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Letter to the Editor

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Author for correspondence:
*Ahmed Naguy
Email: ahmednagy@hotmail.co.uk

Benzodiazepines in autism spectrum disorder—*wise or otherwise?*

Ahmed Naguy[1]*, Saxby Pridmore[2] and Bibi Alamiri[1]

[1]Al-Manara CAP Centre, Kuwait Centre for Mental Health (KCMH), Jamal Abdul-Nassir St, Shuwaikh, State of Kuwait, and [2]Department of Psychiatry, University of Tasmania, Hobart, Australia

Clinicians are generally reluctant to prescribe benzodiazepines (BDZs) in autism spectrum disorder (ASD) on the ground that children and especially those with neurodisabilities are at a heightened risk of paradoxical reactions. Anticognitive actions of BDZs in this special population with limited cognitive reserve (circa a quarter has comorbid intellectual disability as well) is also detracting.[1]

Although BDZs are by no means a panacea, its use in ASD population may still have some merits to mull over. Apart from a rescue medication in behavioural decompensation, BDZs might address comorbid social or other anxiety disorders that can be difficult to tease out from social deficits in this population, yet ubiquitous in 30% to 40% of cases and largely contributing to functional disability and overall caregiver burden. BDZs can also be both diagnostic and therapeutic for comorbid catatonia in ASD-reported in 4% to 17%.[2]

Aberrant sleep patterns have been reported in 45% to 86% of ASD, BDZs can then ease it out.

Epilepsy has a bimodal distribution in these children; before age of 5 and after puberty—BDZs can safeguard against this possibility as a cause of medical decompensation.

Many children of ASD are commonly prescribed atypical antipsychotics (AAPs; typically risperidone or aripiprazole) for associated severe irritability (tantrums, aggressivity, or self-injurious behaviors). Given young age and diagnostic susceptibility to extrapyramidal side effects (EPS), those children, especially the nonverbal or minimally verbal (low-functioning) might silently experience distressing akathisia, for instance, that can masquerade as behavioral dyscontrol and readily overlooked on clinical grounds. This problem is quite ubiquitous, as we see, notably with generics (vs branded) antipsychotics (Naguy, Personal communication). Use of BDZs can alleviate these EPS.

Pharmacodynamically, BDZs are GABA potentiators. This mechanistically translates into an enhancement of dopamine (DA) blockade and hence, potentiating AAPs use in ASD.

Of related interest, there is a confluence of evidence implicating altered basal ganglia function in the mediation of the restricted and repetitive behaviors in autism.[3] This together with emerging evidence accruing speaking to the idea of GABA dysfunction in autism would give kudos for BDZs as of potential therapeutic value in ASD.

Besides an altered glutamatergic synaptic transmission, dysfunction in the GABAergic system is considered an emerging signature of ASD. As a consequence, an altered balance between excitatory and inhibitory neurotransmission (E/I imbalance) has been proposed to contribute to the pathogenesis of ASD. In mice, elevation, but not reduction of cellular E/I balance within the medial prefrontal cortex was found to elicit impairments in social behavior, and compensatory elevation of inhibitory cell excitability partially rescued social deficits. Several genetic mouse models of ASD show a reduction in the number of cortical GABAergic interneurons, especially the parvalbumin subtype.[4] Thus, increasing GABAergic signaling might improve behavioral outcome by compensating a potentially excessive glutamatergic neurotransmission. In the same vein, the BDZ, clonazepam, has also proven to ameliorate symptoms in preclinical models of neurodevelopmental disorders associated with autism.[5]

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