Sex and Parkinson's disease

Sex and Parkinson's disease: a world of difference?

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Do women with Parkinson's disease have a more benign phenotype?

The literature concerning gender effect on the incidence and expression of Parkinson's disease (PD) is far from clear.[1] In this issue of *J Neurol Neurosurg Psychiatry*, Taylor and colleagues[2] present a meta-analysis of age adjusted male to female incidence ratios for PD ***(see page 905)***. Seventeen relevant studies and over 2500 people with PD were identified. The authors determined an overall male:female (M:F) ratio of 1.46 (95% confidence intervals 1.24, 1.72) but also found a high level of heterogeneity. M:F difference in the incidence of PD increased with age of onset and, notably, while a M:F incidence difference in Western populations was observed, no such difference was found in Asian populations. The latter was, however, based on only three studies, so this observation needs to be treated with caution.

In a second article in this issue of the journal, Haaxma and colleagues[3] examined gender differences in a clinic based cohort of 253 PD patients ***(see page 819)***. Key findings from this work were that women were 2 years older than men at symptom onset and more likely to present with tremor (67%) than men (48%). Tremor dominance was associated with a slower rate of decline on rating of motor impairment. Women had 16% higher FP-CIT binding than men at symptom onset with a similar rate of decline in tracer binding between the sexes (3.1%/year) thereafter. In women, age at onset correlated positively with parity (but not with nulliparous women), age at menopause and fertile life span. Taken together, these findings could suggest that women with PD have a more benign phenotype. Additionally, oestrogens may exert a beneficial effect in the preclinical phase, with women having no further advantage over men once their disease becomes clinically manifest, as evidenced by the rate of motor and single photon emission computed tomography deterioration, being comparable in both gender groups.

Attractive though Haaxma and colleagues' hypothesis is,[3] the epidemiological data reported by Taylor *et al*[2] argue against a fundamental protective effect of oestrogen. Given the apparent gender differences between Western and Asian PD studies, additional genetic factors may be involved that modify the risk. Possible differences between the natural history of PD in Asian, as compared with Western, patients have also recently been suggested by a cohort study of 1183 clinic patients in Japan.[4] Although this study replicated Haaxma *et al*'s finding of an older age at onset in women (59.9 vs 58.6 years), the times to reach bilateral disease with axial involvement, to develop wearing off and dyskinesias were all significantly shorter in Japanese women than men, implying a more aggressive disease course in Asian women with PD. When interpreting clinic based cohort studies, it is salutary to bear in mind that patients of female gender may be less likely than men to access secondary and tertiary medical care.[5]

There may, therefore, be significant geographical differences in gender effects on the incidence and natural history of PD. Before coming to this conclusion, however, there is a need for further high quality studies to determine whether these recent observations may be replicated and are not merely a result of study design.

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