Valproic acid augmentation in an adolescent with comorbid autism spectrum disorder and obsessive-compulsive disorder: A case report

Elif Betül Aydoğan[1], Zeynep Kübra Göksu[1], Ali Karayağmurlu[2]

[1]M.D., [2]Assoc. Prof., Istanbul University, Istanbul Medical Faculty, Child and Adolescent Psychiatry Department, Istanbul, Türkiye
https://orcid.org/0009-0000-7535-5920-https://orcid.org/0000-0003-4316-5043-https://orcid.org/0000-0001-5464-2891

SUMMARY

Valproic acid is a mood stabilizer and antiepileptic drug that acts through GABA and glutamate. Glutamatergic and GABAergic dysfunction is thought to be a common mechanism in the pathophysiology of autism spectrum disorder and obsessive-compulsive disorder. The use of valproic acid may be effective in treatment-resistant cases of obsessive-compulsive disorder associated with autism.

A 15-year-old male with autism was administered 2 types of SSRIs in appropriate doses and duration separately for OCD. Aripiprazole was added to the treatment of the patient whose obsessive-compulsive disorder symptoms did not decrease. The patient who responded partially to augmentation was started on valproic acid.

The patient's obsessive-compulsive disorder complaints decreased significantly after valproic acid treatment, and his functionality improved. The valproic acid blood level was 68 mg/L. While the Children's Yale Brown Obsessive Compulsive Scale score was 36 points before valproic acid treatment, the score decreased to 19 points after 2 months of valproic acid treatment.

GABAergic agents such as valproic acid may be considered for treatment-resistant obsessive-compulsive disorder in autism.

Key words: Autism, valproic acid, adolescence

INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social communication and interaction, repetitive behaviors, and restricted interests. Children and adolescents diagnosed with ASD are known to exhibit high rates of lifelong comorbidity. One such comorbid condition is obsessive-compulsive disorder (OCD), characterized by the presence of obsessions and compulsions. Previous studies have reported OCD prevalence rates from 17.4% to 37% among individuals with ASD (1,2). More recently, a meta-analysis reported a prevalence of 11.6%, confirming that OCD occurs more frequently in individuals with ASD than in the general pediatric population (3).

Diagnosing OCD in children and adolescents with ASD may be challenging because of difficulties related to insight, communication, and symptom expression, as well as the phenomenological overlap between compulsions and ASD-related repetitive behaviors. Furthermore, interventions that are effective for OCD in neurotypical youth, including psychopharmacological approaches and cognitive behavioral therapy, may have limitations in individuals with comorbid ASD (4,5).

The high prevalence of OCD in individuals with ASD, together with the challenges associated with diagnosis and treatment, represents a significant clinical concern. The co-occurrence of OCD and ASD has been associated with increased symptom severity, greater functional impairment, behavioral

DOI: 10.5505/kpd.2026.32956

Cite this article as: Aydogan EB, Goksu ZK, Karayagmurlu A. Valproic acid augmentation in an adolescent with comorbid autism spectrum disorder and obsessive-compulsive disorder: A case report. Turkish J Clin Psych 2026; 29:250-254

The arrival date of article: 20.02.2026, **Acceptance date publication:** 24.07.2026

Turkish J Clinical Psychiatry 2026;29:250-254

This work is licensed under Creative Commons Attribution-NonCommercial NonDerivatives International License

dysregulation, and reduced quality of life (6,7). Emerging evidence also suggests that the relationship between ASD and OCD extends beyond simple comorbidity, with overlapping neurobiological mechanisms potentially contributing to symptom expression and treatment responses (6,7).

Due to the high rate of comorbidity, diagnostic complexity, and treatment challenges associated with OCD in ASD, further clinical observations may add to our understanding of potential treatment approaches in this population. This report describes an adolescent with comorbid ASD and treatment-resistant OCD who exhibited clinical improvement following valproic acid augmentation in combination with ongoing sertraline and aripiprazole treatment.

CASE

M. D., a 15-year-old male adolescent with ASD, was referred to our clinic due to excessive handwashing behaviors. ASD had been diagnosed at the age of 11 years based on comprehensive clinical and psychometric assessments conducted by two experienced child and adolescent psychiatry residents. His Childhood Autism Rating Scale score was 37.

According to information obtained from the patient and his caregivers, he experienced contamination-related and uncertainty-related obsessions accompanied by washing compulsions and reassurance-seeking behaviors directed toward his mother. A detailed clinical evaluation was performed in the light of the phenomenological overlap between ASD-related repetitive behaviors and OCD compulsions. The patient described contamination and uncertainty-related thoughts perceived as intrusive, distressing, and difficult to control. These symptoms had been present since the age of 14. The patient demonstrated partial insight into the excessive nature of these thoughts and behaviors. His handwashing behaviors were primarily performed to reduce anxiety associated with contamination concerns, rather than for sensory gratification or adherence to routines. Nevertheless, anxiety persisted following the compulsive behaviors, and he preferred to have a parent present while engaging in them.

The compulsions occupied more than one hour per day and resulted in skin irritation secondary to repetitive handwashing, causing clinically significant distress and functional impairment. Following psychiatric evaluation, the patient was diagnosed with OCD. His Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS) score was 36, the Clinical Global Impression Scale Severity (CGI-S) score for OCD was 6, and the Children's Global Assessment Scale (CGAS) score was 33 at baseline.

Fluoxetine treatment was initiated and titrated to 40 mg/day. Medication adherence was regularly monitored during follow-up visits. After 12 weeks with no clinically meaningful response, fluoxetine was discontinued and sertraline treatment was initiated and gradually increased to 100 mg/day. Following eight weeks of sertraline treatment without sufficient improvement and in the context of emerging aggressive behaviors, further dose escalation was considered. However, considering the more heterogeneous and less predictable selective serotonin reuptake inhibitor (SSRI) response observed in individuals with ASD compared with neurotypical populations, aripiprazole 5 mg/day was added to the treatment regimen.

A partial reduction in OCD symptoms was observed following one month of combined sertraline and aripiprazole treatment, although functional improvement remained limited, and his CY-BOCS score remained at 29. Before the initiation of valproic acid augmentation, the patient's height and weight were 163 cm and 54 kg, respectively. Baseline laboratory investigations, including liver function tests and complete blood count, were within reference ranges.

Valproic acid was subsequently added as an adjunctive treatment for persistent OCD symptoms and irritability. The decision to initiate valproic acid was based on its clinical utility in affective and behavioral dysregulation, as well as its putative effects on excitatory–inhibitory balance, which is considered relevant in both ASD and OCD pathophysiology. The dose was gradually increased to 500 mg/day.

Substantial clinical improvement was reported at one-month follow-up following valproic acid initiation, with no adverse effects being observed. The patient's serum valproic acid level was 68 mg/L. His CY-BOCS score decreased to 19 and the CGI-S score to 4, while the CGAS score rose to 60. A 47.2% decrease in the CY-BOCS score compared to the baseline and a significant decrease in the patient's complaints were interpreted as representing a significant response to treatment. However, due to the concomitant use of sertraline and aripiprazole, as well as the possibility of delayed or cumulative treatment effects, the specific contribution of valproic acid cannot be determined exactly. The patient continues to attend follow-up visits every two months while maintaining the current treatment regimen.

Written informed consent was obtained from the patient's parents for the publication of this report, and assent was obtained from the subject.

DISCUSSION

This report describes an adolescent with comorbid ASD and OCD who exhibited clinical improvement following valproic acid augmentation in the context of ongoing sertraline and aripiprazole treatment. Current clinical guidelines for the psychopharmacological treatment of pediatric OCD recommend adequate trials of at least two SSRIs before considering augmentation strategies (8). Augmentation with agents from different pharmacological classes, including antipsychotics, antidepressants, antiepileptic medications, and other agents, has been described in treatment-resistant cases (9).

The neurobiology of OCD has been strongly linked to dysfunction within the cortico-striato-thalamo-cortical circuits. Hyperactivity of the orbitofrontal cortex and striatum is thought to contribute to impaired inhibitory control over intrusive thoughts and compulsive behaviors (10,11). In addition, increasing evidence suggests that abnormalities in glutamatergic neurotransmission may play an important role in the pathophysiology of OCD (12).

In contrast, ASD has been conceptualized as a neurodevelopmental disorder characterized by atypical synaptic development and altered patterns of brain connectivity. Neuroimaging studies have demonstrated abnormalities in both long-range and local functional connectivity, supporting models of disrupted network integration in the disorder (13). Disturbances in excitatory–inhibitory balance, particularly involving glutamatergic and GABAergic systems, have also been implicated in the emergence of restricted and repetitive behaviors (12).

Although ASD and OCD differ in terms of their developmental origins and clinical manifestations, growing evidence suggests that both disorders involve abnormalities within overlapping fronto-striatal networks. Neuroimaging studies have demonstrated associations between frontostriatal functional connectivity and repetitive behaviors across both disorders (14). Shared alterations in glutamatergic and GABAergic neurotransmission may therefore contribute to the clinical overlap between compulsions in OCD and restricted or repetitive behaviors in ASD (12).

This overlap provided a potential neurobiological rationale for considering valproic acid augmentation in the present case. Valproic acid exerts effects on both GABAergic and glutamatergic neurotransmission and has previously been investigated in relation to repetitive behaviors in ASD (15). Other glutamatergic agents, such as memantine, were not employed in the present case since evidence supporting their efficacy in pediatric OCD remains limited and their use in this population is largely off-label. Topiramate was avoided due to concerns regarding potential adverse cognitive effects. In addition, clomipramine was not considered appropriate in light of concerns regarding the existing polypharmacy burden and the potential for adverse cardiac effects.

Published reports regarding the use of valproic acid in OCD remain scarce, particularly in pediatric patients with comorbid ASD and OCD. Ekinci et al. described rebound compulsive behaviors following abrupt discontinuation of valproate in a child with ASD, suggesting a possible associa-

tion between valproate treatment and compulsive symptoms, although the patient was not formally diagnosed with OCD (16). Corá-Locatelli et al. reported clinical improvement in an adult patient with OCD who received valproate monotherapy following discontinuation of fluoxetine due to intolerance (17). In addition, Deltito et al. reported that valproate pretreatment facilitated subsequent tolerance of standard OCD treatments in a small group of treatment-resistant patients and was associated with symptom improvement (18).

The present case differs from these reports in that it involves an adolescent with formally diagnosed comorbid ASD and OCD. Although the observed reduction in CY-BOCS scores and improvement in functioning are broadly consistent with previous reports, these findings should be interpreted with caution. Our patient received concomitant sertraline and aripiprazole treatment, and delayed or cumulative treatment effects cannot be excluded. Furthermore, sertraline had not reached the maximum recommended dose for OCD. Causal inferences regarding the specific contribution of valproic acid cannot therefore be made on the basis of this single, uncontrolled case.

Valproic acid is an antiepileptic agent with mood-stabilizing properties that has occasionally been used off-label as an augmentation strategy in adult psychiatric disorders, including OCD. However, evidence regarding its use in pediatric OCD, particularly in children with comorbid ASD, remains limited. The present case represents a preliminary clinical observation regarding the potential role of valproic acid augmentation in treatment-resistant OCD symptoms in an adolescent with comorbid ASD. However, these findings should be interpreted with caution, since the patient received concomitant sertraline and aripiprazole treatment, and delayed or cumulative treatment effects cannot be excluded. Further studies are now needed to clarify the efficacy and safety of valproic acid augmentation in this population.

Correspondence address: M.D., Elif Betul Aydogan, Department of Child and Adolescent Psychiatry, Istanbul University, Istanbul Medical Faculty, Istanbul, Türkiye
eaydogan@istanbul.edu.tr

REFERENCES

1. Van Steensel FJ, Bögels SM, Perrin S. Anxiety disorders in children and adolescents with autistic spectrum disorders: a meta-analysis. Clin Child Fam Psychol Rev. 2011;14:302-317.

2. Leyfer OT, Folstein SE, Bacalman S, Davis NO, Dinh E, Morgan J, Tager-Flusberg H, Lainhart JE. Comorbid psychiatric disorders in children with autism: interview development and rates of disorders. J Autism Dev Disord. 2006 Oct;36(7):849-61. doi: 10.1007/s10803-006-0123-0. PMID: 16845581.

3. Aymerich C, Pacho M, Catalan A, Yousaf N, Pérez-Rodríguez V, Hollocks MJ, Parellada M, Krebs G, Clark B, Salazar de Pablo G. Prevalence and Correlates of the Concurrence of Autism Spectrum Disorder and Obsessive Compulsive Disorder in Children and Adolescents: A Systematic Review and Meta-Analysis. Brain Sci. 2024 Apr 13;14(4):379. doi: 10.3390/brainsci14040379. PMID: 38672028; PMCID: PMC11048346.

4. Murray K, Jassi A, Mataix-Cols D, Barrow F, Krebs G. Outcomes of cognitive behaviour therapy for obsessive–compulsive disorder in young people with and without autism spectrum disorders: a case controlled study. Psychiatry Res. 2015;228(1):8-13.

5. Martin AF, Jassi A, Cullen AE, Broadbent M, Downs J, Krebs G. Co-occurring obsessive–compulsive disorder and autism spectrum disorder in young people: prevalence, clinical characteristics and outcomes. Eur Child Adolesc Psychiatry. 2020;29(11):1603-1611.

6. Dell'Osso L, Amatori G, Bonelli C, Nardi B, Massimetti E, Cremone IM, Pini S, Carpita B. Autism spectrum disorder, social anxiety and obsessive-compulsive disorders: beyond the comorbidity. BMC Psychiatry. 2025;25(1):37.

7. Jassi AD, Vidal-Ribas P, Krebs G, Mataix-Cols D, Monzani B. Examining clinical correlates, treatment outcomes and mediators in young people with comorbid obsessive-compulsive disorder and autism spectrum disorder. Eur Child Adolesc Psychiatry. 2023;32(7):1201-1210.

8. Geller DA, March J. Practice parameter for the assessment and treatment of children and adolescents with obsessive-compulsive disorder. J Am Acad Child Adolesc Psychiatry. 2012;51(1):98-113.

9. Del Casale A, Sorice S, Padovano A, Simmaco M, Ferracuti S, Lamis DA, et al. Psychopharmacological treatment of obsessive-compulsive disorder (OCD). Curr Neuropharmacol. 2019;17(8):710-736.

10. Calzà J, Gürsel DA, Schmitz-Koep B, Bremer B, Reinholz L, Berberich G, Koch K. Altered Cortico-Striatal Functional Connectivity During Resting State in Obsessive-Compulsive Disorder. Front Psychiatry. 2019 May 10;10:319. doi: 10.3389/fpsyt.2019.00319. PMID: 31133898; PMCID: PMC6524661.

11. Menzies L, Chamberlain SR, Laird AR, Thelen SM, Sahakian BJ, Bullmore ET. Integrating evidence from neuroimaging and neuropsychological studies of obsessive-compulsive disorder: the orbitofronto-striatal model revisited. Neurosci Biobehav Rev. 2008;32(3):525-49. doi: 10.1016/j.neubiorev.2007.09.005. Epub 2007 Oct 17. PMID: 18061263; PMCID: PMC2889493.

12. Naaijen J, Zwiers MP, Amiri H, Williams SCR, Durston S, Oranje B, Brandeis D, Boecker-Schlier R, Ruf M, Wolf I, Banaschewski T, Glennon JC, Franke B, Buitelaar JK, Lythgoe DJ. Fronto-Striatal Glutamate in Autism Spectrum Disorder and Obsessive Compulsive Disorder. Neuropsychopharmacology. 2017 Nov;42(12):2456-2465. doi: 10.1038/npp.2016.260. Epub 2016 Nov 21. Erratum in: Neuropsychopharmacology. 2017 Nov;42(12):2466-2467. doi: 10.1038/npp.2017.163. PMID: 27869141; PMCID: PMC5645732.

13. Zikopoulos B, Barbas H. Altered neural connectivity in excitatory and inhibitory cortical circuits in autism. Front Hum Neurosci. 2013;7:609.

14. Akkermans SEA, Rheinheimer N, Bruchhage MMK, Durston S, Brandeis D, Banaschewski T, Boecker-Schlier R, Wolf I, Williams SCR, Buitelaar JK, van Rooij D, Oldehinkel M; TACTICS consortium. Frontostriatal functional connectivity correlates with repetitive behaviour across autism spectrum disorder and obsessive-compulsive disorder. Psychol Med. 2019 Oct;49(13):2247-2255. doi: 10.1017/S0033291718003136. Epub 2018 Oct 26. PMID: 30362446.

15. Hollander E, Soorya L, Wasserman S, Esposito K, Chaplin W, Anagnostou E. Divalproex sodium vs placebo in the treatment of repetitive behaviours in autism spectrum disorder. Int J Neuropsychopharmacol. 2006;9(2):209-213.

16. Ekinci Ö, Çelik T, Toros F. Otistik çocuk hastada valproatın ani kesilmesine bağlı rebound kompulsif davranışlar. İzmir Dr Behçet Uz Çocuk Hast Derg. 2013;3(1):71-74

17. Corá-Locatelli G, Greenberg BD, Murphy DL. Valproate monotherapy in an SRI-intolerant OCD patient. J Clin Psychiatry. 1998;59(2):207-208.

18. Deltito JA. Valproate pretreatment for the difficult-to-treat patient with OCD. J Clin Psychiatry. 1994;55(Suppl):30-33.