Reviewer's report

Title: Transcranial sonography for diagnosis of Parkinson's disease

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Reviewer: Annemarie Vlaar

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In this study, Mehmert and colleagues investigated 199 patients with idiopathic Parkinson’s disease (IPD) and 201 healthy subjects. All patients were investigated by three sonographers. They found that transcranial sonography (TCS) is a reliable and highly sensitive tool for differentiation of patients with IPD from healthy controls.

In general:
1. Is the question posed by the authors well defined? yes
2. Are the methods appropriate and well described? see comments
3. Are the data sound? yes
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? yes
5. Are the discussion and conclusions well balanced and adequately supported by the data? yes
6. Are limitations of the work clearly stated? see comments
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? not relevant
8. Do the title and abstract accurately convey what has been found? see comments
9. Is the writing acceptable? yes

Major compulsory revisions:

1) Especially the differentiation between patients with IPD and other parkinsonian disorders like multiple system atrophy, progressive supranuclear palsy, drug induced parkinsonism and vascular parkinsonism can be difficult. Unfortunately, in this study only patients with IPD and healthy controls are studied.

2) Secondly, the authors only included patients that were already diagnosed with IPD. However, this does not resemble the situation in clinical practice, where the neurologist would want to used TCS to reach a diagnosis in patients with a clinically unclear parkinsonism.

Minor essential revisions:

Abstract:
1) not all of the subjects that were investigated and that were described in the methods are handled in the results and discussion (i.e. inter-observer reliability, Perdue pegboard test, Webster gait test, echogenicity of raphe, red nuclei, thalamus, caudate, lenticular nuclei, width ventricles). Please remove these items from the methods or discuss the results shortly.

2) the abbreviation TCS is not explained in the last sentence of the abstract.

Background:
page 3 (Until now studies using the same ultrasound machine only involved small subjects groups......)
One study of Vlaar et al is not mentioned. In BMC neurol 2008 nov (9;8:42) Vlaar et al used SONOS 5500 in their TCS study. They included a mixed group of patients and found lower diagnostic accuracy.

Patients and methods:
1) in which time period were the subjects included?
2) since the size of the SN size changes with age one would prefer similar age groups for both the IPD group and the control group. In this study the mean age of the IPD patients was 66 (range 62-71). The mean age of the control group is not mentioned, only the range (20-79 years).
3) Unfortunately the three investigators were not blinded. Since the age distribution of both groups was so different, the investigators could have assumed that everyone aged below 62 would be healthy.

Results:
Table 1 Inter-observer difference
1) The difference in means of the SN area of both groups, and the standard deviation, is extremely small. Is this caused by the fact that almost all healthy controls had a SN area of 0 cm2?
2) In how many of the IPD patients did the observers come to another conclusion (cut-off point of 0.2cm2)? Hier klopt nog iets niet, door die koppeling met het cut-off point
3) In table 1. Number of individuals tested by both investigators. In the methods the authors mentioned three observers.

Discussion:
1) page 10, first sentence.
.....since this is the basis to advocate TCS as the method of choice in the diagnostic workup...
Please include the shortcomings of this study (not a mixed patient group, already diagnosed patients, .......).

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests