Matters arising

Could Parkinson’s disease follow intra-uterine influenza? A speculative hypothesis

Sir: We read with interest the speculative hypothesis advanced by Mattock et al., proposing an intrauterine influenza infection as the possible aetiology of Parkinson’s disease.

We feel that this hypothesis, although intriguing and obviously requiring further substantiation, appears to be basically flawed by already existing data from the various twin studies in Parkinson’s disease. These studies designed to examine concordance for Parkinson’s disease in mono and dizygotic twins have demonstrated that the concordance rate for monozygotic twins is extremely low. This evidence confirmed by several studies indicates that genetic factors do not play a prominent role in the development of Parkinson’s disease.

The data from these studies can also be used as an argument against the intrauterine infection hypothesis of Parkinson’s disease since it seems very unlikely that an intrauterine infection would affect only one of two twins sharing the same environment. Although congenital malformations have been reported in one of two monozygotic twins, the incidence of a viral infection affecting only a single twin, we reason, must be very low.

We can look, for example, at congenital cytomegalovirus infection in twins. CMV is the commonest cause of congenital infection in man with an incidence ranging from 0.5–2% of all live births. Of these infected infants, 10% will suffer from mental retardation. Twins with CMV infection are described to usually have concordant clinical or laboratory evidence of disease. There are no reports of monozygotic twins where only one of two CMV infected twins is symptomatic or where only one twin of the set is actually infected. The latter situation, although possible, is the least common and these cases reported are either dizygotic twins or situations suggestive of dizygotic twins (two placenta). In the case of herpes simplex virus, perinatal infection with HSV will also affect both twins in a clear majority of cases.

Toxoplasmosis, a non-viral but also haematogenously spread intrauterine infection, similarly has a distinct difference in clinical patterns of infection between monozygotic and dizygotic twins. In monozygotic twins the clinical pattern of involvement tends to be similar in both twins. In dizygotic twins, discrepancies in clinical findings are more frequent and marked. However, only in a minority of dizygotic twins is one of the twins exclusively infected.

If an intrauterine influenza infection predisposed an individual to develop Parkinson’s disease, then it would appear, based on the pattern of viral and nonviral intrauterine infections, that monozygotic twins (and perhaps even dizygotic twins) should have a high rate of concordance for Parkinson’s disease. Since the concordance rate for Parkinson’s disease is only 2–5% in monozygotic twins, the hypothesis of Mattock et al. seems to be an error and there may be some other reason for the relationship they described between year of birth and crude mortality data for influenza.

CARLOS SINGER
WILLIAM J WEINER
Movement Disorder Center,