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Jesse Mu

REVIEW FORUM   Submitting Author

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Parkinson's Disease Subtypes Identified from Cluster Analysis of Motor and Non-Motor Symptoms

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Original Research, Front. Aging Neurosci.
Submitted on: 01 Aug 2017, **Edited by:** Atsushi Takeda ✉

Keywords: Parkinson's disease, subtypes, non-motor symptoms, Motor symptoms, Cluster analysis

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History	Reviewer 1 Active	Reviewer 2 Active

Reviewer 2
Independent review report submitted: 20 Aug 2017
Interactive review activated: 20 Aug 2017

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▼ S1. GENERAL EVALUATION

▼ ARTICLE TYPE

Q 1 ▷ **Does this manuscript conform to the definition below of Original Research articles? If not, please contact the Frontiers Editorial Office (editorial.office@frontiersin.org).**

Original Research articles report on primary and unpublished studies and should describe the aims and hypothesis, methods, results and interpretation of the research. Original Research articles may also encompass confirming studies, as well as disconfirming results which allow hypothesis elimination, reformulation and/or report on the non-reproducibility of previously published results. The manuscript should include the following: Abstract, Introduction, Material and Methods, Results, Discussion.

👤 **Reviewer 2** | 20 Aug 2017 | 10:42   #1

Yes

[Add comment]

▼ LANGUAGE AND GRAMMAR

Q 2   Is the language, specifically the grammar, of sufficient quality? If no, please specify if the authors should send this manuscript to an expert in English editing and academic writing.

Reviewer 2 | 20 Aug 2017 | 10:42   #1

Yes

[Add comment]

MAIN MESSAGE

Q 3   What are the main findings reported in this manuscript?

Reviewer 2 | 20 Aug 2017 | 10:42   #1

The manuscript examines motor- and non-motor symptom groups in Parkinson's disease with a view of assessing symptom-dominant clusters and inter-correlates.

[Add comment]

S2. INDIVIDUAL SECTIONS

TITLE

Q 4   Does the title clearly and precisely reflect the findings of the manuscript, as described in the author guidelines?

Reviewer 2 | 20 Aug 2017 | 10:42   #1

Yes

[Add comment]

ABSTRACT

Q 5   Please comment on the Abstract section. Key elements to consider:
– **appropriateness of context**
– **purpose of study**

Reviewer 2 | 20 Aug 2017 | 10:42   #1

The abstract is appropriate in the context of the manuscript.

[Add comment]

INTRODUCTION

Q 6   Please comment on the Introduction section. Key elements to consider:
– **appropriateness of context**
– **purpose of study**

Reviewer 2 | 20 Aug 2017 | 10:42   #1

The introduction is well-written and is appropriate for the study. My only comment is that postural instability/ gait disorder was omitted as a classical symptom in PD (page 1, line 36)

[Add comment]

MATERIAL AND METHODS

Q 7   Please comment on the Material and Methods section. Key elements to consider:
– **objective errors**
– **correct choice of methods**
– **comprehensive description of methods**
– **accuracy of procedures**
– **quality of figures and tables**

Reviewer 2 | 20 Aug 2017 | 10:42   #1

The approach using cluster analysis has been used in other studies in a similar context.

The quality of figures and tables are appropriate.

> Add comment

Q 8   Are the statistical methods used valid? Key elements to consider:
– appropriateness of statistical test applied
– statistics applied on independent experiments (biological replicates)
– sample size
– statistical significance
– error bars

Reviewer 2 | 20 Aug 2017 | 10:42   #1

Yes

> Add comment

Q 9   Have any ethical issues been identified in the proposed methodology?

Reviewer 2 | 20 Aug 2017 | 10:42   #1

No

> Add comment

Q 10   For research involving human subjects or animals, do the author(s) identify the committee approving the study and have all patients provided their written informed consent?

Reviewer 2 | 20 Aug 2017 | 10:42   #1

Yes

> Add comment

Q 11   For research involving biohazards, biological select agents, toxins, restricted materials or reagents, have the standard biosecurity or institutional safety procedures been carried out?

Reviewer 2 | 20 Aug 2017 | 10:42   #1

Not Applicable

> Add comment

▼ RESULTS

Q 12   Please comment on the Results section. Key elements to consider:
– objective errors
– correct presentation of results
– quality of figures and tables

Reviewer 2 | 20 Aug 2017 | 10:42   #1

The presentation of the results, and quality of figures and tables are appropriate

> Add comment

▼ DATA COMPLIANCE

Q 13   For any complementary data (e.g. nucleotide/amino acid sequences, crystallographic or NMR data, RNAseq) submitted to an online repository or database, do the author(s) provide the accession number?

Reviewer 2 | 20 Aug 2017 | 10:42   #1

Not Applicable

> Add comment

Q 14 ▶ **For any grouped images (gels, blots, etc), are the original images provided in the supplementary material?**

👤 **Reviewer 2** | 20 Aug 2017 | 10:42   #1

Not Applicable

[Add comment]

▼ **DISCUSSION**

Q 15 ▶ **Please comment on the Discussion section. Key elements to consider:**
– adequate discussion of research questions or hypothesis (posed in introduction)
– conclusions supported by data
– exhaustive discussion of previously published material (in context to current study)

👤 **Reviewer 2** | 20 Aug 2017 | 10:42   #1

Do the authors need to factor in cognitive impairment into the clusters and also acknowledge this as a potential weakness in the study?

In paragraph 3, page 6 (of Discussion), the authors state that the initial depression and anxiety scores for cluster D2 have a general improvement, and juxtaposed this with an 'untreated' PD cohort. I believe the immediate study group would have participants who have been treated for PD +/– depression, thus making this conclusion inaccurate.

The discussion does reference only a few papers that assess similar subject matter. It may be worth expanding the discussion to factor in current hypotheses of disease. e.g. Braak hypothesis, prion hypothesis, non–dopaminergic dysfunction in PD (i.e. could some of the clusters described represent this? i.e. a minority group of patients that clinicians have noted to be 'resistant' to dopamine replacement therapy even in early stage disease). There is a good body of evidence that has assessed synergistic pathological burden (i.e. tau– and amyloid burden in–conjunction with synuclein), synuclein propagation, neurotransmitter dysfunction, pathological burden by distribution resulting in symptoms (e.g. visual hallucinations), etc.

[Add comment]

▼ **REFERENCES**

Q 16 ▶ **Is prior work properly and fully cited?**

👤 **Reviewer 2** | 20 Aug 2017 | 10:42   #1

Yes

[Add comment]

▼ **S3. FINAL COMMENTS**

Q 17 ▶ **Please provide your further comments and overall recommendation to the authors, including the level of revisions (minor, moderate, substantial).**

👤 **Reviewer 2** | 20 Aug 2017 | 10:42   #1

The senior authors are established in the field of Parkinson's research. The manuscript is overall well–written and approaches a subject matter that is especially relevant as our understanding expands in Parkinson's.

Minor revision recommended

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