

Against this background, the longitudinal study of Kok et al. is a particularly valuable contribution to our understanding of this subject because it reflects a research investment that was initiated a generation ago. The data derive from the Medical Research Council National Survey of Health and Development, which is a representative cohort that includes approximately 2,500 women followed up since birth in March 1946. Critically valuable for the question of cognition in menopause is that cognitive function was assessed in childhood at 8 years of age, and later at 43 years, and these assessments provide a valuable context against which to interpret the results of cognitive assessment at 53 years of age as reported in the article. The prospective collection of socioeconomic data, potentially relevant to cognitive ability, is also useful.

The researchers have used validated tests of several dimensions of cognitive function, including measures reflecting full-scale IQ, verbal memory, and concentration. These same tests had been conducted 10 years previously, at the age of 43 years. At the previous assessment, postmenopausal status was hardly a feature, but clearly, at 53 years, this is an important variable. It was a sensible precaution that the attribution of postmenopausal status at 53 years was only finalized in retrospect when the group had reached 57 years.

What has been learned? This study reports weak evidence of an influence of the onset of menopause on cognitive function on some measures, but there was no trend in verbal memory across menopause. Comparing the women classified by postmenopausal status, there was a significant trend across the menopausal transition for the predictors of full-scale IQ and concentration to decrease into the postmenopausal phase. However, with adjustment of the IQ predictor based on childhood cognitive ability and lifetime socioeconomic circumstances, the menopausal effect was no longer detected. When the assessment of concentration by search speed was adjusted for the results at 43 years of age, the menopause effect was attenuated to a trend.

Again, we have evidence that any effect of the menopausal transition on different parameters of cognitive function is limited or absent when taken in context of previous ability. This perspective goes beyond the impression that a clinician can form when consulting with a postmenopausal woman and should be influential. The investment in this cohort has been considerable. I would like to think that the longitudinal data would be supplemented by a further assessment after another 5 or 10 years.

Currently, through a selective reading of the literature, it is possible to construct a view that estrogen does or does not have a positive effect on parameters of cognitive function, and it is possible to argue for differences depending on the stage of postmenopausal life involved. More fundamentally, we have an important study of cognitive function with a lifelong perspective where any effects of menopause itself are weak or absent, depending on the parameter concerned. I suppose there may be small subgroups of women whose neuroendocrine activity renders them more vulnerable to the physiological loss of estrogen at menopause in terms of a negative cognitive effect and who may not be detected in the broad categories studied here. If that is not so, I must accept that the best evidence available fails to detect a major effect. In that case, I need to revise my long-held clinical impression.

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REFERENCES