Author's response to reviews

Title: Diagnosing migraine in research and clinical settings: The Validation of the Structured Migraine Interview (SMI)

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Author's response to reviews: see over
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Re- Manuscript “Diagnosing migraine in research and clinical settings:
The Validation of the Structured Migraine Interview (SMI)

Dear Dr. Norton,

We have the pleasure in re-submitting our revised manuscript “Diagnosing migraine in research and clinical settings: The Validation of the Structured Migraine Interview (SMI)” for your consideration for publication in BMC Neurology.

We enclose a point by point response to reviewers’ comments. We thank the reviewers for their helpful observations and suggestions that we believe have improved the manuscript.

Yours sincerely,

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Response to Reviewer 1 (Michael Bjørn Russell) Comments

We thank the reviewer for a very thorough review and helpful comments.

Abstract

R. The notion on specificity is overemphasized in the results as the result is based on evaluation of only 6 persons.

A. The modest number has been addressed under results in this response and added under discussion pages 12-13 in the manuscript as described below:

“Although the numbers are small, we believe that the results are able to demonstrate specificity and sensitivity, and are in keeping with larger sample sizes (Rasmussen et al 1991 Headache 31(5): 290-295). A previous study employing similar methodology also included a modest sample size of 61 headache sufferers concluded a combination of using a diary and a clinical interviewing was more effective than either method alone (Russell et al Cephalalgia 1992). In addition to the 41 individuals who their diagnoses were confirmed by the headache specialist in this study, 646 subjects who were attending the headache clinic and received formal diagnosis for their headaches were tested using the SMI. Although the reported diagnoses were by self report, the diagnosis obtained by the SMI was significantly correlated with self reported migraine (Spearman’s rho = 0.16, p = 0.001). In a study of self recognition of migraine, Lipton et al (Neurology 2002, 58 s21-26) reported that individuals who reported that they had migraine were 3 times more likely to meet the ICHD criteria for migraine.

Background

R. The sentence “An even smaller fraction.....” gives a wrong impression. The majority of migraineurs have very few attacks per year, while only a few percent have frequent attacks that might qualify for prophylactic treatment. However, after the introduction of the triptans in the 90ies the need for prophylactic has changed, as many migraineurs have excellent effect of a triptan and does not necessarily need prophylactic treatment even if they have many attacks. The authors need to consult ref. 13 which encompasses frequency of migraine attacks.

A. In this sentence we are trying to highlight the nature of migraine underrecognition and undertreatment. Triptans did indeed offer a great relief from acute migraine headache. However, the response rate to triptans varied from 44-70% and only Sumatriptan s.c. administration achieved 80% response rate (Saxena et al 2006). In addition, triptans are expensive and not all patients have access to them. In a large population study of US households, only 20% of migraine sufferers used prescription treatment for acute migraine (Diamond et al 2006). Migraine attacks were reported to occur at a rate of more than 3 per month in 31.3% of migraineurs and over half of migraineurs reported severe impairment. Over a quarter met the
criteria for preventative treatment, however only 13% reported current use of such treatment (Lipton et al Neurology 2007).

R. 3rd paragraph first sentence. The International Headache Society is usually described as International Classification of Headache Disorders (2004), while the former classification (1988) is denoted as described in the sentence.

A. This has changed and now reads “In order to identify migraine in a systematic fashion, the International Headache Society (IHS) produced diagnostic criteria and classification system for primary headache disorders including migraine [7]. This provided a method for targeting a group of headache patients in need of care [8] to ensure accurate identification and a measurable way to assess outcome.”

We have also used ICHD consistently throughout the manuscript.

Methods

R. Site is usually denotes locations. Associated symptoms are usually denoted accompanying symptoms.

A. This now reads: “As well as the presence of headache, enquiry was made about severity, frequency, duration, location, character, aura and other accompanying symptoms.”

Fig. 1.

R. The structured migraine interview (SIM) relates to recurrent headaches. However, about 80% of migraineurs have co-occurrence of tension-type headache, and 15% of people with cluster headache have co-occurrence of migraine. The SIM only relate to one type of headache. What if a person has several recurrent headaches?

A. We agree with the reviewer that it is very likely to have more than one headache type. We designed this questionnaire with migraine as the main interest.

R. The following questions are phrased wrong in relation to the International Headache Society classification from 1988 and the International Classification of Headache Disorders from 2004.

Q2. Migraine with aura (MA) can be ascertained if a person experienced two attacks. However, if a tick occur in the box 1-4 times, one can not determine whether the person have MA or not.

A. The diagnosis of migraine with aura here is based on having the diagnostic features of migraine without aura that must include at least 5 attacks in a life time. In addition for the diagnosis of migraine with aura, there must be at least 2 attacks accompanied by aura symptoms as in question 4 (figure1).
Q3. In order to have migraine without aura (MO) you need both hypersensitivity to sound and light. Thus, the diagnosis MO can be given to persons not fulfilling the criteria for MO.

A. We agree with the reviewer that the question (Q3) should be worded to say “Have ever had moderate to severe headache accompanied by hypersensitivity to sound AND light?” however this question will unlikely cause over-diagnosing patient with migraine since it is reported that a quarter of patients with migraine tend to under report these symptoms on routine questioning (Evans et al Headache 2008;48:395-397). In addition each symptom alone is similarly correlated with migraine headache (Kelman and Tanis Cephalalgia, 2006,26, 548–553). On the other hand Sensitivity to sound and light assessed alone was also found to be different predictors of migraine when compared to the gold standard (clinical diagnosis) led to selecting only one (photosensitivity) for use in screening questionnaires (Lipton et al 2003 Neurology 61 (3) 375-382). It was also reported that the use of self administered headache symptoms in a diary led to under-reporting of accompanying symptoms such as photophobia and phonophobia (Russell et al Cephalalgia 1992). The use of this question 3 is therefore unlikely to have led to diagnosing MO in persons not fulfilling the criteria for MO.

Q5. This question encompasses both pain quality and location. Since only one box can be ticked, as the notion “(can tick more than one)” is not added, diagnosis of migraine will sometime be missed.

A. All questions did not constrain answers to one only and indeed most responders have selected more than one answer.

Q7. Certain food is not part of the headache classifications from 1988 nor 2004.

A. That is correct. Certain foods were added in as results of the initial pilot were it was commonly reported that certain foods such as chocolate have triggered headache. This item was not considered as part of the diagnostic criteria.

Q8. Only one box can be ticked as the notion “(can tick more than one)” is not added. This question is not part of headache classifications from 1988 nor 2004.

A. Same as question 7 above.

Q10. Does not relate to classification.

A. The reviewer is rightly pointing out that this question is not part of the classification criteria. This question was added for 2 reasons. 1st: to identify any causes for headache to distinguish primary from secondary headaches. And 2nd: to identify proportion of people who were identified as migraine sufferers and if they actually knew that they had migraine.
Results

R. The number validating the SIM is too small: a total of 41, and a total of 6 persons without migraine is a very small number.

A. Although the numbers are small, we believe that the results are able to demonstrate specificity and sensitivity, and are in keeping with larger sample sizes (Rasmussen et al 1991 Headache 31(5): 290-295). A previous study employing similar methodology also included a modest sample size of 61 headache sufferers concluded a combination of using a diary and a clinical interviewing was more effective than either method alone (Russell et al Cephalalgia 1992). In addition to the 41 individuals who their diagnoses were confirmed by the headache specialist, 646 subjects who were attending the headache clinic and received formal diagnosis for their headaches were tested using the SMI. Although the reported diagnoses were by self report, the diagnosis obtained by the SMI was significantly correlated with self reported migraine (Spearman’s rho = 0.16, p = 0.001). In a study of self recognition of migraine, Lipton et al (Neurology 2002, 58 s21-26) reported that individuals who reported that they had migraine were 3 times more likely to meet the ICHD criteria for migraine.

Discussion

R. The Copenhagen group has previously evaluated a headache diary based on the criteria of the IHS Cephalalgia 1992; 12: 369-74, which actually is quite similar to the SMI, but without the flaws of SIM mention above.

A. The Copenhagen group employed similar study design to the SMI based on the IHCD 1988 criteria. The study included 61 participants from a specialized headache centre. The sensitivity of the headache Diary for migraine with out aura was excellent at 0.94, the specificity however was modest at 0.50, and this specificity was based on 4 individuals only. For migraine with aura the sensitivity and specificity were 0.73 and 0.72 respectively. The authors concluded that the use of the diary should be supplemented by a clinical interview to improve accuracy (Russell et al Cephalalgia 1992). The SMI had a sensitivity of 0.66 and specificity of 1.0 indicating a useful instrument in identifying strict migraine in settings where headache expertise is not available.

R. Paper 27 should be discussed in more details. The main conclusion is that a questionnaire is not valid, due to equal positive and negative misclassification. A method for screening migraine was employed based on paper 27 and described in paper 12. A single question “Have you ever had migraine” is valid (Kappa 0.77) in the Danish population, but not necessarily in other population. So if this method is employed elsewhere it should be validated.

A. We have discussed the findings of Rasmussen and colleagues 1991 in more details (discussion page 13):
“The validity parameters presented here were similar to the results of a study of 713 individuals. Ninety three subjects were identified as having migraine in clinical interviews and 94 subjects classified as having migraine using the questionnaire method (a self administered questionnaire based on the ICHD 1988 criteria) [27]. The sensitivity of a self administered questionnaire in Rasmussen and colleagues study was lower than the SMI (0.51 compared to 0.66) with high specificity 0.92. The study using McNemar test for symmetry in a 2X2 table similar to table 2 found that the two types of inconsistencies (false positive by the questionnaire “b” and false positive by the clinical interview “c” were equally common ($\chi^2 = 0.01$, df = 1, p<0.9). The authors concluded that the use of self administered questionnaire was less sensitive but highly specific, therefore the use of self administered questionnaire in the clinical settings will lead to under-reporting of true cases of migraine [27]. “

R. Rewrite the discussion so it is in line with well conducted studies, i.e. physician evaluation, general population etc., and adjust the discussion relating own results so it reflect the flaws of the questionnaire and the small number validated.

A. The discussion is re-written and clarified based on the reviewer’s helpful comments. It now reads more clearly as what type of study is being discussed (pages 11-14).
Response to Reviewer 2 (Paola Torelli) Comments

We would like to thank this reviewer for comments that helped us to re-write the paper in a more focused fashion that also improved the overall flow of the paper.

Here are our specific responses to the comments raised:

1. The aim stated by the authors is not consistent with what is reported in the Results and Discussion sections. On page 4, they write: “... practical screening tool to identify migraine in order to plan treatment and improve the prognosis of both migraine and the comorbid psychiatric conditions”. In fact, the aim of the study is to validate a questionnaire that will enable investigators to make a correct diagnosis in a clinical setting. As regards the correlation between migraine treatment and prognosis, literature data are scarce and there is no evidence that a correct treatment improves migraine prognosis. Moreover, the validation of a diagnostic tool cannot be additionally aimed at improving also the comorbid psychiatric conditions associated with migraine. In my opinion, the aim of the study should be stated more clearly and more consistently with what is reported in the Results.

   A. We have now changed the paragraph on page 4 to read as “The aim of the current study was to design a short and practical screening tool to identify migraine in settings were clinical interviews are not possible or practical such as large population studies and clinical practice were neurological expertise are limited.”

2. In the Results section the authors do not provide any data about the questionnaire’s sensitivity and specificity for migraine with aura and probable migraine. If the tool makes it possible to establish a migraine diagnosis at the one-digit level of the International Classification of Headache Disorders (ICHD-II), there is no need to include in the paper the criteria for migraine with aura and probable migraine, which require diagnosis at the two-digit level of ICHD-II (1.1, 1.2, 1.6). On the other hand, if the tool has been designed and validated for diagnosis at the two-digit level, as seems to be the case from what the authors themselves report in the Methods section, the data should be presented specifically in the Results section.

   A. We designed the questionnaire with different types of migraine (with aura, without aura and probable migraine) in mind and we have included the ICHD criteria pertaining to the different types at the 2 digit level. However when we looked at the clinical diagnosis, there were no cases of probable migraine diagnosed and most cases of migraine with aura were also diagnosed with migraine without aura that is not uncommon in clinical settings. In addition, to avoid making the cells numbers fewer we decided to include all cases of migraine with and without aura as migraine. We added a paragraph under Results page 9 “The clinical diagnosis included only 3
categories: migraine with aura 41.5%, migraine without aura 43.9% and other non-migraine headache 14.6%. In addition many cases of migraine with aura also had migraine without aura. There were no cases of probable migraine according to the clinical diagnosis. Therefore we combined the diagnostic categories into migraine to include migraine with and without aura and none-migraine headaches.

3. The tool was designed and validated in a number of subjects who were referred to a Headache Clinic and the results of the study demonstrate that the SMI is valid in a clinical setting. I would then leave out from the Discussion and Conclusions any statements regarding the application of the SMI in a research setting: in a survey in clinical or general population it is necessary a face-to-face interview to make the correct diagnosis.

A. The tool was also tested against self reported diagnosis, taking migraine treatment and analgesic treatments in addition to the clinical diagnosis by a headache specialist. Although we fully agree that the best approach to identify migraine in clinical and research setting is by face to face interviews, we are fully aware that in many circumstances such as large studies and clinical settings where headache expertise are limited, the use of a screening tool can be useful. Indeed, in two different large studies we did use the SMI tool to screen for migraine (Samaan et al BJPsych 2009 and Ball, Samaan et al Cephalalgia 2009). Therefore we included the argument for using the tool in research settings as a conservative estimate of migraine can be drawn by using this tool.
Response to Reviewer 3 (Csaba Ertsey) Comments

The authors would like to thank the reviewer for the detailed and specific comments that helped us to reshape this manuscript.

1. The purpose of the study is well defined. As the instrument had been used in two studies, mentioning ‘Development’ in the title does not seem fully justified. (Discretionary Revision)

A. We revised the title of the paper to read “Diagnosing migraine in research and clinical settings: The validation of the Structured Migraine Interview (SMI)”

2. Generally speaking, the Methods section is ample and well-written. The SMI and the diagnostic criteria used by the authors are in keeping with the criteria of the International Headache Society. Nevertheless a couple of points need a significant improvement.

a) Page 7. The method the City of London Migraine Clinic used for selecting patients should be clarified (eg. previous diagnosis of migraine, all patients visiting the Clinic in a given time frame etc). (Major Compulsory Revision)

A. We have added further clarification (page 7 1st paragraph): “Patients attending the clinic were referred to the clinic because they suffered from significant headaches that were not managed by general practice and other health care providers. These patients were not all migraine sufferers but had other types of headaches. All patients who were registered with the clinic at the time of the study conduction (2003) were considered as potential study participants.”

b) The diagnosis by the SMI was compared with the migraine diagnosis given by the headache specialist in a sub-sample of 41 randomly selected patients. This is less than 7% of the 646 patients who completed the study. The authors should explain why such a small fraction was chosen for comparison and whether it is safe to suggest that this sub-sample is representative of the whole study population. (Major Compulsory Revision).

A. A clarification of the rational for selecting this subset of modest number is added (page 7 last paragraph): “For practical reasons (time and resources available at the time of the study conduct) we selected a random sample form the original sample to test for the validity of the questionnaire. The selection ensured an equal opportunity for each participant to be selected by generating a random list of 57 study ID numbers that were assigned to participants arbitrary to conceal subjects identity. This random and blind selection ensured a representative sample to be selected from the original study participants.”

c) Paragraph 4 on page 7: Twenty patients who had been administered the SMI in a face to face interview as part of a previous study were re-interviewed by phone to assess the reliability of the instrument, a mean 2.5 years after the face to face interview. This is a rather small sample size. Also, the time gap is rather long as the test & retest method of testing reliability usually
recommends a time span of about 1 month. The authors should clarify whether is it safe to think that reliability can be assessed this way. (Major Compulsory Revision).

A. The sample of 20 subjects was selected for re-interviewing. We believe that a sample of 20 was adequate to test for repeatability. The study aimed to investigate a life time diagnosis of migraine and for that reason we decided to leave a significant time between 1st and second interviews. A month would have been too short to achieve this aim.

d) Using self-reported migraine and antimigraine drug use as the main (and in the majority of patients, only) means of assessing the SMI's validity seems inadequate as self-reported migraine can be twice as frequent as migraine diagnosed by the IHS criteria (Svensson et al, The Journal of Headache and Pain, 2004;5(3):171-176)). The authors should indicate why they preferred using these data. (Major Compulsory Revision)

A. Using self reported migraine and using treatment was justified in the discussion (1st paragraph): “It has been suggested that a disorder associated with impairment or requiring treatment is usually associated with good reliability of recall [24].” Although the reviewer is making an important point regarding self reported diagnosis versus ICHD diagnosis, there is a significant correlation between self report and ICHD migraine diagnosis (kappa 0.81 Rasmussen et al Headache 1991; 31: 290-295).

Also, the authors could add Spearman's rho values for the SMI diagnosis and self-reported migraine / antimigraine drug use for the sub-sample of patients with a clinically verified diagnosis of migraine in the Results section. (Minor Essential Revision)

A. To add such comparison we are comparing the diagnosis in 3 ways in the same subset. We do not believe that this will add a significant validation to the SMI. Besides for the verified subsample of migraine sufferers we expect to have treatment received and therefore the results will be expected.

e) Finally, the first sentence of paragraph 2 of the Methods section (on page 5), probably referring to the experience of the staff members pilot testing the questionnaire, might be omitted as the info is not relevant for the further use of the questionnaire by migraineurs. Instead, information on what migraineurs think about the difficulty and time consumption of filling in the SMI would be interesting. As the present study is not suited for posing this question, data from the previous studies (if available) could be mentioned in the Discussion section. (Discretionary Revision).

A. this paragraph was added to show the overall efforts and type of questions addressed during the piloting of the study.
3. Are the data sound? The authors have studied a total of 646 patients. Generally speaking this is a more than adequate number. Some parts of the study, however, could benefit from some data improvement:

a) As mentioned above, the number of the subjects in whom the SMI diagnosis was compared to the clinical one (41) is rather small. Also, knowing the time elapsed between the two diagnoses (clinical and SMI) could be important, as well as knowing how many times the headache specialists had seen the patients before they were selected in the study, and whether, in those seen several times, there was a change in the clinical diagnosis. (These data may be important because it is not always possible to establish a correct diagnosis at the first visit and patients’ complaints and symptoms may change over time. Was the diagnosis of migraine still valid at the time when the patient filled in the SMI questionnaire?) (Minor Essential Revision)

A. the small number of participants is explained as in 2 (b) above. The clinical diagnosis assigned by the headache specialist was the final working headache diagnosis. Since we are interested in a life time ever diagnosis of migraine, we wanted to compare the SMI to the current working diagnosis.

b) In the first paragraph after Table 1 the authors report the percentage of patients reporting migraine and receiving migraine pharmacological treatment. As the patients only completed the SMI and reported their demographic details, this information was most likely based on questions 8 and 10 of the SMI. If so, how can we be sure that “migraine pharmacological treatment” refers to specific migraine treatment? For some patients the name of a non-specific drug eg. Migraleve may be misleading, and also people with other conditions such as cluster headache could also use specific antimigraine drugs such as triptans, so this info is not 100% relevant for the diagnosis of migraine. (Minor Essential Revision)

A. The study participants were asked if they were taking any medications and what were the indications for taking such medications as part of the study data collection. Participants had to write the names of each medicine and why did they take it. It is possible that certain medication have multiple indications. For this study purposes we classified a migraine medication that is taken specifically for migraine as indicated by the participant.

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?

The discussion is thorough and well balanced. Some points were not self-evident, so these might benefit from re-editing.

a) I agree that the study population was a highly selected one (patients from a
specialized headache centre), probably with an increased awareness about their headaches, so the comment about SMI detecting a significant number of migraineurs is not really surprising. (Discretionary Revision)

b) Speaking about the (modest) sensitivity of the SMI the authors state that ‘the validity sample was unbalanced by lack of subjects without headache’. The way sensitivity is defined (see also Table 2 of the manuscript) I can’t see how including headache-free subjects could improve the sensitivity. (Minor Essential Revision)

A. This statement refers to the validity of the SMI in general as the lack of non-headache subjects would make the sample unbalanced. The reviewer is correct in stating that the sensitivity is not necessarily affected by the having headache free subjects.

The conclusion that “a structured interview is a useful and valid tool to use in research for the identification of migraine” holds, as the specificity of the SMI was 1. However, I feel that with a misclassification rate of 29% the SMI should not be recommended for clinical use. (Major Compulsory Revision).

A. We have revised this paragraph: “The use of a questionnaire based on the ICHD criteria for migraine is shown to be a valid and simple method to use in diagnosing migraine in research settings and with caution in clinical settings due to limited sensitivity.”

6. Are limitations of the work clearly stated?

I think that more emphasis should be put on the limitations posed by the methods and sample sizes (sections 2b, 2c and 3a of this report). (Major Compulsory Revision)

A. These sections have been addressed as above.

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes.

8. Do the title and abstract accurately convey what has been found? As mentioned above, the ‘Development’ part of the title may be superfluous. The Methods section of the abstract is not informative (the methods of validation are not described). (Major Compulsory Revision)

A. The title has been edited as stated earlier in this report.
The methods section in the abstract was revised and now reads; “The structured migraine interview (SMI) based on the International Classification of Headache Disorders (ICHD) criteria was used in a clinical setting of headache sufferers and compared to clinical diagnosis by headache specialist. In addition to the validating characteristics of the interview; different methods of administration were also tested.”

9. Is the writing acceptable?

Yes. There are some typos as in ‘under diagnosed’ and ‘under treated’ (mentioned in the Abstract), both of which are commonly written as a single word, or “none migraine recurrent headaches” (page 5, paragraph 3). Also, “analgesia” in the last row of page 8 probably refers to analgesics and not a pathological state of the sensory system; for the sake of non-native English speakers I’d recommend the use of the latter, more widely accepted term. (Minor Essential Revision)

A. Typographical errors were addressed throughout the manuscript.