Reviewer’s report

Title: Autism, Spectrum or Clusters? An EEG Coherence Study

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Reviewer: Federico Sicca

Reviewer’s report:

In this manuscript, the authors propose a cluster analysis of 40 EEG-coherence features, which they obtained in their previous research demonstrating a reliable separation between individuals in the autism spectrum and neurotypical controls. The 40 EEG coherence parameters were applied in this study to a large sample of subjects with ASD (n=430), and the optimal cluster number was established using the recently published software package NbClust. The Authors identified two distinct clusters among subjects with autism, which in turn differed sharply from a large control sample (n=554) not involved in the clustering process.

The main value of this interesting work is, in my opinion, that the two-cluster distribution, based on objectively detected neurophysiological parameters, once again suggests that ASD does not exist on a continuous spectrum, but rather consists of discrete sub-populations. The different clinical, neuropsychological, and behavioral patterns seen in clinical practice and, too often, simplistically incorporated under the unitary umbrella of autism spectrum disorders, likely reflect in fact distinct pathophysiologies, as well as different genetic and epigenetic mechanisms leading to ASD.

The limitations of the study are also well described by the authors, in particular the lack of clinical parameters, such as neuro-behavioral and MRI data, that could have validated the EEG-based clustering.

I think, however, that two further points should be added, and more clearly discussed in the "limitation" section of the manuscript.

First, the degree of intellectual disability since it is a domain that, similarly to the core neurobehavioral dysfunctions of autism, may influence neural complexity and, ultimately, the coherence features and clustering.

Second, in order to reliably exclude the presence of epileptiform activity, which potentially influences brain network organization and coherence features, a sleep EEG would have been necessary. Research by myself (Valvo et al., Eur Child Adolesc Psychiatry, 2016) and others (Chez et al, Epilepsy Behav, 2006; Hrdlicka et al., Eur Child Adolesc Psychiatry, 2004; Mulligan et al, J Autism Dev Disord, 2014) have shown that EEG abnormalities can only be seen during sleep, in up to 59% of children with ASD. I think this is an important limitation to discuss, considering the potential clustering role of epileptic activity (Cuccaro et al, 2012; Hrdlicka, 2005), which may escape an EEG assessment only based on an awake recording.
Minor considerations: a typo at page 8 line 33 (best represent best) should be corrected.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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Please indicate the quality of language in the manuscript:

Acceptable

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