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Response to "Cortico-accumbens circuitry in schizophrenia: merely a reward system?" by Rolland and Jardri (SCHRES-14-D-00731)

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To the Editor

We appreciate the interest of Rolland and Jardri in our paper (Fischer et al., 2014). The authors suggest that the circuitry we observed to be abnormal in patients with schizophrenia and cannabis use disorder, that we and others have noted to be involved in reward processing (Blum et al., 2000; Di Martino et al., 2008; Green, 2007) has also been implicated in "other functional (e.g., salience processing) and dysfunctional (e.g., psychosis)" processes. We agree, and as we noted in our paper, that the use of resting state functional connectivity "does not directly measure response to reward, and the brain regions implicated in the brain reward circuit are also involved in processes other than reward." Potentially, future research correlating resting state functional connectivity of the implicated circuitry with analyses of task-based data would be helpful, although others have noted correspondence between resting state networks and task-based findings (Di Martino et al., 2008; Fox and Greicius, 2010; Whitfield-Gabrieli and Ford, 2011)

In their recent publication, Rolland and colleagues (Rolland et al., 2014) linked hallucinations in patients with schizophrenia to connectivity between the nucleus accumbens (NAc), ventral tegmental area (VTA), and a number of other regions generally consistent with what we referred to as the brain reward circuit. Moreover, they noted in their letter that

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Dr. Fischer wrote the first draft of this response letter, and co-wrote the final version with Dr. Green. This letter has been reviewed and approved by all the co-authors.

Conflict of Interest

None

the circuitry that we found to be affected by THC and smoked cannabis has also been implicated in psychosis in schizophrenia, and that cannabis smoking can increase positive symptoms in these patients. As indicated in our paper, however, we noted no global increase in positive or negative symptom severity on the PANSS after cannabis or THC. We recently conducted further analyses on our data, and we found no significant changes in any of the individual positive symptoms of the PANSS, or significant associations between individual positive symptoms and connectivity of reward circuitry, at the dose of THC and the amount of cannabis administered. In our paper, we did propose that the effects of cannabis on reward circuitry may be dose-dependent, and thus it is possible that higher doses of cannabis and THC might have worsened positive symptoms. However, while there are important methodological differences between our study and that of Rolland et al (2014), in our study the modest amount of cannabis smoked (1/2 of a 3.6% THC cigarette) and the relatively low dose of THC administered (15 mg THC pill) improved the functional connectivity between regions of the brain reward circuit, primarily observed between the bilateral NAc and regions of the prefrontal (i.e., ventral anterior cingulate) cortex, without worsening psychosis.

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