Author's response to reviews

Title: Neuroleptic-induced movement disorders in a naturalistic schizophrenia population: diagnostic value of actometric movement patterns

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Author's response to reviews: see over
Dear editor-in-chief,

Thank you for the valuable reviewers comments on our manuscript. We have revised the manuscript according to their suggestions.

Reviewer I

1. Naturalistic schizophrenia patients means in our paper a nonselected patient population. We evaluated almost all patients in the nursing home, who were in suitable age and agreed to participate.
2. The reviewer is right: we changed spelling „electromyogram“ – „electromyography“ in Introduction paragraph 1.1.
3. We added mean daily chlorpromazine equivalent dose with range.
4. Participants did not receive any special instructions, evaluation was during neutral clinical interview. Examinations were taken between 9.00 and 11.00 AM. We added the time window to Methods chapter of our manuscript.
5. Description of TD in the paragraph was directed to affected body regions – what means in our study, that if we measured ankle movements, then it is limitation of our study, that we possibly could not catch the affected body region movements.

Reviewer II

1. Actometry is useful method for differentiating NIA from other NIMDs because the actometric activity count discriminates patients with NIA and PsA from other patients. Questioning of patients discriminates NIA patients from PsA patients.
2. Accurate differential diagnosis of NIMD is valuable for patients directing the following clinical decisions. The issue was not included in our research, although we added it to discussion: "Actometry is useful for measuring change in the overall movement count or patterns after a change of risk factors (dosage, antipsychotic type, time course etc) in experimental conditions, and further research can show the ability of actometric data to drive treatment decisions in a clinical setting". We are very happy that reviewer raised up this valuable idea.
3. We had no possibility to make the qualitative analysis by computer with our technology. This was the reason of using raters. But we hope that our research results can give opportunity to following researchers to design technology that does not need human judgments in finding movement activities in actometric findings.
4. We did not used duration of activity in our study. We used an amount of activity periods, which is different output parameter.
5. Actually was excluded only one person with extremely severe rheumatoidarthritis, who was not able to follow the instructions of investigator. We did not collect information about other somatic or neurological illnesses in our population. We did not studied the ability of actometry to differentiate drug-induced from idiopathic or degenerative neurologic disease. So, we can not present such data.
6. We presented the amount (number) of patients who met criteria for particular movement disorder in Table 3, so we did not presented the percentages of patients in Table 2.
7. We did not calculated the summarized activity.
8. Lower limb activity index is confusing, indeed. We are very happy about this comment. We used in other parts of manuscript lower limb activity count. We changed it in manuscript text page 7, paragraph 1, and Figure 1.
9. The ROC curves are based on diagnoses, NIMD as presented in DSM-IV and PsA as presented in literature, against lower limb activity count. Although diagnoses against single subjective question.
10. The ROC Curves were compared to discriminate particular disorders from the whole population. Actometry offers advantage discriminating NIA and PsA from the population, and subjective question has advantage discriminating between them.

Reviewer III

1. Our study showed that lower limb actometric measurement have few (if any) value in diagnosing other NIMDs than NIA and PsA.
2. We collected data of using concomitant medications. We did not find any significant correlations for this population in NIMD and using of anticholinergics or benzodiazepines what we reported in our first manuscript. No one used beta blockers.
3. We could not detect the subclinical movement disorders in our study. We suspect, that actometry can detect subclinical movement disorders (in continuum), but the design of our study did not allowed to demonstrate it. Actometry can be reliable method in measurement of change, our study has an impact how different neuroleptic-induced movement disorders are seen in actometric data.
4. Actometry discriminated PsA patients from TD patients. The discriminative power was not so high in distinguishing TD patients from non-NIMD patients.

Discretionary revisions

1. We tried to focus in introduction an overview of objective measurements in the field of NIMD. So we were not able to concentrate detailed overview of studies involving actometry.

Reviewer IV

Minor essential revisions

1. We are very happy about the comment. We changed in Introduction paragraph 1: „with objective symptoms like akathisia“ to „with objective signs of akathisia“.
2. Qualitative analysis of movement patterns involves several parameters like rhythmical activity, frequency, etc. Quantitative evaluation involves activity count.
3. We are very happy about the comment and we added the issue of limitations of single question in discussion: „Although the single question has its limitations and is not enough to evaluate the various subjective discomforts associated with NIMD. Our results show that even single question can be a useful method of diagnosing NIA in a clinical setting.“
4. The reviewer is right: we added necessary legends to the Tables (IQ).
5. The aim of our study was to analyze characteristic actometry patterns of NIMDs and PsA in a naturalistic schizophrenia population. Previous studies were more devoted to validation of scales (BARS and SAS) using actometric activity count.

Discretionary revisions

1. Actometers were attached to both ankles.
2. We did not add definitions of actometric variables believing it will not necessary for scientists with similar interests.
3. AUC values of the actometric activity count for NIA is presented in our previous study (24) and for NIP and TD the AUC showed to have no discriminatory power.
4. NIP tremor vs. NIA/PsA descriptions are given in Table 3. The statistical comparison did not give much more by our opinion.
5. We are happy about the suggestion to add recent literature on PsA, but our study was focused more on instrumental measurement.

On behalf of all authors

Sven Janno