Letter to the Editor

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Is There an Effect of Medications on Neural Response to Threat in Patients Who Have Attempted Suicide? A Response to Lewine

To the Editor,

We thank Dr. Lewine (2018) for raising these important questions. We did not initially test the effects of different classes of medication on the magnitude of the late positive potential (LPP), largely because most patients were taking multiple classes of medication and because more severe dysfunction is often confounded with increased use of multiple medications. Nonetheless, below we outline evidence from our sample regarding the LPP and psychiatric medications.

First, in the study by Dietz et al. (2013) that Dr. Lewine cites, many of the patients with Parkinson's disease were taking antidepressants (unlike the healthy comparison group) and, more importantly, were tested while taking Parkinson's medications (see Levodopa equivalent dosages listed in Table 1 of that publication). Given this, we would not conclude that the observed effect of Parkinson's diagnosis on the magnitude of the LPP in that study can be directly attributed to the effect of dopamine (DA) dysfunction, particularly given prior direct tests of DA receptor agonists and antagonists, which did not find an effect of such medications on the magnitude of the LPP (Franken, Nijs, & Pepplinkhuizen, 2008).

Second, turning to our study (Weinberg et al, 2017), 45 of the 83 attempters were currently taking neuroleptics, as were 40 of the nonattempters. Participants in the attempter group were also taking lithium (n = 7), anxiolytics (n = 19), anticonvulsants (n = 39), antidepressants (n = 66), hypnotics (n = 8), stimulants (n = 5), and "other psychiatric medications" (n = 5). Thirty-six attempters were taking both neuroleptics and antidepressants. Many patients in the nonattempter group were also on multiple classes of medications. The use of multiple medication classes, as well as unknown interactions between medications, makes it difficult to isolate the effects of any single class of medication.

Nonetheless, we first examined the simple effects of classes of medication associated with altered dopamine functioning on the LPP: neuroleptics, stimulants, lithium, and antidepressants. Unlike the patients with Parkinson's disease in Dietz et al. (2013), who differed only in the magnitude of their neural response to unpleasant pictures, in our study, lithium and neuroleptic use were independently associated with a blunted LPP in response to all picture types. This nonspecific blunting combined with the confounding of medication use with more severe psychopathology make it difficult to attribute this effect directly to medication. Antidepressants and stimulants were not significantly associated with the magnitude of the LPP.

Next, we included lithium and neuroleptic use in the repeated measures analysis of covariance examining whether suicide attempts significantly predicted modulation of the LPP, controlling for suicidal ideation. In this analysis, only picture type significantly predicted the magnitude of the LPP; the effect of suicide attempts reported in our article was reduced (from η_p^2 = .02 to .01), and was no longer significant (p = .09). Despite this, use of neither lithium (η_p^2 = .001) nor neuroleptics (η_p^2 = .008) significantly interacted with picture type to predict the magnitude of the LPP, suggesting that the interaction of suicide attempt and picture type that we observed previously was not driven by use of these medications.

Finally, we compared the threat-elicited LPP between the 34 attempters and 111 nonattempters who were not currently taking neuroleptics or lithium. Attempters were characterized by a smaller threat-elicited LPP (M = 4.52, SD = 5.06) compared with the non-attempters (M = 6.58, SD = 5.53), $F(1, 144) = 3.75$, p = .055. The two groups did not significantly differ in the LPP elicited by pleasant or neutral images, consistent with the results reported.

In sum, although attention should be paid to the influence of medication on neural responses, this is often difficult in representative samples. Further, our additional

Corresponding Author:
Anna Weinberg, McGill University, Department of Psychology, 2001 McGill College, Montreal, Quebec H3A 1G1, Canada
E-mail: anna.weinberg@mcgill.ca

analyses demonstrate that, in our study, considering medications does not change the conclusions.

Anna Weinberg
Department of Psychology, McGill University

Alexis M. May
Department of Psychology, University of Utah

E. David Klonsky
Department of Psychology, University of British Columbia

Roman Kotov
Department of Psychiatry, Stony Brook University

Greg Hajcak
Department of Psychology, Florida State University

Author Contributions

All the authors approved the final version of the manuscript for submission. A. Weinberg and A. M. May contributed equally to this work.

Declaration of Conflicting Interests

The author(s) declared that there were no conflicts of interest with respect to the authorship or the publication of this article.

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