

Partial validation of a French version of the ADHD-rating scale IV on a French population of children with ADHD and epilepsy. Factorial structure, reliability, and responsiveness



Catherine Mercier^{a,b,c,d,*}, Sylvain Roche^{a,b,c,d}, Ségolène Gaillard^{e,f,g}, Behrouz Kassai^{e,f,g}, Alexis Arzimanoglu^{h,i}, Vania Herbillon^{h,i}, Pascal Roy^{a,b,c,d}, Sylvain Rheims^{j,k,l}

^a Service de Biostatistique, Hospices Civils de Lyon, Lyon, France

^b Université de Lyon, Lyon, France

^c Université Lyon 1, Villeurbanne, France

^d CNRS UMR5558, Laboratoire de Biométrie et Biologie Evolutive, Equipe Biostatistique-Santé, Villeurbanne, France

^e INSERM CIC 1407, Bron, France

^f CNRS UMR 5558, Laboratoire de Biométrie et Biologie Evolutive, Equipe Evaluation et modélisation des effets thérapeutiques, Villeurbanne, France

^g Service de Pharmacologie Clinique, Hospices Civils de Lyon, Bron, France

^h Service Epilepsie, sommeil et explorations fonctionnelles neuropédiatriques, Hospices Civils de Lyon, Bron, France

ⁱ DYCOG team, Centre de Recherche en Neurosciences de Lyon, INSERM UMR_S1028, CNRS UMR 5292, Bron, France

^j Service de Neurologie Fonctionnelle et d'Epileptologie, Hospices Civils de Lyon and Université de Lyon F-69500, Bron, France

^k Centre de Recherche en Neurosciences de Lyon, INSERM UMR_S1028, CNRS UMR 5292, Bron, France

^l Institut des Epilepsies, Bron, France

ARTICLE INFO

Article history:

Received 25 November 2015

Revised 9 February 2016

Accepted 10 February 2016

Available online xxxx

Keywords:

Attention deficit hyperactivity disorder

Epilepsy

Child

Adolescent

Confirmatory factor analysis

Validity

ABSTRACT

Objective: Attention deficit hyperactivity disorder (ADHD) is a well-known comorbidity in children with epilepsy. In English-speaking countries, the scores of the original ADHD-rating scale IV are currently used as main outcomes in various clinical trials in children with epilepsy. In French-speaking countries, several French versions are in use though none has been fully validated yet. We sought here for a partial validation of a French version of the ADHD-RS IV regarding construct validity, internal consistency (i.e., scale reliability), item reliability, and responsiveness in a group of French children with ADHD and epilepsy.

Method: The study involved 167 children aged 6–15 years in 10 French neuropediatric units. The factorial structure and item reliability were assessed with a confirmatory factorial analysis for ordered categorical variables. The dimensions' internal consistency was assessed with Guttman's lambda 6 coefficient. The responsiveness was assessed by the change in score under methylphenidate and in comparison with a control group.

Results: The results confirmed the original two-dimensional factorial structure (inattention, hyperactivity/impulsivity) and showed a satisfactory reliability of most items, a good dimension internal consistency, and a good responsiveness of the total score and the two subscores.

Conclusion: The studied French version of the ADHD-RS IV is thus validated regarding construct validity, reliability, and responsiveness. It can now be used in French-speaking countries in clinical trials of treatments involving children with ADHD and epilepsy. The full validation requires further investigations.

© 2016 Elsevier Inc. All rights reserved.

Abbreviations: ADHD, attention deficit hyperactivity disorder; ADHD-RS IV, ADHD-rating scale IV; ANCOVA, analysis of covariance; CFA, confirmatory factor analysis; CFI, comparative fit index; CI, confidence interval; CS-EPC, completely standardized expected parameter change; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders – Fourth edition; MI, modification index; RMSEA, root mean square error of approximation; SD, standard deviation; SRM, Standardized Response Mean; TLI, Tucker–Lewis index; VCI, Verbal Comprehension Index; PRI, Perceptual Reasoning Index; WISC-IV, Wechsler Intelligence Scale for Children – Fourth edition; WLSMV, mean- and variance-adjusted weighted least squares; WRMR, weighted root mean square residual.

* Corresponding author at: Service de Biostatistique, Hospices Civils de Lyon, 162, avenue Lacassagne, F-69003 Lyon, France. Tel.: +33 472 115 267.

E-mail address: catherine.mercier@chu-lyon.fr (C. Mercier).

1. Introduction

Attention deficit hyperactivity disorder (ADHD) is a well-known comorbidity in children with epilepsy. Its prevalence in these children is nearly 30%; that is, five to ten times higher than in the general population [1]. However, unlike what is seen in the general population, nearly half of children with ADHD and epilepsy have ADHD-I subtype (i.e., with predominance of attention deficit) [2–4].

One of the most robust and frequently used tools in clinical trials on children with ADHD without epilepsy is the ADHD-rating scale IV (ADHD-RS IV) [5]. This tool was initially developed in the English

language and has undergone various investigations of its psychometric properties [6,7]. To date, only the total score was validated for use in multicentric clinical trials in American and European populations [7]. This validation concerned internal coherence, interrater coherence, test–retest reliability, convergence and divergence validity, discriminant validity, and responsiveness under treatment.

The English version of the ADHD-RS IV has been already used as the main outcome in various clinical trials on children with ADHD and epilepsy [8]. However, the properties of this scale might not be suitable for all ADHD contexts, of such as ADHD in epilepsy, where its use might have introduced a methodological bias. Indeed, attention deficit being predominant vs. hyperactivity/impulsivity in children with epilepsy and ADHD [3], the discriminant abilities of the ADHD-RS IV total score or subscores may differ vs. children from the general population. Actually, the attention deficit subscore may be less sensitive than the hyperactivity/impulsivity subscore.

Furthermore, despite the presence of several French versions already in use, none of these versions has been validated yet.

The present study investigated some psychometric properties of a French version of the ADHD-RS IV in children with ADHD and epilepsy and assessed the validity of its total score and subscores in this population. This partial validation focused especially on the scale construct validity, internal consistency of the dimensions, reliability of the items, and responsiveness (i.e., sensitivity to change) in children with and without pharmacological treatment for ADHD.

2. Material and methods

2.1. The study population

Between November 2011 and September 2014, 168 children were screened in 10 French neuropsychiatric units (the PERENE network). Of these, 167 (55 girls and 112 boys) were included in the present study and one excluded on medical decision.

The inclusion criteria for the present study were: age between 6 and 15 years 11 months, diagnosis of epilepsy (any type), diagnosis of ADHD (inattentive or combined type according to the Diagnostic and Statistical Manual of Mental Disorders – Fourth edition (DSM-IV) criteria), and agreement to comply with the study protocol (children and parents).

The exclusion criteria were: the diagnosis of ADHD of exclusively hyperactivity/impulsivity type (according to the DSM-IV criteria), the use of pharmacological treatment for ADHD initiated before inclusion (methylphenidate, amphetamine, atomoxetine, or antidepressant), the presence of mental retardation (either clinically or neuropsychologically

determined with the Wechsler Intelligence Scale for Children – Fourth edition (WISC-IV)), and the presence of a psychiatric comorbidity (pervasive developmental disorders, including autistic disorders, psychotic disorders, and bipolar disorders according to the DSM-IV criteria).

2.2. The questionnaire

The 18-item French version of the ADHD-RS IV is shown in Table 1 (for the original English version, please visit <http://www.healthchoiceaz.com/docs/providers/screeningtools/child%20adhd%20rating%20screeener.pdf>). In each neuropsychiatric unit, all and entire questionnaires were administered by the same physician at the inclusion visit and at the follow-up visit 12 to 16 weeks later. Sixteen questionnaires were missing at the follow-up visit (5 lost to follow-up in the group without pharmacological treatment for ADHD). Thus, the records of 151 patients were kept for responsiveness analysis.

2.3. The data

The data were the scores for the 18 items that quantify the two dimensions of the French version of the ADHD-RS IV: i) Inattention; i.e., impair items 1 to 17 and ii) Hyperactivity/impulsivity: i.e., pair items 2 to 18. Each item was rated on a 4-point Likert scale: 0 for “Jamais ou rarement” (Never or rarely) to 3 for “Très souvent” (Very often) (see Table 1).

2.4. The statistical analysis

2.4.1. The confirmatory factor analysis

A Confirmatory Factor Analysis (CFA) [9] checked the four hypotheses of the baseline CFA model (or Model 1) applied to the French ADHD-RS IV: i) ADHD responses can be explained by two factors (also called, latent variables, or dimensions): inattention and hyperactivity/impulsivity; ii) each item has a nonnull coefficient of regression on the dimension it was designed to measure (factor loading) and null factor loadings on the other dimension; iii) the two factors are correlated; and iv) the residual errors associated with each item are uncorrelated.

As the items are ordinal variables, the parameters of the CFA models were estimated from polychoric correlation matrices [10] using mean- and variance-adjusted weighted least squares (WLSMV).

Items and latent variables were standardized to provide standardized parameters, thus standardized factor loadings. Such an approach enables interpreting and comparing these factor loadings as correlations.

Several indexes (with their distinct rules for good fit) were used to assess the fit of the CFA models: i) the Comparative Fit Index (CFI)

Table 1
The French version of the ADHD-RS IV used for the study.

| Cochez la case qui décrit le mieux le comportement de l'enfant pendant la semaine | Jamais ou rarement (0 point) | Parfois (1 point) | Souvent (2 points) | Très souvent (3 points) |
|---|---------------------------------|--------------------------|--------------------------|----------------------------|
| 1. Ne fait pas attention aux détails ou fait des fautes d'inattention en classe | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Agite les mains ou les pieds ou se tortille sur sa chaise | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. A du mal à rester attentif pendant le travail ou le jeu | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Se lève en classe ou dans d'autres situations où il aurait dû rester assis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Ne semble pas écouter lorsque l'on s'adresse à lui directement | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Court dans tous les sens ou grimpe partout dans des situations où il ne devrait pas faire cela | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. N'exécute pas complètement les instructions et ne finit pas son travail | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 8. A du mal à jouer ou à faire autre chose tranquillement | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 9. A du mal à organiser ses tâches et ses activités | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 10. Semble toujours “sous tension” comme s'il “fonctionnait sur piles” | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 11. Evite les tâches qui nécessitent un effort mental soutenu (travail scolaire, devoirs, ...) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 12. Parle trop | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 13. Perd des objets nécessaires à son travail ou à ses activités | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 14. Lance des réponses avant que l'on ait fini de poser la question | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 15. Est facilement distrait | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 16. A du mal à attendre son tour | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 17. Oublie des choses dans ses activités de tous les jours | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 18. Interrompt les autres ou s'impose à eux | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

[11,12] and the Tucker–Lewis Index (TLI) [13], with “good fit” if >0.95 ; ii) the root mean square error of approximation (RMSEA) and its 90% confidence interval (CI) with “good fit” if <0.08 [14]; iii) the weighted root mean square residual (WRMR), with “good fit” if ≤ 1.0 [15]; and iv) the modification indexes (MIs) [16].

The MIs were used to select additional parameters and improve the model fit. A high MI indicates an important improvement. Alternative models may thus be obtained by adding, to the baseline model (Model 1), one parameter at a time, starting with the parameter with the highest MI. This purely statistical approach was associated with pragmatic fit-improvement criteria: 1) the completely standardized expected parameter change (CS-EPC) associated with each MI is ≥ 0.3 (an item cannot reflect a given dimension if its standardized factor loading is <0.30 [17,18] or <0.40 [19]) and 2) the modifications and parameters (factor loadings or residual correlations between items) are clinically meaningful (the wordings of the items are consistent with knowledge that underpins the development of the scale).

2.4.2. Item reliability

Item reliability was estimated through R^2 ; that is, the part of the item variance that may be explained by its underlying dimension. It is equal to the square of the standardized factor loading of the item [9].

2.4.3. Dimension internal consistency

The internal consistency of each dimension was estimated using Guttman’s lambda 6 reliability coefficient [20]. Usually, the items of each dimension are considered heterogeneous, consistent, or redundant at values <0.7 , close to 0.8, or >0.9 , respectively.

2.4.4. Responsiveness

The responsiveness of a rating scale measures the scale’s ability to detect small but clinically significant changes in patient symptom severity. It was assessed by the change in score between inclusion and end of follow-up. To be able to compare the results regarding responsiveness with those published by other authors, the Standardized Response Mean (SRM) was also computed. The SRM is the mean change between the baseline and end of follow-up scores divided by the standard deviation of the change. The higher the SRM value, the higher the sensitivity to change. The published SRM values for the total score of the English version were 1.2 in an American population [6] and 1.8 in a French subgroup of a European population [7].

An ANCOVA was used to evaluate responsiveness in the group treated with methylphenidate only compared with the control group (methylphenidate being a proven effective compound for ADHD symptoms) [21]. The comparability of the groups was checked, and potential confounding factors were studied: age, sex, center, type of epilepsy, frequency of seizures (during the four weeks before inclusion), number of treatments for epilepsy, duration of epilepsy, duration of ADHD, and delay between pre- and postevaluation. The confounding factors finally kept for the ANCOVA model (group comparisons) were: the pediatric unit, the type of epilepsy, the frequency of seizures, and the delay between pre- and postevaluation; this led to adjusted differences in scores.

2.5. Software programs

The CFA and item reliability were estimated using *Mplus*, version 7.11 [22]. All other analyses used R, version 3.0.1 (<http://www.r-project.org/>). All tests were two-tailed, and $P < 0.05$ was considered for statistical significance.

3. Results

3.1. Description of the participants

The mean age was 9.5 (SD: 2.4) years and the ages ranged from 5 years 8 months to 15 years 9 months. The types of epilepsy were:

idiopathic generalized epilepsy (33%), idiopathic focal epilepsy (28%), symptomatic focal epilepsy (31%), and others (8%). The median duration of epilepsy was 2 years (range: one month to 6 years 7 months). Epilepsy was treated with antiepileptic drugs in 85.5% of the children and controlled in 53.9%. Among the 167 children, 42.5% had an inattentive type of ADHD; the others had the mixed type.

At inclusion in the study, 61 patients were prescribed a specific pharmacological treatment for ADHD (namely, methylphenidate; no other treatment was given for ADHD), and 106 were followed up without pharmacological treatment for ADHD.

3.2. Validation of the factorial structure

The factor loadings, the correlation coefficients between the two dimensions, and the residual correlations were all statistically significant (meaning nonnull coefficient of regression regarding each item on its dimension and nonnull correlation coefficients; see Fig. 1); however, the statistical indexes used for the fit of Model 1 (Table 2) were not satisfactory. The CFI and the TLI were both <0.95 (0.865 and 0.845, respectively), the RMSEA was ≤ 0.08 (0.093, 90% CI: [0.080–0.106]), and the WRMR was greater than 1 (precisely 1.263). Thus, Model 1 could be subject to improvement using the MIs.

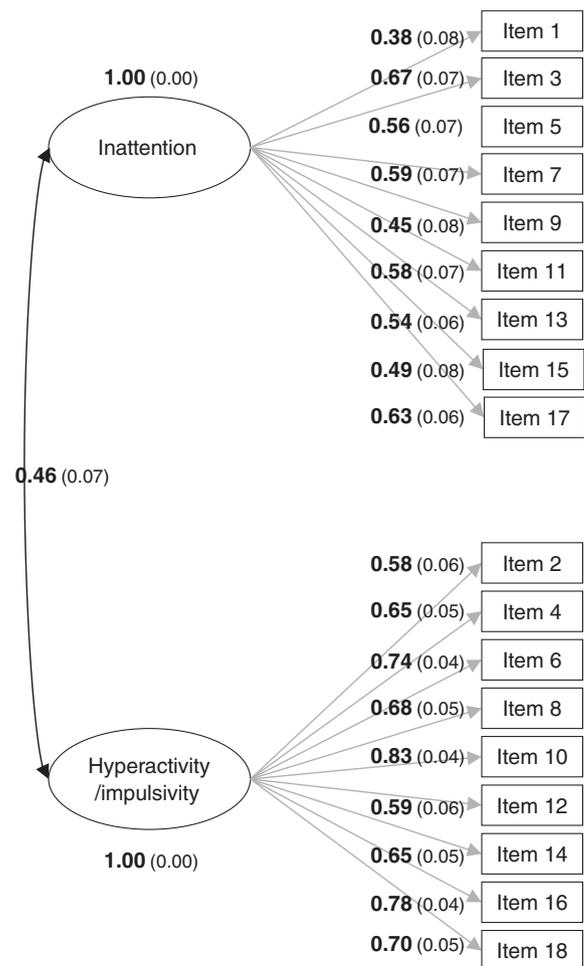


Fig. 1. Standardized parameter estimates and their standard errors stemming from the baseline model (Model 1) run with the French version of the ADHD-RS IV on a French population of children with ADHD and epilepsy. In this diagram, each circle corresponds to a single dimension and each rectangle to a single item. The circles are linked to the rectangles by single-headed arrows only for items that reflect the dimension (i.e., Items 1 and 3 for “Inattention” and not for the other dimension). The lack of arrows means that the factor loading is set at 0. The relationships between dimensions are represented by double-headed arrows between circles. This relationship is a correlation since the latent variables are standardized.

Table 2
Model fit on the basis of the statistical indexes.

| Model and characteristics | Chi ² | df | CFI | TLI | RMSEA | | WRMR | Model improvement | | | |
|---|------------------|-----|-------|-------|----------------|----------------|---------|-------------------|--|--------|--------|
| | | | | | Value [90% CI] | P-value | | Parameter to add | MI | CS-EPC | |
| Model 1: Baseline model | 327.28 | 134 | 0.865 | 0.846 | 0.093 | [0.080; 0.106] | <0.0001 | 1.263 | Residual correlation between Items 13 & 17 | 42.121 | 0.701 |
| Model 2: Model 1 + residual correlation between Items 13 & 17 | 290.19 | 133 | 0.891 | 0.874 | 0.084 | [0.071; 0.097] | <0.001 | 1.160 | Item 5 reflecting Hyperactivity | 24.320 | 0.353 |
| Model 3: Model 2 + Item 5 reflecting Hyperactivity | 269.25 | 132 | 0.904 | 0.889 | 0.079 | [0.065; 0.092] | <0.001 | 1.098 | Item 3 reflecting Hyperactivity | 19.738 | -0.309 |

df: degrees of freedom – CFI: comparative fit index – TLI: Tucker–Lewis index – RMSEA: root mean square error of approximation – CI: confidence interval – WRMR: weighted root mean square residual – MI: modification index – CS-EPC: completely standardized expected parameter change.

The MIs suggested adding, in the first step, a residual correlation between Item 17 “Oublie des choses dans les activités de tous les jours” (“Is forgetful in daily activities”) and Item 13 “Perd les objets nécessaires à son travail ou à ses activités” (“Loses things necessary for tasks or activities”) of Dimension Inattention and, in a second step, a correlation between Item 5 “Ne semble pas écouter lorsque l’on s’adresse à lui directement” (“Does not seem to listen when spoken to directly”) and Dimension Hyperactivity/impulsivity. This led successively to Models 2 and 3 (Table 2) and to an improved fit at each step. Model 3 showed the best fit: a CFI equal to 0.904, a TLI equal to 0.889, a RMSEA of 0.079 (90% CI: [0.065–0.092]), and a WRMR close to 1 (1.098). No further changes to Model 3 could be considered relevant regarding the statistical and pragmatic criteria: the MIs suggested that Item 3 would also reflect Dimension Hyperactivity (Model 3 in Table 2), but this modification led to a weak improvement of the fit and did not satisfy the pragmatic fit-improvement criteria (standardized factor loading of Item 3 = 0.309).

The standardized parameter estimates of Model 3 are shown in Fig. 2. The fit of this model was satisfactory according to the pragmatic criteria, but the items of Dimension Inattention remained less discriminant than those of Dimension Hyperactivity/impulsivity. Indeed, in Dimension Inattention, the standardized factor loadings ranged from 0.283 (Item 5) to 0.734 (Item 3) whereas, in Dimension Hyperactivity/impulsivity, they ranged from 0.308 (Item 5) to 0.834 (Item 10). The factor loadings, the correlation coefficients between the two dimensions, and the residual correlations were all statistically significant. The correlation between the latent variables was not too high: 0.42 between Inattention and Hyperactivity/impulsivity. This indicated that the model with two dimensions is relevant.

3.3. Item reliability

Table 3 shows the estimated reliabilities of all items (with Models 1 and 3) in decreasing order within each dimension. These values ranged between 0.137 and 0.696. They were all, statistically speaking, significantly different from 0 ($P < 0.05$). The lowest values belonged to Item 13 that showed a residual correlation with Item 17. The reliability of Item 5 in Model 3 was 0.249 (it was 0.336 in Model 1).

3.4. Internal consistency

The coefficient of internal consistency was 0.73 for Inattention and 0.87 for Hyperactivity/impulsivity. The two dimensions are thus internally consistent.

3.5. Responsiveness

Regarding the total score, the mean score change between baseline and end of follow-up was – 13 points in the group treated with methylphenidate (61 patients) vs. – 4 in the control group (106 patients). The corresponding SRMs were – 1.19 vs. – 0.53. At end of follow-up, the raw difference in the mean score change between the two groups

was – 9 points and the adjusted difference – 8 points. The corresponding SRMs were – 0.90 and – 0.83, respectively.

Concerning the Inattention subscore, the mean score change between baseline and end of follow-up was – 7 points in the group treated with methylphenidate and – 2 points in the control group. The corresponding SRMs were – 1.08 vs. – 0.42. At end of follow-up, both the raw difference and the adjusted difference in mean score change between the two groups were – 4 points. The corresponding SRMs were – 0.87 for the raw difference and – 0.68 for the adjusted difference.

Concerning the Hyperactivity/impulsivity subscore, the mean score change between baseline and end of follow-up was – 6 points in the group treated with methylphenidate and – 2 points in the control

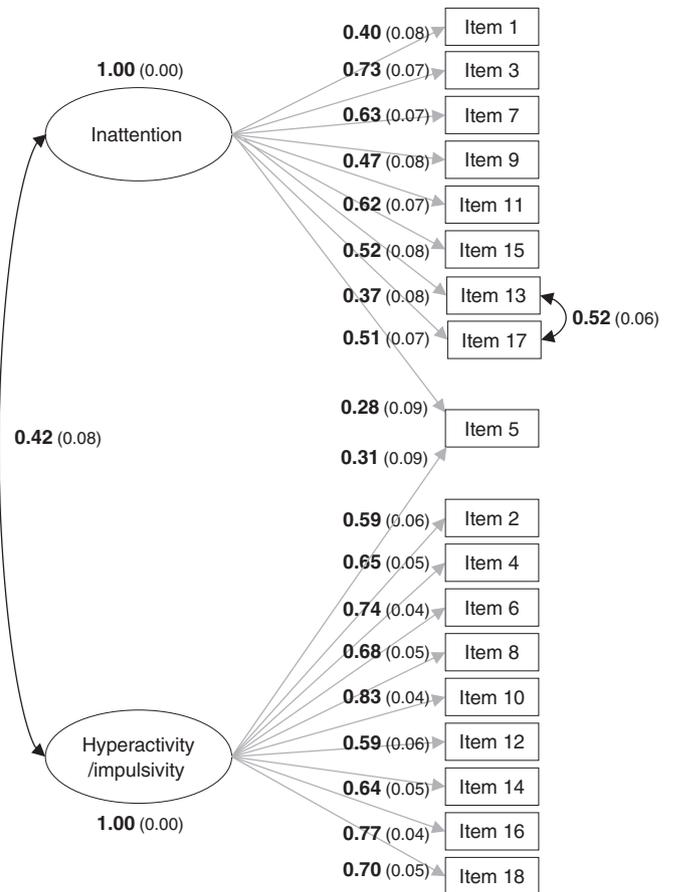


Fig. 2. Standardized parameter estimates and their standard errors stemming from the final Model (Model 3) run with the French version of the ADHD-RS IV on a French population of children with ADHD and epilepsy. In this diagram, the two circles are linked to the same rectangle of Item 5 by single-headed arrows. This means that Item 5 reflects both of the dimensions “Inattention” and “Hyperactivity/impulsivity”. A relationship between Item 13 and Item 17 is represented by a double-headed arrow between the two rectangles. This relationship (covariance between error terms) is a residual correlation because the parameters are standardized.

Table 3
Reliability of the items per dimension according to Models 1 (the baseline model) and 3 (the best model fit).

| Dimensions and items | Model 1 | | | Model 3 | | |
|--|-----------------------|----------------|-------------------|-----------------------|----------------|-------------------|
| | Estimated reliability | Standard error | Residual variance | Estimated reliability | Standard error | Residual variance |
| Inattention | | | | | | |
| 3 | 0.503 | 0.101 | 0.497 | 0.538 | 0.105 | 0.462 |
| 7 | 0.362 | 0.081 | 0.638 | 0.393 | 0.085 | 0.607 |
| 11 | 0.353 | 0.082 | 0.647 | 0.384 | 0.086 | 0.616 |
| 5 | 0.336 | 0.080 | 0.664 | – | – | – |
| 15 | 0.243 | 0.078 | 0.757 | 0.273 | 0.080 | 0.727 |
| 17 | 0.233 | 0.072 | 0.767 | 0.255 | 0.075 | 0.745 |
| 9 | 0.202 | 0.075 | 0.798 | 0.220 | 0.079 | 0.780 |
| 1 | 0.136 | 0.058 | 0.864 | 0.157 | 0.062 | 0.843 |
| 13 | 0.130 | 0.058 | 0.870 | 0.137 | 0.060 | 0.863 |
| Hyperactivity/impulsivity | | | | | | |
| 10 | 0.695 | 0.061 | 0.305 | 0.696 | 0.060 | 0.304 |
| 16 | 0.603 | 0.066 | 0.397 | 0.598 | 0.066 | 0.402 |
| 6 | 0.543 | 0.062 | 0.457 | 0.547 | 0.061 | 0.453 |
| 18 | 0.495 | 0.073 | 0.505 | 0.498 | 0.072 | 0.502 |
| 8 | 0.471 | 0.071 | 0.529 | 0.468 | 0.071 | 0.532 |
| 4 | 0.419 | 0.068 | 0.581 | 0.420 | 0.067 | 0.580 |
| 14 | 0.417 | 0.068 | 0.583 | 0.412 | 0.069 | 0.588 |
| 12 | 0.348 | 0.069 | 0.652 | 0.347 | 0.069 | 0.653 |
| 2 | 0.340 | 0.074 | 0.660 | 0.346 | 0.074 | 0.654 |
| Inattention & hyperact./impulsivity | | | | | | |
| 5 | – | – | – | 0.249 | 0.059 | 0.751 |

group. The corresponding SRMs were -0.91 and -0.52 , respectively. At end of follow-up, both the raw difference and the adjusted difference in mean score change between the two groups were -4 points. The corresponding SRMs were -0.68 (raw difference) and -0.72 (adjusted difference).

The differences in scores and subscores between the two groups were statistically significant (raw and adjusted differences). The precise adjusted differences were -7.7 (95% CI: $[-11.5, -3.8]$) for the total score, -3.8 $[-6.0, -1.5]$ for Inattention-specific score, and -3.9 $[-6.1, -1.7]$ for the Hyperactivity/impulsivity-specific score.

4. Discussion

In ADHD, the common tool used in clinical trials is the ADHD-RS IV though its validation in children with epilepsy has not been reported yet. Furthermore, its French versions have never been validated even in children without epilepsy. In testing the factorial validity and estimating item and dimension reliability of a French version, we wanted to provide French-speaking physicians and researchers a valid and dependable tool to use in children with ADHD and epilepsy.

4.1. Validation of the factorial structure

Regarding construct validity, two of the four hypotheses investigated with a CFA were fully supported: i) ADHD responses can be explained by two factors: inattention and hyperactivity/impulsivity; and ii) the two factors are correlated.

The two other hypotheses were only partially supported. First, each item had a nonnull coefficient of regression on the dimension it was designed to measure (factor loading), but Item 5 had nonnull factor loadings on the two dimensions (inattention and hyperactivity/impulsivity). This has been already found in children with ADHD without epilepsy but not explicitly mentioned by Zhang et al. [7]: Item 5 “Does not seem to listen when spoken to directly” had a factor loading of 0.35 for Inattention and 0.27 for Hyperactivity/impulsivity. Second, correlated residual errors were found between Item 13 “Perd les objets nécessaires à son travail ou à ses activités” (“Loses things necessary for tasks or activities”) and Item 17 “Oublie des choses dans les activités de tous les jours” (“Is forgetful in daily activities”).

Thus, allowing for a residual correlation between Items 13 and 17 and a correlation between Item 5 and Dimension Hyperactivity/

impulsivity led to a better model fit. However, the residual correlation may stem from features specific to the study sample; it should thus be checked in other independent samples.

4.2. Item reliability and internal consistency

The results confirmed the internal consistency of the ADHD-RS IV dimensions; both are thus reliable. Item reliability was lower for Inattention items than for Hyperactivity/impulsivity items. This was already found by previous studies using the English version [7], especially regarding Items 5 and 13 which had low factor loadings (the square roots of item reliabilities). These properties make the ADHD-RS IV an objective tool for behavior assessment in children with ADHD and epilepsy.

4.3. Responsiveness

The responsiveness of the total score, that of the Inattention subscore, and that of the Hyperactivity/impulsivity subscore were assessed in children with epilepsy receiving methylphenidate. The scale was found more responsive (sensitive to change) in the group treated with methylphenidate than in the control group.

Regarding the total score, the SRM in the treatment group (i.e., 1.19) was similar to the SRM published by other authors [6,7]. The SRMs relative to the subscores were slightly lower (-1.08 for Inattention and -0.91 for Hyperactivity/impulsivity). In the control group, the SRMs relative to the total score and subscores were fairly close (-0.53 for the total score, -0.42 for Inattention, and -0.52 for Hyperactivity/impulsivity). The adjusted differences between the two groups were statically significant and clinically significant according to the minimal clinically important difference in ADHD (i.e., a 6.6-point difference in total score) [7]. This demonstrates the responsiveness of the total score and subscores.

One facet of the present study is that the final model we kept was slightly different from the one used for the English version. Actually, in the French version, Item 5 could as well belong to any of the two dimensions of the ADHD-RS IV. Thus, one would like to put weight on this item in each subscore. However, according to Steiner and Norman [23], this would probably bring no change to the total score and subscores; thus, probably no change in the responsiveness.

One potential limitation may be that all participants did not undergo IQ testing. In fact, at first, a detailed neuropsychological evaluation was not required by the study protocol; IQ testing was carried out at the discretion of the treating physician. However, in all participating centers, full neuropsychological evaluation is usually performed in children suspected of mental retardation, and children with scores <70 for Verbal Comprehension Index (VCI) and Perceptual Reasoning Index (PRI) or with clinically determined mental retardation were not eligible for the study. Thus, in the absence of systematic IQ testing of included patients, we cannot formally exclude that some of them had scores <70. In other words, the relationship between ADHD severity and IQ score could not be evaluated. Therefore, we cannot rule out that different IQ levels between patients might have been a confounding factor.

5. Conclusions

To our knowledge, this is the first validation study of a French version of the ADHD-RS IV in a population of children with ADHD and epilepsy. The responsiveness of the total score and subscores under treatment or between a treatment and a control group allows use of this scale in clinical trials of treatments for ADHD in epilepsy.

The validation of other aspects of the scale (test–retest validity, interrater validity, etc.) in patients with epilepsy and ADHD requires further investigations. A partial or full validation in other children (with other diseases or without disease) requires an entirely new investigation protocol in the appropriate population.

Ethics

The study was carried out with agreements from: i) Comité de Protection des Personnes Lyon Sud-Est II (France) obtained on October 5, 2011; ii) Comité Consultatif sur le Traitement de l'Information en matière de Recherche dans le domaine de la Santé (France), Agreement Nr. 11.530, issued on September 22, 2011; and, iii) Commission Nationale de l'Informatique et des Libertés (France), Agreement Nr. 911501, issued on February 23, 2012.

Acknowledgments

The authors thank Catherine Cereser (Direction de la Recherche Clinique et de l'Innovation), Fanny Abad, and Camille Ménard (Centre d'Investigation Clinique) for their participation. They also thank Jean Iwaz (Hospices Civils de Lyon, France) for many helpful comments, suggestions, and revisions of the manuscript.

The study was conducted with a grant from the French Ministry of health (grant number 27.23) (PHRC 2011). Patients were recruited by the Pediatric Epilepsy Research Network, France (PERENE, RIPPS, <http://ripss.eu/en/paediatric-epilepsies/perene-network>): Doctors Stéphane Auvin (Paris, Robert Debré), Patrick Berquin (Amiens), Claude Cances (Toulouse), Pierre Castelnau (Tours), Julitta de Bellescize (Lyon), Hervé Isnard (Lyon), Pascale Keo-Kosal (Lyon), Mathieu Milh (Marseille), Rima Nabbout (Paris, Necker-Enfants Malades), Silvia Napuri

(Rennes), Sylvie N'guyen The Tich (Angers), Karine Ostrowsky-Coste (Lyon), Eleni Panagiotakaki (Lyon), and Frédéric Villega (Bordeaux).

Conflicts of interest

None.

References

- [1] Kaufmann R, Goldberg-Stern H, Shuper A. Attention-deficit disorders and epilepsy in childhood: incidence, causative relations and treatment possibilities. *J Child Neuro* 2009;24:727–33.
- [2] Hesdorffer DC, Ludvigsson P, Olafsson E, Gudmundsson G, Kjartansson O, Hauser WA. ADHD as a risk factor for incident unprovoked seizures and epilepsy in children. *Arch Gen Psychiatry* 2004;61:731–6.
- [3] Hermann B, Jones J, Dabbs K, Allen CA, Sheth R, Fine J, et al. The frequency, complications and aetiology of ADHD in new onset paediatric epilepsy. *Brain* 2007;130(Pt 12): 3135–48.
- [4] Sherman EM, Slick DJ, Connolly MB, Eyrl KL. ADHD, neurological correlates and health-related quality of life in severe pediatric epilepsy. *Epilepsia* 2007;48(6): 1083–91.
- [5] DuPaul GJ, Power TJ, Anastopoulos. ADHD rating scale IV: checklists, norms, and clinical interpretations. New York (NY): Guilford Press; 1998.
- [6] Faries D, Yalcin I, Harder D, Heiligenstein JH. Validation of the ADHD rating scale as a clinician administered and scored instrument. *J Atten Disord* 2001;5:107–15.
- [7] Zhang S, Faries DE, Vowles M, Michelson D. ADHD rating scale IV: psychometric properties from a multinational study as a clinician-administered instrument. *Int J Methods Psychiatr Res* 2005;14:186–201.
- [8] Gonzalez-Heydrich J, Whitney J, Waber D, Forbes P, Hsin O, Faraone SV, et al. Adaptive phase I study of OROS methylphenidate treatment of attention deficit hyperactivity disorder with epilepsy. *Epilepsy Behav* 2010;18:229–37.
- [9] Bollen KA. Structural equations with latent variables. New York: John Wiley & Sons; 1989.
- [10] Muthén B, du Toit SHC, Spisic D. Robust inference using weighted least squares and quadratic estimating equations in latent variable modeling with categorical and continuous outcomes. Available at: http://www.statmodel.com/bmuthen/articles/Article_075.pdf; 1997. [Last accessed December 2014].
- [11] Hu L, Bentler PM. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct Equ Model* 1999;6:1–19.
- [12] Bentler PM. Comparative fit indexes in structural models. *Psychol Bull* 1990;107: 238–46.
- [13] Tucker LR, Lewis C. A reliability coefficient for maximum likelihood factor analysis. *Psychometrika* 1973;38:1–10.
- [14] Browne MW, Cudeck R. Alternative ways of assessing model fit. In: Bollen KA, Long JS, editors. Testing structural equation models. Beverly Hills (CA): Sage Publications; 1993. p. 136–62.
- [15] Yu CY. Evaluating cutoff criteria of model fit indices for latent variable models with. Available at: <http://statmodel2.com/download/Yudissertation.pdf>. [Last accessed December 2014].
- [16] Sörbom D. Model modification. *Psychometrika* 1989;54:371–84.
- [17] Kim JO, Mueller CW. Factor analysis: structural methods and practical issues. Beverly Hills (CA): Sage Publications; 1978.
- [18] Brown TA. Confirmatory factor analysis for applied research. New York: The Guildford press; 2006.
- [19] Ford JK, MacCallum RC, Tait M. The application of factor analysis in applied psychology: a critical review and analysis. *Pers Psychol* 1986;39:291–314.
- [20] Guttman L. A basis for analyzing test–retest reliability. *Psychometrika* 1945;10: 255–82.
- [21] Storebo OJ, Krogh HB, Ramstad E, Moreira-Maia CR, Holmskov M, Skoog M, et al. Methylphenidate for attention-deficit/hyperactivity disorder in children and adolescents: Cochrane systematic review with meta-analyses and trial sequential analyses of randomised clinical trials. *BMJ* 2015;351:h5203.
- [22] Muthén LK, Muthén BO. Mplus user's guide. 7th ed. Los Angeles: Muthén & Muthén; 1998–2012.
- [23] Steiner DL, Norman GR. Health measurement scales. A practical guide to their development and use. 4th ed. Oxford Univ. Press; 2008.