Reviewer's report

Title: Cortico-cerebellar functional connectivity and sequencing of movements in schizophrenia

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Reviewer: Neeltje van Haren

Reviewer's report:

The authors focus on the abnormalities that are present in patients with schizophrenia while executing movements in a sequence. As such motor acts require correct integration of cortico-subcortical processes, among others with the cerebellum, the authors assume that abnormal connectivity between cortical and cerebellar regions results in cognitive dysmetria. A total of 29 patients and 29 controls underwent an fMRI experiment performing a modified finger tapping task. In addition the Neurological Evaluation Scale (NESSQ) was administered. Patients with sequencing abnormalities showed less connectivity in motor cortex – cerebellum and supplementary motor cortex – cerebellum relative to patients without these abnormalities. The authors conclude that abnormal cortico-cerebellar functional connectivity is linked with movement sequencing abnormalities in schizophrenia, but not with the diagnosis of schizophrenia per se.

This is an interesting approach and studies involving the cerebellum are relatively rare. I have a few issues:

Introduction:
The authors introduce a rather narrow definition of neurological soft signs, i.e. “Abnormalities of the motor system…” while in my opinion neurological soft signs are minor neurological signs indicating non-specific cerebral dysfunction. Please rephrase this.

Method:
Exclusion criterion is drug dependence. Table 1 shows 7 patients with abuse. Can the authors explain this? I suppose those with drug abuse (not dependence) were included. Which scale was used? Also, what kind of abuse is present among these 7 patients?

Can the authors explain what the motor rest-condition means? Does this come close the resting-state fMRI? This is important as activation patterns while sequential tapping were contrasted to the motor rest condition. On page 10 the authors refer to resting state functional connectivity parameters having the largest discriminative value for classification of schizophrenia patients and controls. Isn’t this effect removed from the data by the correction for the motor rest condition? If so, the statement in the conclusion that abnormal connectivity is
not linked with the diagnosis of schizophrenia per se lacks validity. In other words, were there differences between the groups during the motor rest condition? If not, how does it relate to the paper the authors refer to?

Can the authors elaborate (in the discussion) on the validity and (clinical) significance of the seeds that were used in the analyses?

Can the authors explain why a median split was used to categorize the patients in two groups instead of using the expression of movement sequencing abnormalities as a continuous variable?

Results:
I do not understand the sentence on differences in education: “Healthy controls had more frequently university…..more frequently primary education (…)”. I suppose all controls who went to university also had primary education. Please rephrase.

In the results groups are compared on several scales (BAS, SAS, AIMS) that were not described in the method section. Provide a rationale for administering these scales, also in discussion.

Discussion:
Last sentence of first paragraph, add: “Which means, abnormal cooperation between cerebellum and motor cortex during a motor task manifest itself by impaired ability to sequence movements in time.”

Typo’s
Introduction: second paragraph, one before last sentence: have should be has.
Page 8, first paragraph, change sentence: “however, SQ+ patients more frequently had at least….”
Discussion starts with 1.
Page 10, 2nd paragraph: start new sentence with “Moreover, there is evidence…..”.
Check typo in reference list: ref 2

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.