Comment on: "Disulfiram-induced *De novo* Convulsions Without Alcohol Challenge: Case Series and Review of Literature" (Kulkarni and Bairy, Indian J Psychol Med, Jul-Sep; 37(3): 345-8, 2015)

Sir,

We read with great interest the recently published article by Kulkarni and Bairy in the Indian J Psychol Med[1] regarding disulfiram (DSF)-induced convulsions in alcoholic patients, and we really find the issue very interesting. However, we would like to comment briefly on this report.

In the aforementioned paper, the authors present eight subjects with alcohol dependence who developed epileptic seizures while under therapy with DSF. Since no other causes of seizures were detected the convulsions were attributed to the use of DSF and the authors concluded that this was a dose-dependent phenomenon. In addition, the main underlying mechanism suggested was the impairment of the metabolism of brain catecholamines, due to inhibition of dopamine-beta-hydroxylase (DBH), a copper-containing glycoprotein enzyme that catalyzes the conversion of dopamine to noradrenaline in the peripheral and central adrenergic neurons.[1]

In a previous work of our laboratory team increasing doses of DSF were administered to Wistar rats and the activity of the hepatic aldehyde dehydrogenase (ALDH) along with the levels of brain catecholamines were determined.[2] ALDH was inhibited by DSF in a dose-dependent way. Similarly, the detected changes in the levels of the brain catecholamines correlated well with the doses applied. As expected, the known inhibitory effect of DSF on DBH[3] resulted in an accumulation of dopamine and a respective decrease of the levels of noradrenaline. However, the lowest dose of DSF produced no effect on brain catecholamines. Our results clearly showed that the hepatic ALDH is highly sensitive to the inhibitory effect of DSF while on the contrary, the levels of brain catecholamines, and hence the activity of DBH, seemed to be more refractory to the action of this drug.

Neurological complications of DSF are usually dose-related and may be reversible if the offending agent is removed early. This has been shown by others[4,5] and was also confirmed by Kulkarni and Bairy.[1] The precise mechanism by which DSF produces its neurotoxic side effects is not fully understood. A key role, however, has been attributed to the inhibition of DBH,[4,5] which was also suggested in the paper of Kulkarni and Bairy.[1]

In conclusion, we suggest that Kulkarni and Bairy should refer our work in their paper, in order to strengthen their findings regarding the dose-dependent nature of DSF-induced convulsions, as well as their assumption toward an implication of DBH inhibition in this phenomenon. In addition, we should keep in mind that DSF affects the level of brain biogenic amines at dose levels higher than those inhibiting the activity of ALDH and it seems reasonable to conclude that there is a safety margin in the dosage of DSF between therapeutic and toxic effects. Therefore, in clinical practice treatment of alcoholic patients with low DSF doses could retain the aversion effect toward ethanol, with a reduced risk of neurotoxicity (e.g., convulsions).

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Conflicts of interest
There are no conflicts of interest.

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