SEX HORMONES
and cognitive health

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Although less studied than the female sex steroids, androgens are important for cognition in women.

SEX steroid hormones have important roles in cognition, with oestrogen and androgen receptors found in various anatomical locations throughout the brain.

Teasing out the individual impacts of these hormones on cognitive function is challenging. Whereas traditionally the focus in women has been on the effects of oestrogen and progestogens on cognition, androgens are also likely to play an important role.

Most of the study data to date examining the relationship between exogenous sex steroids and cognitive function in women is from studies in which the oestrogen component administered was conjugated equine oestrogens.

Studies such as the Women's Health Initiative (WHI) gave us the benefit of following a large group of women over time, but in this study we only have information for one form of HRT, and with the average age of WHI participants at 63 years, the likelihood is that cognitively this study had 'missed the boat'.

Mild cognitive impairment is thought to precede the development of dementia by at least 20 years, and for a study to give us meaningful information about the influence of HRT on cognition long term, study participants need to be women around the time of perimenopause or menopause and the study needs to involve long-term HRT versus placebo. Unfortunately, after the negative messages from the WHI study, large, long-term RCTs of HRT are not likely to be conducted.

Perimenopausal or menopausal women commonly report cognitive symptoms such as foggy thoughts and memory issues.

This may be due to changes in sex steroid hormone levels, particularly oestradiol, but may also be due to menopause-related mood disturbance, or secondary to sleep disruption due to nocturnal vasomotor symptoms.

Both women and men have a normal age-related decline in cognitive function, however the reasons underlying this decline are not clear.

While men typically have a small reduction in testosterone levels over their adult life, women have both the dramatic fall in oestradiol levels around menopause (median age 51–52 years), coupled with an age-related decline in androgen levels even from the early reproductive years.

Women have twice the risk of developing dementia compared to men, and it has been postulated that both the decline in oestradiol at menopause, and the gradual decline in androgen production over the adult years may contribute to this difference.

Projections for dementia prevalence suggest that 2.8% of the population will have dementia by 2050 and it will become the most important disease burden in women by 2016.

In the setting of dementia therefore being a significant public health issue, a focus has been on identifying contributing factors to cognitive decline, with an aim of therapeutic intervention.

Economic projections have postulated that even a five-month delay in diagnosis of Alzheimer's disease could lead to significant cost savings and reduce the number of cases per year by 5%.

Studies have attempted to determine the relationship between both endogenous and exogenous androgens and cognition. Surgical or chemical reduction in testosterone levels in men has been associated with impaired memory.

In premenopausal women, higher levels of testosterone have been linked with superior performance on mathematical and spatial tasks.

In elderly women, higher testosterone levels have been associated with superior performance on verbal fluency and verbal memory tasks.

In postmenopausal women higher levels of DHEAs have been linked positively with executive function, working memory and concentration.

Recent RCTs have demonstrated cognitive benefits in both men and women administered testosterone.

Healthy men and men with early cognitive decline/ dementia showed improved visuospatial ability and verbal fluency following testosterone administration.

Women given testosterone have demonstrated improvements in visuospatial task performance, complex information processing, visual memory, verbal memory and concentration.

At this point the evidence is insufficient to recommend general use of androgens such as testosterone as an intervention strategy to prevent cognitive decline.

However, in the absence of other effective intervention strategies, this is an exciting area that warrants further investigation.

Jean Hailes for Women's Health is a national, not-for-profit organisation focusing on clinical care, innovative research and practical educational opportunities for health professionals and women. **www.jeanhailes.org.au**