Author's response to reviews

Title: Frequency of impulse control behaviours associated with dopaminergic therapy in restless legs syndrome

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Author's response to reviews:

Dear Sirs,

First we would like to thank the editors and the reviewers for their valuable suggestions for improving our work.

We hereby submit a revised version of our manuscript MS 9919921584290797. Following the reviewer’s suggestions (A. Antonini) we changed the title to “The frequency of impulse control behaviours associated with dopaminergic therapy in restless legs syndrome”. We also restructured the abstract according to your specifications.

Below, we respond to the reviewers' comments in detail.

We hope our manuscript may now be considered for publication in your esteemed journal.

Sincerely yours

Friederike Sixel-Döring and Claudia Trenkwalder

Reviewer A. Antonini:

- We changed the title according to the reviewer’s suggestion to “The frequency of impulse control behaviors associated with dopaminergic therapy in restless legs syndrome”.

We addressed the limitations of the study and mentioned the proposed references: …”

One limitation of the study is the lack of a control group. However, all RLS patients with ICBs were on dopaminergic therapy and none of the RLS patients with non-dopaminergic medication was identified with an ICB. In accordance with previous findings [24-27] we therefore assume a risk for developing ICBs with
dopaminergic medication in RLS patients. We can also confirm the previous
association between the occurrence of ICBs in RLS and the treatment with
higher dosages of dopaminergic agents compared to RLS patients who did not
develop ICBs [24, 26]. As depression may present an individual susceptibility
factor for abnormal behaviours in PD patients [28] and neuropsychological
testing revealed preserved executive functions in a previous study on PD
patients with pathological gambling [29], the lack of further psychiatric and
neuropsychological evaluation in our cohort further limits the study presented
here. Comparative assessment of psychiatric comorbidities and cognitive profiles
should be addressed in further studies.”

- The data on dopaminergic medications is included in Tables 1& 2. Apparently
there has been some problem for both reviewers with uploading the tables
properly. We apologize for this inconvenience and hope that all information is
now included in the resubmission. Dosage of dopamine agonists calculated as
LEDD was significantly higher in the RLS + ICB group (p = 0.001).

- Clonazepam and gabapentin are not licensed as first-line treatment of RLS in
Germany. Therefore it was not possible to create a sufficiently large control
group of idiopathic RLS patients with monotherapy of dopaminergic agents.
There are, however, few patients with non-dopaminergic medications included in
this cohort, who did not show any ICB. This is now pointed out in the discussion.

- All patients identified with ICBs during this study were offered to have their
treatments changed. Accordingly we added this information at the end of the
discussion: “Although all RLS patients identified with ICBs in this study were
advised to have their treatment regimen changed, none of the affected study
subjects felt sufficiently impaired by their behaviours to stop dopaminergic
medications completely, but agreed to a reduced dosage or combination therapy
with non-dopaminergic agents.

Reviewer D. Muresanu:
We apologize for the erroneous Figure and the problems with uploading the
tables. Some numbers were part of the overall group, others should have been
placed as a parallel group. We now corrected Fig 1 for more clarity and revised
Tables 1&2.

We received 140 completed questionnaires from 274 questionnaires that were
mailed out. Of these 140 completely filled out questionnaires 27 scored indicative
of a possible ICB. A psychiatrist or a psychologist performed interviews with
these 27 subjects to correctly diagnose ICB according to clinical criteria. In the
end 10 subjects were identified with an ICB.

We hope the revised study tree (Fig 1) as well as the table 2 now clarifies our
data.

We agree with the reviewer that the number of patients affected is small.
However, the frequency of ICB’s in RLS patients with dopaminergic treatment is
higher than estimated numbers of the German population. Therefore we feel
justified in publishing these results to increase physicians’ and patients'
awareness for these potentially deleterious behaviors under dopaminergic therapy.