Reviewer's report

Title: Pulmonary Function in Patients with Huntington's Disease

Version: 2
Date: 23 March 2014

Reviewer: Helena Backman

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In my opinion, this paper is an important contribution to this field of research. The design is simple and straightforward and the message is clear; patients with HD have lower pulmonary function than the healthy controls in the study. Also, pulmonary function for HD patients is negatively correlated with motor severity (UHDRS-TMS score). However, some questions regarding the paper must be answered before acceptance for publication.

Major Compulsory Revisions

1) With an expected difference of 30 cmH2O difference in MEP between groups (SD=30), alpha=0.05 and 80% power, I argue that the sample size should be at least 13 participants per group, not 12 (as described in the Participants section). Please elaborate on why you base the sample size calculation on the largest expected difference? I also suggest that the sentence “To achieve statistical significance of 5% and a statistical power of 80%, an adequate … …” is revised into the more accurate “With alpha 0.05 and 80% power, an adequate …”. And in connection to this matter, do you have sufficient power to make comparisons of mean pulmonary function values between subgroups such as e.g. smoking subgroups of HD patients (n=9 per group) as described in the Result and Discussion sections?

2) The description of the sampling of the control group is insufficient. Since there are several factors which can affect lung function which are not accounted for in the exclusion/inclusion criteria, please explain from where the controls are sampled. Are they sampled from hospitals, specific work places or other areas? Factors such as e.g. occupational exposure to gas/dust/fumes (related to lower lung function) or high socioeconomic status (related to higher lung function) which possibly could be overrepresented among controls may be a confounding factor not described in the paper. Also, please elaborate on why the gender (sex) matching was not exact between HD patients and controls.

3) Please consider displaying 95% Confidence Intervals for the mean values in table 2 and 3.

4) Why did you choose the Stanojevic 2009 prediction equations as reference values for spirometric values, and not the GLI-2012 equations which currently are recommended by most recognized respiratory societies? Both the Stanojevic and the GLI reference values are evaluated on a population sample from Australia/New Zealand and found to be applicable. And, why is % of predicted
not presented for the FEV1/FVC ratio? Additionally, does the Stanojevic reference value for SVC predict Slow Vital Capacity or the highest value of Forced and Slow Vital Capacity? Also, please provide a reference to the Stanojevic reference values (describing all spirometric indices) where the reader can find this information.

5) The controls have mean values well below 100% for the spirometric measurements of SVC, FVC, FEV1 and PEF although mean % of predicted is expected to be close to 100% for healthy subjects. Is the relatively low mean % of predicted values for the control group due to the fact that six controls have a smoking history? In essence, do the former smokers “lower” the mean (even though the subgroup analysis did not yield significant differences and mean time elapsed since smoking cessation>20 years)? Or may some other factor influence their spirometric performance?

6) Table 1 gives the impression that all participants had a smoking history, i.e. values for packyears and time elapsed from smoking cessation, when in fact only nine HD patients and six controls had values for these variables. This should be explained in the table. Also, do you have sufficient power to test for differences in these variables between HD patients and controls, and are the two variables normally distributed?

Minor Essential Revisions

7) In the Participants section, please consider revising the sentence “Eighteen patients with manifest HD …… scheme database [10], and the Huntington’s Western Australia Association”. One possible suggestion is: “Eighteen patients with manifest HD …… scheme database [10], with assistance from the Huntington’s Western Australia Association”.

8) In the Methods section, page 5, second paragraph: one inclusion criterion is stated as a clinically verified disease expression of UHDRS-TMS<=5. This should be changed into UHDRS-TMS>=5.

9) Please explain how height was estimated. It is important that height is measured at the time of investigation and not estimated merely by asking the participant, preferably by using an accurate and calibrated stadiometer, since self-reported height and weight can be seriously biased. An accurate height estimate is important in order to enable calculation of an accurate reference value. The same goes for weight when using the Stanojevic reference values.

10) The packyears term generally describes the cumulative number of cigarette pack equivalents consumed by a subject up to time of examination, and is usually spelled as either “packyears” or “pack-years”. You use the term “pack/years” throughout the paper, which gives the impression of number of packs per year, which is not the purpose of this term. Also, in the footnote to Table 1, you use the term “Pack year”. Please change this throughout the paper.

11) Was the Shapiro-Wilk test performed for all variables and in all subgroups where statistical tests are performed? Please clarify.
12) Since the significance level is stated in the Statistical Analysis section, you are not required to state both p-value AND “statistical significant” throughout the text, when describing statistically significant differences between groups. Preferably, “(p<0.05)” can be removed in those sentences, e.g. in the Results section, page 9, second paragraph.

13) Please provide equal number of decimals (preferably 2) for mean height and range for height in Table 1. The same goes for number of packyears in Table 1.

14) Please add that the correlations are calculated for UHDRS-TMS and spirometric indices expressed as % of predicted (not for absolute values) to the figure legend of Figure 1.

15) Please consider revising the first sentence in the first paragraph of the Results section, page 8. It should be clear that the groups you refer to are the HD patients and controls. This can be inverted in the second sentence.

16) Regarding the second last sentence in the Results section, page 9; is this sentence referring to Figure 1? More specifically, is this paragraph referring to absolute values or % of predicted? Please clarify.

17) Regarding the last sentence in the Results section, page 9; were the correlations between age and the pulmonary function variables calculated for both absolute and % of predicted values or only for % of predicted? One would certainly expect a significant correlation between age and absolute values. And was this the case among both HD patients and controls? If no correlations with age were found neither for HD patients nor controls, you cannot suggest that this finding is specific for HD patients (as implied in the Discussion section on page 9). Please elaborate on this matter.

18) In the Discussion section, page 10, please consider revising the sentence “In the present study, however smoking history was under 20 pack/years for HD and control groups” and add the word mean into the sentence, e.g. into “In the present study however, both HD patients and controls had mean packyears of smoking less than 20”.

Discretionary Revisions

19) Consider revising the expression “No information is available” (regarding respiratory function in HD patients) which is used in the Abstract and in the Introduction section. Is there truly no information at all available, or should it maybe me more appropriate to express the matter as e.g. “To our knowledge, no publications are available”?

20) Can the terms pulmonary function and respiratory function be used interchangeably, as done in the Introduction section?

21) In the Result section, page 8, please consider revising the sentence “However, MIP values across testing sessions were more variable in the HD (CV 10.8%) than in the control group…..” into “However, the variability for MIP values
across testing sessions was larger in the HD (CV 10.8%) than in the control group.....”.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests