

REVIEW FORUM

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1. Submission

2. Independent
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Review

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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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ON TIME

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History

Reviewer 1
Active

Reviewer 2
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Reviewer 1

Independent review report submitted: 09 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Original Research articles report on primary and unpublished studies and should describe the aims and hypothesis, methods, results and interpretation of the research.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 1 | 09 Aug 2017 | 01:56

#1

Yes

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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 1 | 09 Aug 2017 | 01:56

#1

Yes

Add comment

MAIN MESSAGE

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

Reviewer 1 | 09 Aug 2017 | 01:56

#1

This study is the largest cluster analysis of PD-related motor and non-motor symptoms (NMS) from large international multi-centre cohorts. According to the authors, this is the first study to perform cluster analysis exclusively on NMS to reveal NMS-specific subtypes. From the NMS clustering, six small clusters were identified as follows, S1, mild (similar to D1) ; S2, RLS, pain and others ; S3, significant urinary dysfunction ; S4, high mood/apathy symptoms ; S5, cognitive impairment ; S6, autonomic (cardiovascular and gastrointestinal) symptoms. Many of these subtypes are newly reported.

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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 1 | 09 Aug 2017 | 01:56

#1

Yes

Add comment

ABSTRACT

Q 5 Please comment on the Abstract section. Key elements to consider:

- appropriateness of context
- purpose of study

Reviewer 1 | 09 Aug 2017 | 01:56

#1

Key elements, including purpose of study are clearly and appropriately described.

Add comment

INTRODUCTION

Q 6 Please comment on the Introduction section. Key elements to consider:

- appropriateness of context
- purpose of study

Reviewer 1 | 09 Aug 2017 | 01:56

#1

Key elements, including background and purpose of study are clearly and appropriately described.

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 1 | 09 Aug 2017 | 01:56

#1

Key elements of the "Material and Methods" section are appropriately described. The quality of figures and tables are above the average.

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 1 | 09 Aug 2017 | 01:56

#1

Yes

Add comment

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

Reviewer 1 | 09 Aug 2017 | 01:56

#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 1 | 09 Aug 2017 | 01:56

#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 1 | 09 Aug 2017 | 01:56

#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 1 | 09 Aug 2017 | 01:56

#1

Key elements of the "Results" section are carefully and appropriately described.

Comment on Line 202 ;

Does "grouped loosely" mean "significantly"? If this is not significant, the description of "diplopia" and sexual symptoms seems to be unnecessary.

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 1 | 09 Aug 2017 | 01:56

#1

Not Applicable

Add comment

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

Reviewer 1 | 09 Aug 2017 | 01:56

#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 1 | 09 Aug 2017 | 01:56

#1

The "Discussion" section are well-constructed.

Comments on Line 276–278 and 247–248;

The NMS profiles in PD are significantly influenced and also improved by various treatments, especially dopaminergic therapy. The authors only described "particularly hallucination and orthostatic problems" in advanced PD. However, the authors should not overlook the therapeutic effects on the NMS in early PD. For example, pramipexole can improve depression and rotigotine can ameliorate sleep problems and etc. The authors should elaborate and discuss on this issue "cluster analysis of NMS in treated PD." Otherwise, this study cannot mention the "clinical endophenotyping of NMS" in Line 248.

Add comment

REFERENCES

Q 16 Is prior work properly and fully cited?

Reviewer 1 | 09 Aug 2017 | 01:56

#1

No

Line 367–369 in the references ;

"Ray Chaudhuri K" can be written as "Chaudhuri KR" and the position of this reference has to be moved.

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 1 | 09 Aug 2017 | 01:56

#1

The level of revision ; minor.

The authors should address on the comments in "Discussion" section (Q15 ; Line 276–278 and 247–248).

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OR

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