

Letter to the Editor

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We thank Professor Fagiolini et al (2023) for their interest in our review (Masdrakis et al., 2023), and for drawing our attention again to their important previous publication (Fagiolini et al., 2021). Our review mainly addressed reports of the emergence of apathy manifestations as a consequence of treatment with an antidepressant medication, although we also included publications in which treatment strategies to alleviate antidepressant-induced apathy symptoms were proposed. To be included in our review, there had to be strong indications that the apathy symptoms of the sample patients were definitely or most probably due to the antidepressant medication, and not be a reflection of a domain of depressive psychopathology or the result of a comorbid clinical condition.

Our understanding is that patients included in the Fagiolini et al (2021) study were suffering from major depression and were partial responders to SSRI/SNRI treatment: the authors state that their sample included ‘... patients with MDD who experienced inadequate depressive symptom resolution and emotional blunting after treatment with an SSRI or SNRI...’, but they do not stipulate that the emotional blunting was definitely or probably induced by the antidepressant medication used, before switching to vortioxetine. A reader of their paper could plausibly assume that apathy/emotional blunting was either partly or completely due to persisting, residual post-treatment depressive psychopathology. It would also not be fully clear whether the improvement in apathy manifestations after the treatment switch was due to direct effects of vortioxetine on emotional blunting or through its efficacy in reducing the severity of residual symptoms of depression. The authors note that there was no prospective phase before medication switch (in Abstract) and recognise the limitation described above, as follows: ‘... the absence of a prospective phase to study the incidence of emotional blunting during SSRI or SNRI treatment before switching to vortioxetine makes it difficult to establish if the effect observed on emotional blunting was due to the previous antidepressant or due to depression’ (in Discussion: although the authors undertook an exploratory analysis, adjusting for the effects of change in depressive symptom severity).

In their letter, Fagiolini et al suggest that vortioxetine is ‘an antidepressant that may not cause it’ (i.e. apathy), and that vortioxetine is ‘an antidepressant that does not cause emotional blunting’. However, in our review, we included a paper by the same group (Christensen et al., 2022), which suggests that vortioxetine may induce apathy symptomatology. These authors conducted an internet-based survey of 752 patients with major depression in acute or remission phase, currently receiving vortioxetine or another antidepressant (including agomelatine, bupropion, citalopram, desvenlafaxine, duloxetine, escitalopram, fluoxetine, mirtazapine, paroxetine, sertraline or venlafaxine) and who reported emotional blunting during the previous 6 weeks: up to 44% of those receiving antidepressant medication rated their emotional blunting as ‘extremely severe’. Furthermore, this study suggested that when depressive symptoms and apathy manifestations co-exist, patients themselves were divided as to the potential cause of their apathy: 56% of patients considered their emotional blunting to be caused by their depression (acute phase, 62%; remission phase, 52%), whereas 45% of patients believed that antidepressant medication was the cause of their emotional blunting (Christensen et al., 2022).

Another study included in our review explored reviews in three popular health Internet websites concerning vortioxetine and three other antidepressants (duloxetine, escitalopram, vilazodone) among 3243 individuals who reported suffering from anxiety, depression, or bipolar disorders: up to 5.9% of patients receiving vortioxetine reported ‘emotional numbing’ (Hughes et al., 2017).

In conclusion, there are indications from differing groups of academic researchers (Hughes et al., 2017; Christensen et al., 2022) that vortioxetine may induce apathy. For these reasons, we were reluctant to include the study reported by Fagiolini et al (2021) in the section of our review referring to treatment strategies used to alleviate apathy or emotional blunting symptoms induced by an antidepressant medication. This is not, however, to distract from the merits of this important study: rather, replication of it should ideally include a prospective phase before medication switch. In addition, examining the effects of vortioxetine in patients with major depression who have entered symptomatic remission but who are troubled by clinically important apathy should help to clarify matters.



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