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Violence as a side - effect of antidepressants: Provocation by alcohol

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Objectives: Based on case-reports and epidemiological data, we reported the rare induction of serious violence by antidepressant treatment (PLoS Med 3(9): e372). Given alcohol's prevalence and tendency to disinhibit behaviour, we studied its association with SSRI-induced violence.

Methods: We analyzed some 200 cases drawn from our medicolegal practices, web-based patient discussion lists, and ADR reports to government authorities in Canada and the USA. Assessment was based on standard criteria for drug-effect causality (CIOMS), taking into account apparent sources of bias.

Results: A distinct syndrome of uncharacteristic disinhibition with alcohol was detected in 40 individuals of either sex during treatment with SSRIs or venlafaxine. Outcomes included 12 homicides (2 of which were double), suicide, serious assault, unintended sexual intercourse, and other damaging or markedly embarrassing social behaviour. In the majority of cases, memory for the episode was lacking, often completely so. For most individuals, modest or usual amounts of alcohol were involved, with evidence that these had been well tolerated before antidepressant treatment, and after its discontinuation (challenge-dechallenge). In several cases, re-exposure to the same or related antidepressant reproduced the phenomenon (rechallenge).

Conclusions: We identify a distinct and forensically important interaction between alcohol and SSRI antidepressants. Aggregated pharmacovigilance data (in preparation) corroborate the existence of this phenomenon. We suggest that antidepressant product warnings regarding alcohol, hitherto non-specific and unhelpful, will need to be reconsidered.