Author's response to reviews

Title: Screening for autism and AD/HD. The A-TAC: further validation of a telephone interview in clinical and population samples.

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Author's response to reviews: see over
Dear Dr Alam,

Many thanks for your kind and fruitful attention to our proposed manuscript, submitted as a possible contribution to BMC Psychiatry. We have carefully considered the two reviews, and have tried our best to improve the manuscript in accordance with the suggestion that we received. For a point-by-point discussion and specification of the changes we made, please see below. Remarks on revisions are numbered following the referees, and examples of the corrected text inserted in italics below each point.

Hereby attached is the revised version of the manuscript, which we hope will meet the high standards set by the journal.

The referees suggested new Figures, which are attached to this resubmission and referenced in the paper. We would be glad to include these in a final version of the paper, but this, of course, is up to your discretion, as none of them is strictly necessary to communicate the scientific content.

Yours truly,

Tomas Larson, MSc
PhD-Student

Reviewer 2 Morten Hesse

We have corrected the errors on pages 4-8 as indicated by the referee.

Three discretionary revisions:

1. Detailed information about the interviews has been added on page 9.

   *The full A-TAC interviews used here took on average 32 minutes to conduct.*

2. As a matter of fact, English and French versions are available on the web site of the Swedish Child Neuropsychiatry Science Foundation, and, in addition, there is a Spanish version of just the autism modules. This is now more carefully described in the manuscript on page 6.

   *On this web-site, official free translations of the original Swedish A-TAC into English, French and Spanish (ASD modules only) are also posted.*

3. A sentence addressing the utility of the gate structure has been added on page 8.

   *The motive for establishing the “gate” structure is, of course, to develop a briefer instrument with as good screening and diagnostic properties as the longer, more detailed, full version. The additional items are only asked if one or more of the first items in the module are*
endorsed fully or to some extent. A version containing the gate items only (Short Version, SV) is also available from the web-site.

Reviewer 1 Poul Thorsen

Major revisions

1. New columns have been added to Table 1 specifying the results by gender for each diagnostic category. In the results section, the following phrase was added on page 14:

All analyses were remade separately for boys and girls both with Index I and with both Index groups and the controls. Generally, the small number of girls gave the higher AUCs, but for both genders, they were very similar to those for the collapsed study groups.

2. The background has been extended on page XX

The “Autism – Tics, AD/HD and other Comorbidities inventory” (A-TAC) is a comprehensive screening interview for autism spectrum disorders (ASD), attention deficit/hyperactivity disorder (AD/HD), tic disorders (TD), developmental coordination disorder (DCD), learning disorders (LD) and other related childhood mental disorders that have been associated with these neurodevelopmental disorders in the existing literature. /…/ The overlap across ASD, AD/HD, and TD is considerable [6-8]. In subgroups, considerable overlaps have also been reported with obsessive compulsive disorder (OCD) [9], eating disorders, including anorexia nervosa [10], conduct disorder (CD), oppositional defiant disorder (ODD) [11], and learning disabilities [12].

3. For the time allotted to each interview, see Referee 2 point 1 above. Other requested details are given in this revised version of the Procedures.

All interviews were conducted over the telephone. The first author (T.L.), at the time a graduate student in psychology, who was blind to all diagnostic information and clinical data on the children, interviewed the parents of all children from the CNC, using a paper-and-pencil questionnaire. Parents were specifically asked not to provide any further information about their children, in order not to jeopardize blindness. The CATSS interviews were performed by a professional interview company, Intervjubolaget, by interviewers who had had a brief introduction in child and adolescent psychiatry and twin research, as detailed elsewhere [18]. They followed a computerized version of the A-TAC, and all responses were entered directly on to a database.

4. A new sentence on the frame for use of the A-TAC has been added to the summary.

Although the A-TAC is principally intended for epidemiological research and general investigations, the instrument may be useful as a tool to collect information in clinical practice as well.

The setting for which the A-TAC is validated is now also discussed on page 17. Even if the A-TAC is developed for research purposes, the validation may serve clinical purposes as well. For example, we often use the A-TAC before clinical consultations to gather information beforehand.
Among instruments that are possible to use in large-scale, non-clinical research, the A-TAC is unique in that it (a) identifies caseness across a range of different diagnostic categories, (b) provides dimensional assessments specifically in relation to ASD symptomatology and associated problems, and (c) in that it has been validated as a telephone interview. There are today several instruments that are frequently used as telephone interviewing tools, but are not validated as such. In the clinic, the A-TAC may for instance be used as an easy way to obtain structured information from parents before clinical examinations, making it possible to quickly focus on the most relevant aspects of the child’s mental and/or behavioral problems.

5. The study was designed to compare the A-TAC to independent clinical expert diagnoses from multi-professional teams at Sweden’s leading child neuropsychiatric clinic. Unfortunately, we did not from the beginning plan to compare the A-TAC results to scores from the various instruments established as state-of-the-art. Instead, we used LEAD (longitudinal, expert, all-data diagnoses) as “gold standard”. It may be argued that other instruments in the field have been validated according to similar principles. This was specifically addressed both in the ethical application and the information to parents used to obtain informed consent, where we stated that we would only access the final diagnostics, not any other medical information on the children. We thus conclude that, at this stage, it is not possible to change the design of the study in order to compare the A-TAC results to that from other interviews or instruments used. It is worth mentioning that the Gothenburg CNC is one of the world’s leading research and clinical facilities specialized on the conditions assessed in relation to the A-TAC and, even if we regret that we could not provide the additional information asked for, still consider the LEAD diagnoses as the “correct” standard for a validation of a screening and identification of caseness instrument, rather than convergent validity with other instruments.

Minor essential revisions
a. The theory for the A-TAC is mainly DSM-IV based using the diagnostic classification of child and adolescent mental disorders, in some cases split according to the various symptom profiles ordered in the DSM-IV, such as the three symptom items for autistic disorder and the two for AD/HD. Additional modules for tics, LD and DCD were added in the first version of the instrument, followed by the present, more specific modules for perception and organization. By the statement, we meant that the A-TAC was not constructed based on empirical findings from the general population, such as the CBCL or the MMPI, but based on clinical descriptions of children and adolescents with mental disorders.

The A-TAC items are organized in modules (e.g., attention, impulsiveness and activity, social interaction, communication), targeting hypothetical areas of psychiatric and psychological problems based on theoretical assumptions and the clinical literature in the field.

b. A specimen of an A-TAC module (the relatively long and detailed “social interaction” module) is included as a possible Figure 3.
c. This information was added to the Subjects description on page 10.

165 9-years-olds (84 boys and 81 girls) and 201 12-years-olds (97 boys and 104 girls, totaling 366 children)

122 9-years-olds (89 boys and 33 girls) and 197 12-years-olds (141 boys and 56 controls, totaling 319 children)

We also specified the mean age of the Index I subjects by age instead of the previously given collapsed information.

d. We have tried to be more detailed on how the psychometrics of the A-TAC has been described in the previous paper and in the web-material, as in the following examples.

In a clinical validation based on telephone interviews with 111 parents of clinically diagnosed children and healthy controls [1], a preliminary version of the A-TAC (with 178 items) had “excellent” screening properties for AD/HD and ASD (as assessed by areas under receiver operating characteristics curves around 0.90), and “fair” screening properties for LD, DCD, and TD (as assessed by areas under receiver operating characteristics curves between 0.70 and 0.80). The algorithms based on the DSM-IV criteria were sufficient for screening purposes, and items added from other sources did not improve the prediction of caseness. Inter-rater and test-retest reliability coefficients were good-excellent (intra-class coefficients ranging from 0.97 to 1.0 and from 0.77 to 0.97 respectively, with the exception of eating problems 0.57. The astonishing inter-rater correlations was, of course, due to the two raters participating in a simultaneous telephone interview and demonstrate little more than the clear conceptualization of the response alternatives.

e. We agree with the reviewer: ASDs combined with mental retardation could influence the results by providing a wide range of unspecific differences in relation to healthy controls. We therefore recalculated the analyses for the Index I subjects who had ASDs with a normal intelligence, but arrived at highly similar results. The following paragraph was added to the Results section:

The ROC analyses for ASDs were recalculated for the 34 Index I subjects who had ASD diagnoses with a normal intelligence and controls in order to check for a possible bias by comorbid mental retardation that could have conferred unspecific group differences across many modules, but these analyses yielding very similar AUCs (e.g. for the module gate scores 0.90, 0.95 and 0.94 in the order of the tables and for the total ASD score 0.95).

f. The group numbers are now all given in the format number (percent) in the Tables.

g. The superfluous headline was removed in the revised version of the paper.

h. The study was approved by the ethics review board at the University of Gothenburg (reference number Ö633-03). This is now specifically stated on page 12.

Discretionary Reviews
I. We have added two ROC curves for a possible inclusion in the final paper, one depicting the association between the three modules and total ASD score vs. ASDs and the other the parallel two modules and total score for ADHD among Index I and controls.