Gabapentin for anxiety in autism spectrum disorders: a case series

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Background
Autism Spectrum Disorder (ASD) is a chronic neurodevelopmental condition characterized by impaired reciprocal social interaction and by restricted, repetitive and stereotyped patterns of behaviors or interests [1]. ASD is frequently burdened by medical and psychiatric comorbidities, among which anxiety is one of the most common, affecting nearly 54% of individuals with ASD [2]. Among commonly prescribed anti-anxiety medications (i.e. SSRI), none has been proven extremely effective to treat anxiety in ASD. Gabapentin is an aminoacid derivative of gamma-amino butyric acid (GABA). It was originally developed as an antiepileptic drug, but to date is frequently used to treat anxiety [3] as well as primary insomnia [4]. Despite its effect, gabapentin has never been investigated as an anxiety medication in ASD.

Aim
The present case series evaluated the use of gabapentin in adult patients with ASD who presented a comorbid diagnosis of generalized anxiety disorder (GAD), according to the DSM 5 criteria.

Methods
Three patients were included in the case series. All subjects had significant comorbid anxiety and met the criteria for Generalized Anxiety Disorder (GAD) according to the DSM 5. Two patients were drug naïve, while one was taking carbamazepine for comorbid epilepsy. In order to increase tolerability, gabapentin was started at 300 mg per day and gradually titrated to the reported minimum efficacious dose of 900 mg per day or higher. Maximum dosage was 1200 mg. Improvement was evaluated by means of the Clinical Global Impression-Improvement (CGI-I) scale after four weeks of treatment.

Case description
F, a 20-year-old man, was diagnosed with ASD at 16 years of age. He presented a significantly reduced verbal production with high latency of response to questions without the presence of comorbid intellectual disability (Raven Matrix IQ 128). After 4 weeks of treatment, CGI-I (=1) for anxiety showed a significant improvement, with a significant increase in verbal production. F, a 22-year-old woman, was diagnosed with ASD at 20 years of age (Raven Matrix IQ 128). Apart from GAD, she suffered from severe insomnia. After 4 weeks of treatment, CGI-I for anxiety showed a significant improvement (CGI-I=2), with an improvement also in subjective sleep quality and duration. A, a 26-year-old man, was diagnosed with ASD at 24 years of age. He presented a significantly reduced verbal production without the presence of comorbid intellectual disability (Raven Matrix IQ 128). After 4 weeks of treatment, CGI-I for anxiety showed a significant improvement (CGI-I=1), with a significant increase in verbal production as well as less self-reported difficulties in social interactions. In all patients no significant adverse event was reported, apart from vertigo and dizziness in one patient (F): however, these side-effect disappeared spontaneously after a short period of time and after a reduction of the titration speed.

Conclusions
These data seem to cautiously suggest a potential use of gabapentin for anxiety in ASD. Gabapentin acts on the GABAergic system and literature data have reported the presence of an imbalance between excitatory glutamatergic and inhibitory GABAergic pathways in ASD [5]. However, the exact mechanism of action of gabapentin in ASD remains speculative. Future randomized controlled trials are needed to better elucidate these findings.

References