Cognitive function in late versus early postmenopausal stage

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Received 22 December 2005; received in revised form 7 June 2006; accepted 14 June 2006

Abstract

Objectives: There are relatively few studies of cognitive performance in the first few postmenopausal years and insufficient data on whether there is differential decline in different cognitive abilities. The aim of the present analysis was to determine the nature of cognitive decline across a range of functions within a period of 5 years from early to late postmenopausal stage.

Methods: In a cross-sectional study, 189 postmenopausal women, who had experienced a natural menopause, were not taking hormonal medication and had not done so in the previous 12 months, were divided according to their postmenopausal stage into early (stage +1, ≤ 5 years since the last menstrual period, aged 55.4 ± 0.3 years, n = 80), or late (stage +2, >5 years since the last menstrual period, aged 59.8 ± 0.4 years, n = 109) postmenopausal stages. Participants completed a comprehensive battery of tests measuring attention, episodic and semantic memory, planning and mental flexibility. Participants also completed self-ratings of mood, sleepiness and menopausal symptoms.

Results: There were no differences between the groups in their performance in tests of attention, verbal fluency or memory. However, in the two tests of executive function (planning and mental flexibility) the women in the late postmenopausal stage performed significantly worse than the women in the early postmenopausal stage. These differences remained significant when effects of age and IQ were taken into account by analyses of covariance. There were no differences between the groups in their ratings of mood, of habitual sleepiness, or of feeling sleepy at the start of testing. However, by the end of testing the women in the late postmenopausal stage rated themselves as feeling sleepier than did the women in the early postmenopausal stage. The group differences in executive function remained significant when these differences in sleepiness were accounted for.

Conclusions: Although there were no differences in attention, verbal fluency and memory, executive function was significantly poorer in the late postmenopausal stage women, suggesting that this aspect of cognition deteriorates more rapidly than other functions. This change was independent of change in age, suggesting that hormonal changes between the early and late postmenopausal stages may be responsible.

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Keywords: Menopause; Age; IQ; Executive function; Memory; Attention; Mood

1. Introduction

It is widely accepted within the literature that cognitive ability steadily declines with advancing age from...
early to late adulthood [1–3]. As cognitive functions are diverse processes sub-served by separate neuroanatomical substrates, it is not surprising that age-related decrements in cognitive performance are much greater in certain tasks than in others. For example, healthy older adults tend to perform worse than younger adults in tests of episodic memory (memory for specific events within a spatio-temporal context), whilst only slight effects of age are reported for retrieval from semantic memory (memory for facts and knowledge) [4]. More recent evidence suggests that executive functions, which are dependent on the pre-frontal cortex, e.g. planning ability, mental flexibility, are particularly susceptible to advancing age [5–7].

Cognitive function, assessed by the mini-mental states examination (MMSE), was shown to decline with age and time since the menopause in a cohort of postmenopausal women (aged 50–74 years) [8]. However, the MMSE produces a global score of cognitive function and does not allow for the determination of differential effects on separate aspects of cognitive function. Two longitudinal studies found no change in cognitive function during the menopausal transition [9,10], but these studies were heavily confounded by the well-known practice effects in the tasks used and thus no conclusions can be drawn from them as to the impact of menopausal stage. Kritz-Silverstein et al. [11] demonstrated that a younger group of postmenopausal women (aged 50–59 years) performed better on tests of executive function (trails B), and episodic memory (immediate and delayed recall of a story) than an older group (60–74 years). However, these data are limited by the fact that the women were stratified by age, and not by postmenopausal stage, and it also covered a large age-range particularly in the older group. A recent study on postmenopausal women (aged 51–67 years) found that those in the late postmenopausal stage performed significantly worse on the executive functions of planning and mental flexibility than did those in the early postmenopausal stage, whereas there were no differences in tests of attention and memory [12]. In a much larger group (n = 326) of postmenopausal women aged 52–63 years, episodic memory did not vary with menopausal status during the transition or in the early postmenopausal years, either in the cohort as a whole, or in the sub-group who had never received hormone replacement therapy [13]. The results of these two studies suggest that there may be a differential rate of decline in different cognitive functions postmenopause, with executive function deteriorating more rapidly than memory and perhaps memory only showing a decline in later years. This is important because it contrasts with the frequent complaints of deteriorating memory by peri- and postmenopausal women [14–17].

The purpose of the present study was to analyse data from a larger sample than that used by Elsabagh et al. [12] to test the hypothesis that executive function is significantly worse in the late postmenopausal stage than in the early stage, but that attention and memory do not differ. This hypothesis is specific to women in the under 70 age-range and we further sought to have two groups with similar variability in ages and differing by no more than 5 years in age. Because mood and intelligence can also affect cognitive performance, measures of these were also included in the study.

2. Method

2.1. Participants

The present study presents an analysis of all the postmenopausal women who took part in experiments on the cognitive effects of ginkgo, gincosan (ginkgo + ginseng), and soya supplements [12,18,19]. This gave a sample of 189 women, aged 49–67. They were stratified into two postmenopausal stages, according to a classified system of reproductive ageing [20]. The early postmenopausal stage, or stage +1, is defined as ≤5 years since the final menstrual period and encompasses the period where circulating levels of oestrogen are still declining to a permanent level, in addition to the period of accelerated bone loss [20–22]. The late postmenopausal stage, or stage +2, is defined as >5 years since the final menstrual period and reflects the stage at which levels of circulating oestrogen have reached a steady low level. In our earlier studies, all the women were first tested at baseline, before any treatments began, and it is these scores that were analysed for the present study. The local ethics committee approved the studies and all participants gave written informed consent. All participants were healthy, had undergone a natural menopause and were defined as postmenopausal if they had not menstruated in the previous 12 months. Only women who had not used hormone replacement therapy (HRT) in the previous 12 months
were recruited, and other exclusion criteria were smoking more than 20 cigarettes/day, current illness or use of psychoactive medication and the use of soya, ginkgo or ginseng supplements. As part of a general questionnaire, the women were asked about their usual alcohol (units/week) and caffeine (cups/day) consumption, and their years of secondary education. Their height and weight was measured and their body mass index (BMI) was calculated (BMI = weight (kg)/height (m)^2).

2.2. Mood and menopausal symptoms

2.2.1. Menopausal symptoms

The Greene climacteric scale [23] was used to assess menopausal symptoms yielding four independent symptom measures, psychological, somatic, vasomotor symptoms and sexual dysfunction.

2.2.2. Measures of trait mood

The hospital anxiety and depression scale (HAD) [24] was used to determine levels of trait anxiety and depression. The Epworth sleepiness scale [25] was used to measure habitual levels of sleepiness, and was completed at the end of the test session.

2.2.3. Ratings of mood state

In order to assess the participants' actual mood state at the time of testing, the Stanford sleepiness scale [26] and the Bond and Lader visual analogue mood scales [27] and were used immediately prior to, and just after, the battery of cognitive tests. For the mood scales, each item consisted of a pair of opposite adjectives separated by a 100 mm line. Participants indicated how they felt at the time by placing a vertical mark at the appropriate place along each horizontal line. From the individual items, three-mood factors (alertness, well-being and anxiety) can be extracted [27].

2.3. Cognitive tests

2.3.1. Estimate of IQ

For each participant, an estimate of intelligence quotient (IQ) was obtained from the national adult reading test, revised version [28].

2.3.2. Sustained attention

The paced serial addition test (PASAT) was used to measure sustained attention [29]. Participants had to add together successive pairs of single digits read from a list of 61 numbers. There were four levels of difficulty, with presentation speeds of 2.4, 2.0, 1.6 and 1.2 s between digits. The total number of correct responses (maximum 60/trial) was recorded for each of these four trials.

2.3.3. Episodic memory

There were three tests of episodic memory. In the immediate and delayed paragraph recall test (from the Weschler memory scale—revised) [30], 25 units of information were read at a rate of 1 unit/s, and the participants were told to remember as accurately as possible. Recall was tested immediately and after 25 min, and the number of correctly recalled units was scored (maximum 25 each for immediate and delayed recall). The test of short-term non-verbal memory was the delayed matching to sample test (DMTS) from the Cambridge neuropsychological test automated test battery (CANTAB Cambridge Cognition, Cambridge, UK), which has been shown to be dependent on the temporal cortex [31,32]. In this test, a sample complex pattern is displayed on the computer screen and the task is to select one of four similar patterns that match the sample. The four patterns are either displayed simultaneously with the sample or appear after a delay of 0, 4 or 12 s. The number of correct responses was scored for five patterns at each delay. Long-term episodic memory was also measured by presenting a set of 20 pictures of common objects [33], with a stimulus duration of 5 s. Participants were asked for their recall 25 min later.

2.3.4. Category generation

Participants were asked to name all the animals they could think of that belonged to a particular semantic category (house, farm or jungle) [29]. They were given 20 s for each category. A total score was derived from all admissible answers for each category.

2.3.5. Test of executive function

Two tests of executive function were selected from the CANTAB.

2.3.5.1. Mental flexibility. A test of learning rule reversal and shifting (intradimensional-extradimensional IDED test) provided a measure of mental flexibility dependent on the pre-frontal cortex [34]. In this
test, a series of pairs of patterns was presented on a computer screen and the task was to learn the rule that determined which pattern was correct. Once the rule was correctly learned, this rule was reversed or shifted. There were nine levels of the task. The number of stages completed, the number of errors and trials to complete the task, and the number of errors made at the critical extra-dimensional shift (EDS) stage of the task were recorded.

2.3.5.2. Planning. Planning ability was measured using the stockings of Cambridge (SoC) test, which has also been shown to use the frontal cortex [35]. The computer screen displayed two sets of three coloured balls that could be housed in three stockings. The task was to move the balls in the lower part of the screen so that the pattern exactly matched that shown in the upper part, using the fewest moves possible. The task varied in difficulty with four levels of increasing complexity, so that the match could be obtained in two, three, four or five moves. The first two levels of the task were used for training, and the number of moves and the initial and subsequent thinking times (ms) to complete the four and five-move tasks were recorded.

2.3.6. Statistics

Power analyses from our previous studies [12,18,19,36] indicated that \( n = 50–100 \) would be sufficient to show significant differences in the cognitive tests at \( P < 0.05 \).

The demographic characteristics, HAD scale, Epworth scale, menopausal symptoms and cognitive test measures were initially analysed using one-way analyses of variance (ANOVARs) with menopausal stage as the independent factor. PASAT, SoC and story recall were analysed by two-way ANOVAs, with menopausal stage as the between group factor and task level as the repeated measure factor. The three-mood factors and Stanford sleepiness scales were analysed by two-way ANOVAs, with menopausal stage as the between-group factor, and the repeated measure factor of time (before and after cognitive testing). Analyses of covariance were then conducted on the cognitive measures found to differ significantly between the groups, the covariates being IQ (because this affects performance on these tasks [37]), age and ratings of sleepiness at the end of testing. The statistical package used was SPSS version 10.1 for windows

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Early (n = 80)</th>
<th>Late (n = 109)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.4 ± 0.3</td>
<td>59.8 ± 0.4***</td>
</tr>
<tr>
<td>IQ (based on NART)</td>
<td>114.6 ± 1.1</td>
<td>112.3 ± 1.0</td>
</tr>
<tr>
<td>Secondary education (years)</td>
<td>5.8 ± 0.2</td>
<td>5.8 ± 0.2</td>
</tr>
<tr>
<td>BMI</td>
<td>24.4 ± 0.4</td>
<td>25.0 ± 0.3</td>
</tr>
<tr>
<td>Alcohol intake (units/week)</td>
<td>5.2 ± 0.7</td>
<td>4.1 ± 0.5</td>
</tr>
<tr>
<td>Caffeine intake (cups/day)</td>
<td>4.5 ± 0.3</td>
<td>5.2 ± 0.3</td>
</tr>
<tr>
<td>HADanxiety</td>
<td>6.5 ± 0.4</td>
<td>6.3 ± 0.4</td>
</tr>
<tr>
<td>HADdepression</td>
<td>2.9 ± 0.3</td>
<td>3.5 ± 0.3</td>
</tr>
<tr>
<td>Greene climacteric scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological</td>
<td>8.2 ± 0.6</td>
<td>7.7 ± 0.5</td>
</tr>
<tr>
<td>Anxiety</td>
<td>5.0 ± 0.3</td>
<td>4.4 ± 0.3</td>
</tr>
<tr>
<td>Depression</td>
<td>3.2 ± 0.3</td>
<td>3.2 ± 0.2</td>
</tr>
<tr>
<td>Somatic</td>
<td>3.1 ± 0.3</td>
<td>3.2 ± 0.2</td>
</tr>
<tr>
<td>Vasomotor</td>
<td>2.2 ± 0.2</td>
<td>1.3 ± 0.2***</td>
</tr>
<tr>
<td>Sexual dysfunction</td>
<td>1.1 ± 0.1</td>
<td>1.4 ± 0.1</td>
</tr>
<tr>
<td>Epworth sleepiness scale</td>
<td>6.5 ± 0.4</td>
<td>6.6 ± 0.4</td>
</tr>
</tbody>
</table>

Early vs. late postmenopausal stage, *** \( P < 0.001 \).

### 3. Results

#### 3.1. Demographics, mood and menopausal symptoms

It can be seen from Table 1 that the women in the early and late postmenopausal stages did not differ in their IQ, years of secondary education, BMI, daily intake of caffeine or weekly intake of alcohol, or in their levels of anxiety or depression, as measured on the HAD scale (stage, \( F < 3.1, \ n.s. \) in all cases). The late postmenopausal stage group had a significantly lower rating of menopausal vasomotor symptoms (stage; \( F_{(1,187)} = 12.5; P < 0.001 \)), but there were no group differences in any of the other menopausal symptoms (stage, \( F < 1.6, \ n.s. \) in all cases; see Table 1). There were no differences between the groups in their ratings of habitual sleepiness, as measured by the Epworth scale (\( F < 0.1, \ n.s. \)).

#### 3.1.1. Ratings of mood state

There were no significant effects of postmenopausal stage on any of the three factors extracted from the Bond and Lader mood scale (\( F < 2.1, \ n.s. \) in all cases).
There was a significant time effect on the three-mood factors showing that both groups became less alert (time, $F_{(1,187)} = 169; P < 0.001$), had lower ratings of well-being (time, $F_{(1,187)} = 103; P < 0.001$), and became more anxious (time, $F_{(1,187)} = 168; P < 0.001$) as a result of testing. There were no differences between the groups in these changes over time (stage $\times$ time interactions, $F_{(1,187)} < 3.2$, n.s. in all cases), data not shown.

However, on the Stanford sleepiness scale there was a significant stage $\times$ time interaction, with the late postmenopausal group showing a greater increase in feeling sleepy after completing the test battery than the early postmenopausal group (stage $\times$ time; $F_{(1,187)} = 6.8; P = 0.01$), data not shown.

3.2. Cognitive tests

3.2.1. Sustained attention

There was no significant effect of postmenopausal stage on the PASAT task ($F = 3.4$, n.s.; see Table 2). There was a significant effect of speed of presentation, with fewer correct responses as the speed of the task increased (speed, $F_{(3,144)} = 207.5; P < 0.001$). However, there was no speed $\times$ menopausal stage interaction ($F = 0.37$, n.s.).

3.2.2. Category generation

There were no significant effects of postmenopausal stage on the category generation task ($F < 1.0$, n.s.; see Table 2).

| Table 2 Mean (±S.E.M.) number of correct responses in PASAT, category generation, picture recall, immediate and delayed story recall and DMTS for women in early and late postmenopausal stages |
|---------------------------------------------------------------|-----------------|-----------------|
| PASAT                                                        | Early ($n = 80$) | Late ($n = 109$) |
| 2.4 s                                                       | 35.6 ± 2.1       | 43.4 ± 2.0       |
| 2.0 s                                                       | 28.6 ± 1.7       | 38.3 ± 1.5       |
| 1.6 s                                                       | 21.7 ± 1.5       | 29.1 ± 1.3       |
| 1.2 s                                                       | 17.8 ± 1.2       | 22.7 ± 1.2       |
| Category generation                                        | 23.5 ± 0.6       | 23.0 ± 0.5       |
| Episodic memory                                             |                  |                  |
| Picture recall                                              | 9.5 ± 0.3        | 9.3 ± 0.3        |
| Story recall (immediate)                                    | 12.9 ± 0.6       | 11.9 ± 0.4       |
| Story recall (delayed)                                      | 11.6 ± 0.6       | 11.0 ± 0.4       |
| DMTS (total correct)                                        | 17.4 ± 0.2       | 17.0 ± 0.2       |

3.2.3. Episodic memory

There were no significant effects of postmenopausal stage on performance in the picture recall, immediate and delayed story recall, or delayed matching to sample tasks (stage, $F < 1.5$, n.s. in all cases; see Table 2).

3.2.4. Executive function

3.2.4.1. Mental flexibility. The late postmenopausal group performed significantly worse than the early postmenopausal group by completing fewer stages of the IDED task ($F_{(1,187)} = 15.6; P < 0.001$; see Fig. 1A). This difference remained significant when differences in age and effects of IQ were accounted for (ANCOVA $F_{(1,186)} = 9.2; P < 0.005$ and $F_{(1,186)} = 14.8; P < 0.001$, respectively) and when differences in feeling sleepy at the end of testing were accounted for ($F_{(1,186)} = 14.7; P < 0.001$).

Of the participants who could complete the task up to the eighth level (the extradimensional shift or EDS stage, $n = 175$), the late postmenopausal group made significantly more errors at the EDS level of the task ($F_{(1,173)} = 28.2; P < 0.001$; see Fig. 1A). This difference remained significant when age and IQ were accounted for (ANCOVA $F_{(1,172)} = 22.7; P < 0.001$ and $F_{(1,172)} = 25.3; P < 0.001$, respectively) and when differences in feeling sleepy at the end of testing were accounted for ($F_{(1,172)} = 27.1$).

Only 115 participants out of 189 were able to complete all nine levels of the IDED task. Of these 115 participants, those in the late postmenopausal group performed significantly worse than the early postmenopausal group by taking more trials, and making more errors to complete the whole task ($F_{(1,113)} = 7.5; P < 0.01$ and $F_{(1,113)} = 10.6; P < 0.001$, respectively; see Fig. 1A). These effects remained significant when IQ was accounted for (ANCOVA, $F_{(1,112)} = 5.6; P < 0.02$ for trials, and $F_{(1,112)} = 8.4; P < 0.005$, for errors). The differences between the menopausal stages also remained significant when ratings of sleepiness at the end of testing were accounted for (ANCOVA, $F_{(1,112)} = 7.1; P < 0.01$ for trials and $F_{(1,112)} = 10.3; P < 0.005$ for errors). When differences in age were accounted for, the trials to criterion was no longer significant (ANCOVA, $F_{(1,112)} = 1.2$, n.s.), but the menopausal groups still differed significantly in the number of errors they made to complete the task (ANCOVA, $F_{(1,112)} = 4.7; P < 0.05$).
Fig. 1. Executive function (scores are mean ± S.E.M.) in early and late postmenopausal stages. (A) In the IDED task: stages completed; extradimensional shift (EDS) errors; trials to criterion; errors to criterion. (B) In the stockings of Cambridge planning task: number of moves; subsequent thinking time (ms). ***P < 0.001, **P < 0.01, *P < 0.05 significant difference between postmenopausal stages.
3.2.4.2. Planning. The performance of the late postmenopausal stage participants on this task of planning was significantly worse than those in the early postmenopausal stage. They used more moves to complete the task than did the women in the early postmenopausal stage ($F_{1,187} = 15.4; P < 0.001$) and they took longer to complete the task (subsequent thinking time $F_{1,187} = 5.5, P < 0.03$; see Fig. 1B). The number of moves made to complete the task increased with the task difficulty ($F_{1,187} = 120.7; P < 0.001$) and, on this measure, task difficulty enhanced the difference between the menopausal stages (task difficulty $\times$ stage interaction $F_{1,187} = 12.6; P < 0.001$). The subsequent thinking time also increased with task difficulty ($F_{1,187} = 18.2; P < 0.001$), but there was no task difficulty $\times$ stage interaction on this measure ($F_{1,187} = 0.4, \text{n.s.}$). There was no significant effect of postmenopausal stage or task difficulty $\times$ stage interaction ($F_{1,187} < 0.2, \text{n.s.}$) on the initial thinking time (data not shown).

The difference between the groups in the number of moves to complete the task remained significant when effects of age and IQ were accounted for (ANCOVA $F_{1,186} = 8.0; P < 0.01$ and $F_{1,186} = 13.0; P < 0.001$, respectively). It also remained significant when sleepiness at the end of testing were accounted for (ANCOVA, $F_{1,186} = 15.0; P < 0.001$). With respect to subsequent thinking time, the difference remained significant when IQ and sleepiness at the end of testing was accounted for (ANCOVA $F_{1,186} = 3.9; P < 0.05$ and $F_{1,186} = 5.7; P < 0.02$, respectively), but was no longer significant when differences in age were accounted for (ANCOVA, $F < 1.3, \text{n.s.}$).

4. Discussion

By analysing a far larger sample of women, the results of this study have confirmed the indication from our earlier study [12] that, whilst there are no differences between the performance of early and late postmenopausal stage women in tests of attention, verbal fluency and memory, the latter perform significantly worse in tests of executive function (mental flexibility and planning). It is interesting that we have previously found that the benefits to postmenopausal women of 6 weeks of treatment with soya supplements were limited to performance in these two tests of executive function [19] and that the benefits of 6 weeks of ginkgo were limited to the performance of late postmenopausal stage women in the test of mental flexibility [12]. It is unlikely that the reason for this pattern of results is because the tests of executive function are more sensitive than the others, because we have shown improvements in performance of postmenopausal women ($n = 31$) in PASAT and DMTS after one week of ginkgo treatment [36] and after 12 weeks of treatment with soya supplements, postmenopausal women ($n = 33$) showed improvements in PASAT and picture recall, as well as in the tests of executive function [37]. The large sample analysed in this study should have been powerful enough to detect any group differences. It would therefore seem that executive function is particularly sensitive to deterioration with postmenopausal stage. However, performance in measures of global cognitive function and attention in a group of women aged 52–97 years has been shown to be influenced by a measure of life-long oestrogen exposure [38]. It is therefore possible that oestrogen affects different cognitive functions in different ways. Kritz-Silverstein et al. [11] found poorer logical memory in an older group of postmenopausal women (aged 60–74 years) compared with a younger group (aged 50–59 years). This may suggest that memory impairments might be detected after age 60 in postmenopausal women, but it is also possible that the impairments may be related to age differences rather than postmenopausal stage.

Apart from one measure in each test (trials to criterion in the IDED and subsequent thinking time in the planning task), the effects of postmenopausal stage were found to be independent of age. This suggests that it may be the difference in circulating oestrogen levels between the early and late postmenopausal stages that is responsible for the differences in executive function. Interestingly, the IDED test shows poorer performance for the age-group 50–59, compared with the decade 40–49 [39,40]. The Deluca study [40] found no sex differences in the age-group 50–64, but the numbers were very small (13 women and 6 men). When the Cambridge Cognition data were examined separately for men and women, it was found that for the EDS errors the deterioration was due to the poorer performance of women who showed twice as many errors at age 50–59 as in the previous decade, the men showing little change (Eileen Marshall, personal communication). It would
be interesting to know whether it is the latter half of the
decade (i.e. 55–60) that is the main source of this dif-
ference in women’s performance. The results of other
studies also indicate that postmenopausal women are
more susceptible to age-related cognitive decline than
age-matched men and pre-menopausal women [41,42]
and there is some evidence that this decline in cognitive
performance is associated with reduced levels of circu-
lating oestrogen [8,43,44]. Our findings of impairments
in executive functions are supported by evidence that
oestrogen loss in postmenopausal women may particu-
larly affect functions of the pre-frontal cortex. Keenan
et al. [45] demonstrated that untreated postmenopausal
women were impaired on tests of mental flexibility,
working memory and discriminability compared with
those treated with HRT, whereas memory tasks were
unaffected. One study, however, raises the possibil-
ity that it might be the relative decrease in oestrogen,
rather than the absolute levels, that is important for
impaired executive function. File et al. [46] compared
postmenopausal women who had been treated for 10
years with oestradiol implants, with pair-matched post-
menopausal women who had never received hormone
replacement therapy. The women with implants were
tested at the time of their trough oestradiol levels,
just before they received a replacement implant. Com-
pared with their pair-matched controls, the women with
implants had significantly worse performance in the
IDED task, despite concentrations of oestrogen in the
range 646–727 pmol/l at the time of testing, well above
the levels of <50 pmol/l in untreated women.

Although there were no differences in ratings of
habitual sleepiness on the Epworth scale, and no dif-
fences in ratings of feeling sleepy at the start of
testing, by the end of testing the women in the late
postmenopausal stage had higher ratings of sleepiness
on the Stanford scale than did those in the early post-
enopausal stage. It is possible that the greater increase
in the feeling of sleepiness at the end of testing in the
late postmenopausal stage women reflected the greater
difficulty that they experienced in the two tasks of exec-
utive function, but as there were no differences in rat-
ings pre-test it is unlikely that differences in sleepiness
could account for the differences in test performance.
Furthermore, the differences in performance remained
significant when the differences in ratings of sleepi-
ness were accounted for in an analysis of covariance.
There were no differences between the two menopausal
stages in ratings of alertness (pre- or post-testing), and
therefore it is unlikely that differences in alertness
could explain the cognitive differences between the
two groups. Additionally, changes in alertness would
be expected to have a more general effect on all tasks,
and would be unlikely to specifically affect those mea-
suring executive functions.

The results of the present analysis raise the impor-
tant possibility that there is poorer executive function
at postmenopausal stage 2, that is independent of age,
but that occurs within a period of only 5 years. Both
mental flexibility and planning are important cogni-
tive functions that are required for the execution of
tasks in everyday life. Indeed, it has been demonstrated
that impairments in performance on laboratory tests of
mental flexibility correlate with scores on the cognitive
failures questionnaire, which measures participants’
ratings of mistakes made in simple everyday tasks (such
as failing to hear somebody speaking whilst perform-
ing another task) [47]. The impairments may be linked
either to the lower concentrations of oestrogen, or to
their relative decrease.

**Keypoints**

- Mental flexibility and planning ability were signif-
icantly poorer in women in the late postmenopause
stage compared with those in the early post-
enopause stage.
- These changes were independent of the effects of
age or IQ.

**Acknowledgement**

This work was funded by a grant from the Dunhill
Medical Trust.

**References**

[1] Albert MS. Age-related changes in cognitive function. In:
Albert ML, Knoefel JE, editors. Clinical neurology of aging.
28.

[2] Ardila A, Rosselli M. Neuropsychological characteristics of

tioning in very old age. In: Craik FIM, Salthouse TA, editors.
[39] Robbins TW, James M, Owen AM, et al. A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: implica-


