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Severe psychiatric symptoms associated with paroxetine withdrawal

SIR—To date, selective serotonin reuptake inhibitor (SSRI) withdrawal syndrome has been described predominantly in terms of physical symptoms.[1] We have observed two cases of transient behavioural syndromes with severe aggressive and suicidal impulsivity subsequent to paroxetine withdrawal.

Two healthy white men, aged 36 and 48 years, participated in a controlled double-blind clinical trial of paroxetine treatment for stuttering. Both had a history of brief episodes of minor depression. After completing a 6-week treatment period with 50 mg paroxetine, both men went into a placebo phase. In the first case, 2 days after abrupt drug discontinuation, the subject reported hypomanic-like symptoms, including hyperactivity, decreased need for sleep, and irritability that developed into agitation, aggressiveness, and volatility. After 2 weeks of fluctuating symptoms, he experienced ego-dystonic impulsive behaviour such as shoplifting and suicidal impulses and gestures. All symptoms abated spontaneously after 2½ weeks. In the second case, paroxetine was tapered over a 12-day period. The first week of withdrawal was notable for an uncharacteristic feeling of confidence and optimism, talkativeness, and a subjective feeling of sharpened and quickened thought processes. During the 2nd week, the patient developed physical symptoms of dizziness, blurred vision, nausea, lethargy, and insomnia. He also reported feeling angry, irritable, and short-tempered, with some highly atypical explosive vocal outbursts and tantrums. He became preoccupied with homicidal thoughts and plans, initially directed towards acquaintances and later towards his own children. These became so intense and ego-dystonic that he contemplated suicide. Physical and behavioural symptoms lasted about 9 days and then remitted spontaneously over 2–3 days.

In these two instances, men without a history of major psychiatric disorder developed severe behavioural symptoms when paroxetine was withdrawn. The first few days were characterised by predominantly hypomanic features followed by a period of escalated ego-dystonic aggression, behavioural dyscontrol, and suicidal intention. This biphasic symptom pattern is reminiscent of the case of fluvoxamine-precipitated withdrawal hypomania described by Szabadi.[2]

We believe that the serious behavioural symptoms seen in these cases were adverse effects of paroxetine withdrawal. The reaction was possibly triggered by an insufficiently gradual tapering of the drug and may reflect low central serotonin concentrations in "down-regulated" serotonergic systems. Such a deficiency has been implicated in impulsive and aggressive behaviours.[3] One cannot rule out, though, a delayed hypomanic response to paroxetine. Another possibility is that people who stutter may be unusually vulnerable to SSRI withdrawal because of a neurological abnormality. With the growing number of indications for SSRI treatment, clinicians should be aware of a possible serious withdrawal syndrome with prominent psychiatric symptoms consequent to paroxetine discontinuation.

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Occupational flour exposure and screening for coeliac disease

SIR—A *Lancet* commentary[1] suggested that subclinical coeliac disease could be detected in a healthy European population with antigliadin and antiendomysium antibodies. Catassi et al,[2] using commercial immunoassays and relying on cut-offs established by the manufacturer, calculated a prevalence rate of coeliac disease of 0·32% in children in Italy. Sjöberg et al[3] reported a prevalence of nearly 4% of antigliadin IgG and IgA in serum samples from 384 12-year-old Swedish children. These authors used what they considered a test of relatively low sensitivity but high specificity for diagnosis of coeliac disease. In their adult control group (blood donors and middle-aged women), they found IgG and IgA positivity in 1·17 and 1·43%, respectively, while either IgG or IgA positivity was found in about 5% of the population studied, according to their cut-off choice.

However, high levels of IgG and IgA antibodies to gliadin have been reported in patients suffering from disorders other than coeliac disease, such as rheumatoid arthritis.[4] Primary or secondary increased permeability of digestive mucosa allowing increased amounts of antigen to cross the epithelial barrier may explain these findings. Similarly raised concentrations of antigliadin antibodies are found in juvenile chronic arthritis, psoriasis, and IgA nephropathy, and hyperstimulation of the digestive immune system is considered to be the cause.

We studied healthy French workers exposed to flour dust.[5] Specific IgG and IgA antigliadin antibody levels were investigated in serum samples from 158 millers and bakers and from 41 workers from a salt factory, used as a control group. The test we used was technically similar to that used by Sjöberg et al.[2] No subjects had diagnosed or reported clinical signs of coeliac disease. The cut-off determined from healthy coeliac-disease-free controls was chosen as 3 SD above mean. IgG was positive in 37% of exposed subjects, versus 2% in controls, and IgA antigliadin antibodies in 21%, versus 5% in controls.

These data show that serum antigliadin antibodies may also result from high exposure to flour antigens overcoming the usual oral tolerance. These data also indicate that the occupational status of adult individuals with such serum antibodies should be considered in interpreting screening tests in the general population and before further investigations are performed to diagnose coeliac disease.

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