



Letter to the Editor

Depressive symptomatology, serotonergic activity, and neuroticism: A methodological recommendation



To the Editors:

In a recent positron emission tomography study, [Hirvonen et al. \(2015\)](#) reported a negative correlation between the personality trait neuroticism and serotonin 5-HT_{1A} receptor binding potential (BP) in apparently healthy individuals. Based on the observation that serotonin 5-HT_{1A} receptor density is altered in patients with major depressive disorder, the authors suggest that lowered serotonin 5-HT_{1A} receptor BP may be a trait characteristic. While the efforts of the authors to understand the link between neuroticism and serotonin 5-HT_{1A} receptor BP should be acknowledged, we think that the authors' conclusions should be reconsidered. Indeed, depressive symptomatology was not statistically controlled for in this study.

Neuroticism is known to be positively and strongly associated with depressive symptoms (e.g., [Jylha and Isometsa, 2006](#); [Everaerd et al., 2015](#)). As a result, depressive symptoms constitute a key potential confounder in neuroticism research. Because the authors did not control for depressive symptoms in their statistical analyses, they cannot determine whether neuroticism is independently associated with serotonin 5-HT_{1A} receptor BP. In other words, whether neuroticism explains variance in serotonin 5-HT_{1A} receptor BP that is unaccounted for by depressive symptomatology remains unclear. We noticed that (a) the study participants reported an absence of psychiatric illness and (b) the authors partly verified these declarations using Structured Clinical Interview for DSM-IV Axis I Disorders. However, the presence of subclinical depressive symptoms—whose impact on an individual's life can be significant ([Gotlib et al., 1995](#); [Cuijpers et al., 2013](#))—cannot be ruled out based on such a procedure, leaving the raised problem unresolved.

In our view, this methodological issue should lead to a cautious interpretation of the study results. The authors suggest that lowered serotonin 5-HT_{1A} receptor BP may be a trait characteristic linked to neuroticism. Given the lack of consideration of depressive symptoms in the statistical analyses, the article contributes little to resolving debates over the trait versus state abnormalities related to serotonin function ([Bhagwagar and Cowen, 2008](#)). All in all, further research is needed before conclusions can be drawn

about the link between neuroticism and serotonergic activity.

Neuroticism and depressive symptomatology overlap to such a degree that the distinctiveness of neuroticism with respect to depressive symptomatology has been controversial (e.g., [Farmer et al., 2002](#)). In this context, we suggest that depressive symptomatology should be systematically controlled for in neuroticism research. Importantly, not only the statistical significance but also the size of neuroticism-related effects should be carefully considered, in order to determine whether such effects are of substantial or anecdotal importance once depression is taken into account.

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