

Reply to: Late-Life Depression, Cortisol, and the Hippocampus: On the Need to Consider Depressive, Hippocampal, and Pharmacological Complexities

To the Editor:

We would like to respond to the letter of Dr. Bianchi and Dr. Laurent (1) with regard to our meta-analysis published in *Biological Psychiatry* (2). We think that the three points raised by our colleagues are excellent and important points and also reflect our concerns. First, of the studies included in the meta-analysis, very few studies go beyond age of depression onset in differentiating late-life depression (LLD) subtypes. The recommendation to consider a melancholic depression subtype and a subtype of major depressive disorder with atypical features is important; however, we would like to suggest that studies on LLD should not only consider diagnostic subclassification but also take into consideration symptoms of LLD not fulfilling clinical criteria. For instance, we showed that symptoms of apathy in the absence of depression are related to brain volume reduction in older persons without dementia (3), a relationship that would not been found if the diagnosis of major depressive disorder or a conventional cutoff score on a depressive symptom questionnaire were used. Second, we underscore the recommendation to study the subregions of the hippocampus in relation to LLD and hypothalamic-pituitary-adrenal axis regulation. From our work, we have noted that very few studies have used the recent advances in novel imaging techniques such as 7T magnetic resonance imaging in visualizing hippocampal subfields that may link or differentiate LLD (4). Finally, with respect to medication use, the majority of case-control studies in our meta-analysis included patients who were on antidepressant medication, or medication was not reported. We have shown that antidepressant medication is related to smaller hippocampal volume (5) and increase in white matter hyperintensity volume (6), a relationship that needs further investigation despite its methodological complexity when interpreting these findings.

We thank the authors for the points raised and underscore their invitation to more systematically examine subtypes of LLD, hippocampal complexity, and antidepressant use in the field of neurobiology of depression. Clearly more research is needed, which could increase our understanding

of the etiology and cognitive consequences of depression later in life.

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Acknowledgments and Disclosures

LG is supported by Netherlands Organisation for Scientific Research VENI Grant No. 916-14-016 and Marie Curie intra-European Fellowship of the European Community's Seventh Framework Programme Contract No. PIEF-GA-2011-300355.

The authors report no biomedical financial interests or potential conflicts of interest.

Article Information

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See also associated correspondence: <http://dx.doi.org/10.1016/j.biopsych.2017.04.022>.

Received Jul 1, 2017; accepted Jul 3, 2017.

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