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Antidepressants and REM Behavior Disorder

A reply to Kolla BP, Mansukhani MP. Antidepressants trigger an early clinical presentation of REM sleep behavior disorder: the jury is still out. SLEEP 2014;37:1393.

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We thank Drs. Kolla and Mansukhani for their interest in our article and for the opportunity to provide further clarifications.[1] Regarding their suggestion of "antidepressants-as-depression-proxy," it should first be noted that our study in no way tested whether depression is a risk factor or prodromal marker for synucleinopathies. This would require population-based studies, which in fact do suggest that this is the case.[2] Rather, the hypothesis we tested (and found evidence against) spoke only to the relationship between antidepressants and REM behavior disorder (RBD). We found that antidepressants had no direct connection to RBD, but simply represented the presence of another prodromal marker (i.e. depression itself). If this were true, patients with RBD taking antidepressants should have had a higher risk of neurodegeneration, since they now had *two* prodromal markers of disease (i.e. RBD and depression). However, the observed risk was significantly lower.[3] Note that our analysis was adjusted for age, so the younger age in antidepressant users would not explain the difference in disease risk (furthermore, this age difference would actually argue *for* the central hypothesis of antidepressants as symptom triggers of synucleinopathy; if antidepressants trigger early clinical presentation of an otherwise-latent synucleinopathy, these patients would be younger).

We absolutely agree that the temporal relationship between RBD symptom onset and antidepressant use can often be murky. This was the main motivation for choosing all those taking antidepressants at baseline for the primary analysis. This minimized confounding from inaccurate RBD onset history. Regarding presentation history, all patients in our study had a complaint of dream-enactment behavior (and all had PSG confirming diagnosis); we had no asymptomatic patients diagnosed only on PSG.

With regards to an antidepressant-neuroprotective hypothesis, this would certainly be an exciting possibility. Supporting evidence for this hypothesis would likely have to start with findings from population-based studies. We are unaware of any studies linking antidepressants to a lower risk of neurodegenerative disease. Moreover, considering that persons with depression and anxiety are the primary recipients of antidepressants, but have a *higher* risk of neurodegenerative disease, this possibility may be less likely.

The relationship between antidepressants and RBD is complex, and our study is only one piece of evidence pointing towards a potential explanation. No doubt there are additional complexities not yet understood. Moreover, our study can speak only to the predominant mechanism behind antidepressants and RBD; there may be exceptions, including patients for whom antidepressants only marked depression, or who have a "pure" pharmacologic non-neurodegenerative RBD. We greatly encourage further work on this fascinating area of sleep neurology.

Citation

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REFERENCES

1. Kolla BP, Mansukhani MP. Antidepressants trigger an early clinical presentation of REM sleep behavior disorder: the jury is still out. Sleep 2014;37:1393.
2. Postuma RB, Aarsland D, Barone P, et al. Identifying prodromal Parkinson's disease: pre-motor disorders in Parkinson's disease. Mov Disord 2012;27:617–26.
3. Postuma RB, Gagnon JF, Tuineaig M, et al. Antidepressants and REM sleep behavior disorder: isolated side effect or neurodegenerative signal? Sleep 2013;36:1579–85.

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