Neurotoxicology

Fluoxetine (Prozac) use in children: working towards a customised approach

Dr Mari Golub from the Environmental Toxicology Department at the University of California at Davis, has recently completed a five-year research project looking at the behavioural effects of fluoxetine (Prozac) on brain development. Her findings, which have so far been published in eight academic papers, supplement information on the safety of fluoxetine use in children, and show for the first time that an individual’s genetic make-up can influence their reactiveness to the drug.

Fluoxetine therapy has been used to treat children with Major Depressive Disorder (MDD) and Obsessive Compulsive Disorder (OCD) for over 14 years in the USA, and its use has recently been expanded to other behaviour disorders, including Attention Deficit Hyperactivity Disorder (ADHD), anxiety and autism. The drug, which has been used in adults since 1987, was approved for use in children by the US Food & Drug Administration (FDA) in 2003, following a 19-week clinical trial in children. Apart from the findings of this trial, and those from a later toxicology study in rats, experiments evaluating the safety of fluoxetine use in children are limited. Dr Golub’s work has focused on the potential adverse effects of fluoxetine on brain development, using the juvenile rhesus monkey as a model.

Monkeys were given a dose of fluoxetine each day for two years before the onset of puberty. The dose used was selected because it produced comparable levels of fluoxetine and its metabolites in the monkeys’ blood serum as found in the blood serum of children successfully treated with the recommended dose of 20 mg per day. The monkeys were assessed for growth, impulsivity, activity, sleep, social interaction, attention and emotional response, after one and two years of dosing.

RESPONSES: BEHAVIOURAL AND BIOLOGICAL
The results showed that monkeys treated with fluoxetine had poor sustained attention, were more impulsive, had more disrupted sleep and displayed more social interaction compared to vehicle-treated controls (counterparts who received a sham preparation with no active ingredient). These results confirmed some previously described effects of fluoxetine in adults and children. More startling, and entirely new, was the observation that behavioural responses to fluoxetine were influenced by variations in the monkeys’ genes.
The biomarkers were correlated with impulsivity – a behavioural test affected by fluoxetine after one year of treatment.