Major Depressive Disorder in Autism Spectrum Disorder: A Double Whammy

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In contrast to long-upheld clinical lore, major depressive disorder (MDD) is commonplace in the autism spectrum disorder (ASD) population, with lifetime rates 4-fold greater than in the general population and variable prevalence rates ranging from 7%–40%.[1,2] MDD takes a toll on patients with ASD by negatively impacting adaptive functioning and quality of life, adding to caregiver distress, increasing service utilization, and heightening comorbidities and associated suicidality and self-injurious behaviors. Elevated rates of MDD in ASD have been tied to increasing age and average to above-average IQ, using structured clinical interviews and reliance on self-reports.

Assessment and diagnosis of MDD in ASD is quite challenging. Many factors are at play. Diagnostic overshadowing, overlapping phenomenology, and lack of validated psychometric instruments are all contributory.

ASD has a pathoplastic effect on MDD presentation in the form of irritability; dysphoria nervosa; changes in circumscribed interests (decreased pleasure, increased intensity, or a morbid content); increased restrictive, repetitive behaviors; aggression; regression; and decline in self-care and adaptive functioning. Suicidality, self-injurious behaviors, or even catatonia can complicate these presentations.[3] A more typical picture is seen in cognitively able and socially motivated ASD (high-functioning autism).

Vulnerability factors are protean and include inter alia, genetic loading of mood disorders, older age groups, lower ASD severity and higher cognitive abilities, social motivation, comorbid anxiety, degree of social support, and, most importantly, proximal events/allostatic overload (eg, bullying, stigma). A growing body of evidence supports that both ASD and mood disorders are highly heritable genetic pathologies. A pivotal role in the relationship between ASD and mood disorders could be played by serotonin; hyperserotonemia is observed in one-third of this clinical population.[4]

Clinicians should be cognizant of these diagnostic caveats. Symptom overlap between MDD and ASD (eg, irritability, gaze aversion, restricted affective display, neurovegetative signs/symptoms, social shrinkage) is deceptive. Social communication deficits, alexithymia, and poor insight make it difficult for those with ASD to express MDD.[5,6] Cautious use of generic depressive scales is warranted while assessing patients with ASD. The Psychopathology in Autism Checklist[7] has been developed specifically to discriminate between autism and 4 major psychiatric disorders (psychosis, depression, anxiety, and obsessive-compulsive disorder).

Evidence for effective treatment of MDD in ASD is generally limited, although adapted psychotherapies (eg, psychoeducation, hands-on interactive activities, visual analog scales, technology, group therapy) show some promise like cognitive-behavioral therapy in autism and mindful-based interventions. Selective serotonin reuptake inhibitors remain the first-line treatment despite a lack of randomized controlled trials evaluating their efficacy for MDD, particularly in the ASD population. Behavioral activation has frequently been reported in these patients, so close monitoring and slower titration regimens are strongly recommended.[8]

Further studies are sorely needed on the epidemiology, phenomenology, and proper screening tools for MDD in the ASD population. Longitudinal controlled studies are likewise essential to provide evidence-based guidelines for clinicians.

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