Commentary: Fact and artefact in the secular increase in the rate of autism

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King and Bearman\(^1\) sought to determine whether the increased prevalence of an autism diagnosis in California was due to diagnostic substitution of autism in place of mental retardation (MR). They make good use of systematic administrative data from the California Department of Developmental Services between 1992 and 2005 for this purpose, with the conclusion that changes in diagnostic practices accounted for a quarter of the observed increase in diagnosed autism over this time period. They discuss this finding as reflecting diagnostic substitution or accretion, but it is clear that there was almost no substitution. Thus, in 95% of the cases the change was from ‘pure’ MR to MR plus autism. Figure 3 in King & Bearman indicates a substantial increase in MR between 1992 and 2005, although the proportional increase for autism was greater. Most of the rise applied to ‘pure’ autism, about a quarter to ‘pure’ MR being changed to MR and autism, and very little to MR being replaced by autism. In other words, the main change in diagnostic practice concerned an increased willingness to note co-morbidity. Given that the increase in ‘pure’ autism between 1992 and 2005 was huge (from 4446 to 28046 cases)—a much greater rise than for co-morbidity (3210–10410), it is dubious whether the latter increase does much to help in resolving the key basic issue of whether there has been a true increase over time in the incidence of autism.

That is particularly so when the available evidence suggests that the main rise has not predominantly involved autism associated with intellectual disability; rather, it seems to have particularly involved autism in individuals with non-verbal IQ in the normal range.\(^2\) King and Bearman quite properly pointed out that they could not examine that suggestion in their dataset. Nevertheless, the consequence is that their main focus was off-target with respect to the observed rise.

Almost all reviews have concluded that a substantial part of the rise in the rate of diagnosed autism has been due to a combination of better ascertainment and a broadening of the diagnostic concept, but has there been, in addition, a true rise in incidence? In my view, we simply do not know.\(^2\) The rise has been seen in Europe, the USA and Japan, but there is a geographic variability in whether the main rise began in the 1970s and 80s, or rather in the 1990s. The claims that the so-called ‘epidemic’ of autism was due to either the measles–mumps–rubella (MMR) vaccine or mercury-containing preservative thimerosal that used to be present in many vaccines are not supported by the evidence. Most crucially, in Japan, where MMR was discontinued at a time when it remained in wide use in other countries, the removal of MMR was not followed by any fall in the rate of autism, or even by a reduction in the rate of rise.\(^3\) Similarly, the discontinuation of use of thimerosal in Scandinavia was not followed by any change in the rising rate of autism.\(^4\)

Nevertheless, these findings do not rule out a risk effect from other prenatal or postnatal toxins or other hazards. Large-scale prospective epidemiological/longitudinal studies with good biological measures and good diagnostic procedures are needed to test that possibility. The ongoing MoBa study of mothers and...
babies in Norway constitutes one good example of what is needed in that connection.\textsuperscript{5}

It should be added that the factor responsible for a real rise in autism (if that truly has occurred) need not necessarily be a specific environmental hazard. The trigger could be a rising age of parenthood, given the evidence that high paternal age is associated with an increased rate of autism in the offspring.\textsuperscript{6} How might that operate? One possibility is that it increases the rate of developmental perturbations such as copy number variation (i.e. submicroscopic substitutions or deletion)\textsuperscript{7} or minor congenital anomalies or chromosomal anomalies, all of which have been found to be more common in autism.

Whilst there is value in considering the role of changing concepts and better ascertainment in the observed rise in the rate of diagnosed autism, and there is still uncertainty on whether or not there has been a true rise in incidence, the greater the need is for hypothesis-testing focused research on possible causal mechanisms that could lead to changes in incidence.

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References