HORMONE REPLACEMENT THERAPY AND THE BRAIN: A CLINICAL PERSPECTIVE ON THE ROLE OF ESTROGEN.

By Victor W. Henderson.


Professor Victor Henderson, of the Division of Cognitive Neuroscience and Neurogerontology at the University of Southern California, has written a helpful and catholic monograph concerning oestrogen and brain function. This is a relatively unexplored area of interdisciplinary neurological enquiry, for which this book sets the scene successfully. The early text straightforwardly summarizes potentially cloying facts concerning the wide range of oestrogenic effects upon brain biology and chemistry. The numerous figures are clear and informative. Other chapters address the influence of oestrogen on diseases such as stroke or dementia. These disorders are introduced in a simple manner so as to make the book accessible to non-neurologists.

Those who have ever dared to suspect sex-determined differences in map reading abilities will be interested to learn how perinatal sex hormone exposure in rodents leads to sex-specific behavioural differences, including learning tasks dependent upon spatial cues. Absence of early exposure to gonadal steroids seems to result in eventual patterns of neuronal organization and behaviours typical of female adults so that ‘the female pattern of development is thus the default pattern’. Could postponement of hard-wiring the female brain lead to later virtues of adaptability and aptitude for multiskilling? And there is the intriguing matter of environmental toxins with oestrogenic and anti-oestrogenic activities. Whether such exposure is sufficient to alter brain wiring and sex-dependent behaviours in humans remains unclear, but this does raise speculation about the underlying causes for some changing social mores as well as environmentally determined cancers and malformations. In this regard it is intriguing that male rats show long-term behaviour changes if nursed from mothers with high phyto-oestrogen levels in the diet. That the mature male and female brains are different seems to me to be beyond dispute, as if this question was even worth cogitation in the first place: the next time you are teaching medical students how to use an ophthalmoscope or test the visual fields, you might be intrigued by my observation that many lady medical students cannot maintain sustained closure of just one eye whereas this seems a simple skill for most men.

The relationship between oestrogens and mood, cognition and dementia occupies the bulk of this monograph. That women generally have different attributes of mood, verbal agility and visuo-spatial skills is part of the folklore of human nature, which some of our current social engineers would like to suppress. Of course scientific testing is much more adept at measuring differences in cognitive skills, and is rather poor at assessing those fascinating intangibles of emotion, feelings, adaptability and judgement. This could
affect the balance of how we perceive brain attributes to be distributed between the two sexes without meaning either is ‘better’ than the other. They are just different, and almost certainly designed to be so. Of practical importance is the evidence that oestrogenic hormone replacement therapy (HRT) in post-menopausal women improves mental performance on a variety of measurable tasks. Henderson predicts that widespread use of HRT in the world’s half billion post-menopausal women would substantially reduce the incidence of Alzheimer’s disease, for instance by one million in the US alone. Whether oestrogenic enhancement of cognitive performance occurs through a separate mechanism than its protective effect against Alzheimer’s disease seems unclear from the data, although intuition suggests distinct mechanisms. It will be of importance to hear the results of those trials of oestrogens to prevent dementia which are currently under way. It is not clear how one reconciles these reported benefits of HRT with the statements that ‘oestrogen levels within the cerebrospinal fluid appear not to change substantially with age’ despite ‘the absence of ovarian oestrogen production after the menopause’. During pregnancy the pre-menopausal woman’s brain is often exposed to huge systemic oestrogen levels, but it remains unclear whether it is this, or some other endocrine factor, which causes the alterations in mental abilities and some perceptual tasks noted by many pregnant women.

The influence of oestrogens upon stroke risk is an important topic for neurologists. We are all aware of the 40% reduction in coronary artery disease which is provided by HRT in post-menopausal women. Henderson quite rightly draws a distinction between beneficial cardiovascular effects for the heart, and the uncertain cardiovascular effects as far as stroke is concerned. For a practising clinician, this always seems a slightly difficult area. I recall numerous instances of women who have had strokes within a few weeks or months of starting HRT and in whom the coincidence made me suspect a causative relationship. That carried the implication that HRT should be stopped, despite the favourable epidemiological evidence for cardiovascular disease overall. Henderson summarizes the evidence for stroke by noting that although the mortality is reduced in HRT users, it seems there is no measurable change in the incidence of stroke. This question seems worthy of further epidemiological study, along the same rigorous lines as the WHO Collaborative Study of the increased stroke risk associated with oral contraception in women of childbearing age. One deficiency of the discourse on cerebrovascular disease is the lack of discussion about the influence of oestrogen upon the risk of stroke in migraineurs, an important practical area about which general neurologists are consulted frequently.

This monograph does not contain a lot of useful information for a practising neurologist, nor does it set out to do so. Rather, it ties together evidence from a number of different disciplines about the important effects of sex hormones upon the balance of how we perceive brain attributes to be differences in cognition and mood, for the epidemiology of dementia, and for the occurrence of cardiovascular diseases and stroke in women. Professor Henderson is clearly a passionate advocate of this area and states ‘however, the importance of oestrogen on different aspects of brain activity far exceeds its regulatory role in reproductive physiology’. It is good to know that a tussle continues between the relative attributes of mind and body.

Dr Michael Donaghy
University Department of Clinical Neurology, Radcliffe Infirmary, Oxford, UK