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COGNITIVE IMPROVEMENTS WITH VORTIOXETINE IN SCHIZOPHRENIA: A CASE REPORT

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INTRODUCTION

Cognitive dysfunction is a core feature of schizophrenia, with the patients reportedly scoring 1.5-2.5 standard deviations below healthy-controls across various cognitive assessments (Keefe 2014). The cognitive deficits may develop independently during any phase, including the premorbid and the prodromal stage (Bruno et al. 2020; Keefe 2014), or secondary to the positive, negative and depressive symptoms of the illness (Keefe 2014).

Currently, there is no potent pharmacotherapy for cognitive dysfunctions. Antipsychotics may be useful to some degree by lowering the positive symptoms, but their anticholinergic side-effects can exacerbate cognitive deficiencies (Rehse et al. 2016). Moreover, studies on adjunctive treatments with pro-cognitive agents targeting *N*-methyl-D-aspartate, nicotinic and dopaminergic receptors or anti-inflammatory and antioxidant pathways are sparse and less encouraging (Bruno et al. 2020). Vortioxetine is a serotonin modulator with proven pro-cognitive effects in depression. Moreover, the cognitive improvements with vortioxetine are reportedly independent of its effects on depressive symptoms (Frampton 2016). However, the cognitive effects of vortioxetine have been less studied in schizophrenia. Hereby, we report a case of schizophrenia with cognitive and depressive symptoms benefiting from vortioxetine.

CASE HISTORY

A 22-year-old single male with nil-contributory past, personal or family history with premorbid normal intelligence developed insidious-onset gradually progressive fearfulness, suspiciousness and third-person auditory hallucinations for 8-months, and was diagnosed with paranoid schizophrenia (ICD-10) (Brief Psychiatric Rating Scale, BPRS score 60) (Leucht et al. 2005). The patient was started on risperidone 4mg/d, gradually hiked and maintained at 8 mg/d, on which his psychotic symptoms showed adequate response (BPRS score 46), without any obvious extrapyramidal motor side-effects. The patient also gave a subjective account of persistent slowness in mental activities, difficulty in focusing on complex tasks, forgetfulness, and frequent mistakes during remembering his lessons and calculations, which led him to quit his graduation studies. The subsequent dysfunction and development of insight into the cognitive deficits resulted in the development of low mood, worthlessness and the guilt of becoming a burden to his family over the past 2-months. However, there was no complaint of further deterioration in the cognitive deficits following the development of depression. He was started on Escitalopram, gradually hiked to 15 mg/d with which there was no significant improvement in the mood or cognition.

His present mental status examination revealed depressed affect with poor attention span, recent memory deficits, depressive cognitions, and grade-3 insight. A BPRS score of 41 (moderately ill), Montreal Cognitive Assessment (MoCA) score of 15 (moderate deficits) (Hobson 2015) and Montgomery-Åsberg Depression Rating Scale (MADRS) score of 28 (moderate depression) (Müller et al. 2000) were noted. Given the prominence of neurocognitive deficits in a young individual early in the course of psychosis, we tried to rule out any organic aetiology behind the presentation. However, his brain-imaging and relevant blood reports (complete haemogram, fasting glucose, lipid profile, liver-renal-thyroid function, anti-thyroid peroxidase and Antinuclear-antibody profile) showed normal findings.

Due to minimal psychotic symptoms in the current presentation and the possibility of cognitive slowing/dysphoria due to a higher dose of antipsychotic, risperidone was reduced to 4 mg/d. Also, due to a lack of improvement in depressive and cognitive symptoms, escitalopram was gradually switched to vortioxetine 10 mg/d, considering its additional procognitive profile. A follow-up after 8-weeks showed marked clinical improvements in cognition (especially in sustained attention, calculation, immediate and recent memory; MoCA: 22), depressive symptoms (MADRS: 14) and illness severity (BPRS: 27, improvement particularly in depressive mood, guilt and somatic concerns). No severe side-effects to vortioxetine were reported, except for infrequent nausea well controlled with oral ondansetron 4 mg *pro re nata*.

DISCUSSION

The described patient was a case of first-episode schizophrenia with cognitive deficits and depressive symptoms. The cognitive deficits were prominent in the

areas of sustained attention, calculations, working memory and processing speed, which fall within the ambit of schizophrenia (Keefe 2014). The cognitive dysfunctions probably evolved alongside the paranoid symptoms and got unmasked with the reduction of the active psychotic symptoms. The cognitive deficit profile, including slow information processing, can be due to schizophrenia illness (Keefe 2014). However, the 'mental slowness' seen in our patient could be influenced by the high-dose risperidone (Rehse et al. 2016), although there were no observable extrapyramidal motor symptoms. Furthermore, the cognitive deficits appear unrelated to the depressive features because a) the depressive symptoms appeared later in the course and following the development of insight about the debilities, b) no further deterioration in the cognition was noted following the onset of depression, and c) the cognitive deficits were qualitatively different from that usually described in depression. We reduced the risperidone dose in view of reduced psychotic symptoms at the current presentation and switched over from escitalopram to vortioxetine due to its favourable procognitive profile.

Vortioxetine, like escitalopram, inhibits serotonin-transporter (SERT) and has comparable antidepressant effects. However, it produces greater improvement in cognition (Levada & Troyan 2019) due to its unique actions on the serotonin receptors ($5HT_{1A}$ full-agonism, $5\text{-}HT_{1B}$ partial-agonism, $5\text{-}HT_3$ and $5\text{-}HT_7$ antagonism), which increases the cortical glutaminergic firing by dis-inhibiting γ-aminobutyric acidergic interneurons (Bruno et al. 2020). Though the cognitive benefits of vortioxetine in depression are established, in schizophrenia, there are only anecdotal reports of its procognitive effects in adjunct to lurasidone (Lowe et al. 2018) and clozapine (Bruno et al. 2020).

In our case, there was an improvement in attention, memory and calculation similar to that reported with vortioxetine in previous studies (Harrison et al. 2016). Since depression appeared less likely to influence the cognition of the patient, its alleviation logically has a limited effect on the cognitive improvements. However, there is a possibility of improvement in the patient's 'mental slowness' due to the synergistic effects of vortioxetine and risperidone dose-reduction. Therefore, our experience highlights vortioxetine augmentation as a potential strategy for the improvement of the cognitive dysfunctions in schizophrenia which can be further explored through future RCTs.

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Tathagata Biswas: conceptualization, data collection, first draft.

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Rajeev Ranjan: editing.

Rituparna Maiti: editing, addition of critical intellectual content, writing the final draft.

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