

Author's response to reviews

Title: High prevalence of extrapyramidal signs and symptoms in a group of Italian dental technicians

Authors:

Edito Fabrizio (edito@libero.it)

Nicola Vanacore (vanacore@iss.it)

Marcella Valente (marcella.valente@virgilio.it)

Alfonso Rubino (alf-rub@libero.it)

Giuseppe Mecco (giuseppe.meco@uniroma1.it)

Version: 3 **Date:** 25 May 2007

Author's response to reviews: see over

Editors of **BMC Neurology**

May 25, 2007

Re: **“High prevalence of extrapyramidal signs and symptoms in a group of Italian dental technicians “**, revised version

Dear Editors,

Thank you for your interest in our manuscript and for the comments of the reviewer.

We are very pleased to see that the reviewer found our work interesting and our findings important.

We did our best to address all the points raised, and we feel that the paper has been improved after the revision.

A detailed explanation of how we have responded to each of the reviewer comments is enclosed below.

We have changed the title in: **“High prevalence of extrapyramidal signs and symptoms in a group of Italian dental technicians “**, as suggested by the reviewer.

We hope the manuscript is now acceptable for publication in **BMC Neurology**

We look forward to hearing from you.

With best regards,
Giuseppe Meco and Nicola Vanacore

Prof. Giuseppe Meco
Department of Neurological Sciences
“La Sapienza” University
Viale Università 30
00185 Rome, Italy
tel +390649914706
fax +390649914840
e-mail: giuseppe.meco@uniroma1.it

Reply to the specific points raised by reviewer:

1. **It is important for the authors to decide whether the cases with postural tremor had ET or not. At times (e.g., the abstract), the authors are more tentative, referring to this merely as “postural tremor” whereas in the body of the paper, they are more prone to refer to this as “ET”. I think the approach to these patients and labeling of these patients should be presented consistently.*

We agree with this comment and we have changed in the body of the paper the term “essential tremor” in the “postural tremor”. Now the definitions included in the abstract and in the paper are consistently.

2. **I think the conclusion is too strongly worded. Rather than writing that they found “an unexpectedly high frequency”, I think it would be more appropriate to write “a high prevalence”. Also, rather than writing “that this finding is likely to be due to the presence of toxins...” I think it would be more appropriate to write “that this finding could be due to the presence of toxins...”.*

We have modified the conclusions of the paper, as suggested by the reviewer and we have also changed the term “frequency” in the title of the paper with “prevalence”.

3. *The background section suggests that there are only two studies linking solvents and metals to PD. However, there is a huge literature (case reports, case control studies, outbreak studies) linking metals(e.g., manganese) to parkinsonism and PD.*

We report briefly in the background three case-control studies and two case-report regarding the relationship between exposure to metals and solvents and parkinsonism. Now we have added a specific review on this theme (Gorell et al, 1999)

4. *In several places, they use the word “incidence” when I think they might mean “prevalence”. Perhaps they can check on this. Incidence refers to new cases whereas prevalence, to existing cases.*

We appreciate the comments of the reviewer but we are convinced that the word “incidence” is more appropriate than “prevalence” when are reported the results of a case control study . In fact in this type of the study it has been evaluated the link between exposure to neurotoxins and the onset of a disease, then the use of word “incidence” is correct.

5. *The summary of the ET literature, which cites reference 6, is a bit vague and non-specific. Since much of the focus of this submission is on ET as well as PD, they may wish to expand on this.*

We have reported briefly only a wide review of Essential Tremor literature, with a specific paragraph on risk factors and aetiology. However, we have added two specific case-controls studies (Louis et al, 2004 and 2003) on this argument and we have inserted the review in the results section for the clinical implications.

6. *In the case description, I have several comments. First, was the patient right or left handed? Second, can they expand on what they mean in saying that the patient was referred to them for “PD and other extrapyramidal diseases”? Third, “cupremia” and “ceruloplasmine” should be changed to “serum copper” and “serum ceruloplasmin”. Fourth, can they provide details regarding the methods/interpretation of the acute L-dopa test? Fifth, how was “family history” of ET evaluated and how was it defined?*

We have specified the description of PD case for each of five specific comments of the reviewer. First, the patient is right handed,; second the definition of “PD and other extrapyramidal disease” was referred to our clinical centre; third we have changed the words on biochemical test as suggested by the reviewer; fourth we have reported deeply the acute levodopa test and at last we have clarified the family history of the patients in the methods section.

*7. *A major limitation of this study is that there was no contemporaneously enrolled control group. This greatly lessens the impact of this paper. The second is that there was no attempt to assess exposure level. A third is that there was no attempt to assess workplace measures or biological measures of exposure. These issues should all be discussed in the limitations section.*

We agree partially with this comment because our study from a methodological point of view was a cross-sectional study not a case-control study, then the inclusion of control, group was not required. Instead, we not have could to perform an evaluation of exposure level and a biological measure of neurotoxins present in workplace of these dental technicians. These issues have been included in the discussion of the paper.

8. One concern is that the patient referred many of his colleagues for further evaluation. This raises the issue of selection bias. However, if all 27 dental technicians were evaluated, this reassures the reader that such bias was not operative here.

We agree with reviewer that the selection bias was not operative in our study because all 27 dental technicians have participated at the screen phase of the study.

9. On page 5, they cite reference 7 when I think they might mean reference 8.

We have changes the references 7. The observation of the reviewer is correct.

*10. *Another shortcoming of this paper is that they did not include a formal screen for ET. This is unfortunate as such screens were provided for PD and GH.*

We partially agree with this comments because the self-reported questionnaire on extrapyramidal symptoms include a specific item on tremor

11. I am not I understand the statistical approach. Was the paired t test used or the Student's t test?

We have used the Student's t test. We have deleted the words o “paired t test”.

*12. *Another sizable concern is that there is no sample size calculation so that the study power is not known. This is a concern with the small sample size.*

We believe that the sample size calculation was not appropriate in this study because a “ a priori hypothesis” was not considered. We underline that our study was only an epidemiological and clinical survey.

*13. *In the results section, they note that three subjects met consensus criteria for ET but they do not note whether these are criteria for definite, probable or possible ET. The problem with the consensus criteria are underscored in this study. These criteria do not specify a minimal tremor amplitude or a minimal number of tasks in which tremor must be present in order to qualify for a diagnosis of ET. Hence, they are not designed so that investigators who are conducting*

epidemiological or population-based studies can distinguish between ET and enhanced physiological tremor. This should be mentioned in the limitations section.

We agree with this comment, then we have deleted the adoption of the Consensus criteria for ET. In the new version of the paper we have used only a descriptive clinical approach of the subjects underwent the neurological examination because an adequate follow-up of these subjects was not available. Then we reported three patients with bilateral postural tremor and one with unilateral postural tremor.

14. In general, the terms “symptoms” and “signs” are often used interchangeably here but they should not be. For example, in the first sentence of the discussion, both symptoms and signs should be mentioned.

We agree with this comments and have added in the title and in the body of the paper the term “signs”.

*15. *The first sentence of the discussion is an over-extension of their results. It should be modified and toned down to more accurately reflect their results. They have shown that a relatively high proportion of these individuals have extrapyramidal signs. Not having enrolled a control group, they can not formally assess whether this proportion is excessive or not. Using a historical control group, they can surmise that the proportion is high. However, they can only surmise that this could be due to environmental or toxic factors.*

We have commented the results more accurately and reduced the tone of the findings.

16. In the table, “monolateral” tremor should be changed to “unilateral” tremor.

The term has been changed.

17. In a number of places the English is a little awkward (e.g., “We propose to all 27 dental technician also an neurological examination”).

The quality of the written English has been revised.

18. In summary, the authors present interesting results that merit further study. A number of methodological issues should be highlighted and the authors will want to tone down their conclusions so that they do not over-extend their data.

We have reduced the tone of the conclusions of the paper and we suggest to perform further study.