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Running Title:

Measurement Invariance Study in ADHD

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Abstract

Objectives: To ascertain whether the differences of prevalence and severity of Attention Deficit/Hyperactivity Disorder (ADHD) are true or whether children are perceived and rated differently by parent and teacher informant assessments (INFA) according to gender, age and co-occurring disorders, even at equal levels of latent ADHD traits. Methods: Use of latent trait models (for binary responses) to evaluate measurement invariance in children with ADHD and their siblings from the IMAGE data. Results: Substantial measurement non-invariance between parent and teacher INFA was detected for 7/9 inattention (IA) and 6/9 hyperactivity/impulsivity (HI) items; the correlations between parent and teacher INFA for 6 IA and 4 HI items were not significantly different from zero; which suggests that parent and teachers INFAs are essentially rating different kinds of behaviours expressed in different settings, instead of measurement bias. However, age and gender did not affect substantially the endorsement probability of either IA or HI-symptom criteria, regardless of INFA. For co-occurring disorders, teacher INFA ratings were largely unaffected by comorbidity; conversely, parental endorsement of HI-symptoms is substantially influenced by co-occurring Oppositional Defiant Disorder.

Conclusions: Our findings suggest general robustness of DSM ADHD diagnostic items in relation to age, gender. Further research on classroom presentations is needed.

Keywords: ADHD, measurement invariance, item factor analysis, PACS, co-occurring disorder

Introduction

The DSM5 stipulates an age-related threshold in the number of inattention (IA) and/or hyperactivity/impulsivity (HI) symptoms for an ADHD diagnosis (American Psychiatric Association, 2013). The DSM5 symptom criteria remain largely unchanged from those of DSM-IV. There is, however, no guidance or operationalised algorithm to steer clinicians' judgement on 'developmental appropriateness' for a given age and gender. To establish a reliable clinical diagnosis of ADHD, it is recommended to gather information across settings. However, this introduces the issue of how best to integrate information from multiple settings, in particular, if co-occurring conditions can further blur or affect the thresholds of diagnosis. Two common systems for diagnosis are used (Valo and Tannock, 2010): the 'and-rule' requires the item's endorsement by both parents and teachers; while the 'or-rule' requires only the one or the other. The extent to which the above factors would influence the measurement of the traits - yielded by the 'and' versus 'or' rules - is not yet sufficiently known.

The effects of age, gender, informant assessment and co-occurring conditions on both the endorsement or severity rating of ADHD have been evaluated in a substantial body of studies. The majority of research examined the extent to which the total number of symptoms can vary according to these factors, with the ensuing effects on diagnostic prevalence. The detected

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differences across demographic groups in the total number of symptoms (score differences) have prompted some authors to propose adjusting the criteria threshold with respect to age (Ramtekkar et al., 2010, Biederman et al., 2000 among others) and gender (Rucklidge, 2010; Amador Campos et al., 2006; Monuteaux et al., 2010). Newcorn et al. (2001), identified significant differences in symptomatology according to comorbidity and gender.

The differences in the total scores (total number of symptoms) due to these factors are well documented in the literature. However, for an unbiased comparison of the total number of Inattention (IA) or Hyperactivity/Impulsivity (HI) symptoms across groups (for instance gender or age groups) or conditions (for instance type of INFA), we need first to establish that the probability of endorsing each symptom depends solely on the levels of IA or HI, and that any group membership or condition does not bias the measurement. In psychometrics, this assessment is referred to as measurement invariance (MI) testing, within the framework of factor analysis (for instance see Millsap, 2011), or as differential item functioning (DIF, for instance Osterlind and Everson, 2009) within the item response theory (IRT) context.

For instance, to compare boys' and girls' weights, one would first ensure that the same or an identical weighting scale is employed to measure both groups. Once the scale's MI across groups is established, then one can proceed with comparing the measurement scores. Only then, we expect that the same value (measurement) will occur on the weighting scale for two individuals with the same weight, regardless of their gender. In a similar manner, in this study we seek to establish the invariance of the symptom criteria ratings in the measurement of the latent traits IA and HI across gender, age, INFA and the algorithms to combine INFA' scores (i.e. 'and' versus 'or' rules). If the measurement is invariant (unbiased), then two individuals

with the same IA (or HI) levels should both have equal probabilities of endorsing the symptoms - regardless of their age, gender, co-occurring diagnoses, and/or INFA. One can then proceed with testing the factor's effect on the total score, in a manner similar to that of a researcher who has first to ensure that the same weighting scale can be used for boys and girls and can then proceed with comparing the mean weight across genders. Therefore, there are two questions to be asked with respect to measurement. The first one refers to the objectivity of the measuring instrument (measurement invariance; *MI*) and the second refers to the differences in the scores (in psychometrics, differences in the scores of the traits referred to are termed the *structural invariance*).

Researchers in the field have previously used different assessment tools, statistical methods and target populations, in their exploration of MI due to age and/or gender (Burns et al., 2006; Derks et al, 2007; Gomez and Vance, 2008; Gomez et al., 2012; Geiser et al., 2014; Gomez, 2013; Zeeuw et al, 2015; Wiesner et al, 2015; Gomez et al, 2016; Morin et al, 2016; Caci et al, 2016, Fumeaux et al. 2017; and Cogo-Moreira et al., 2017) and invariance due to the informant (for instance Gomez, 2007; Burns, 2009; Makransky and Bilenberg, 2014; King et al 2016). Overall, the results of MI studies so far suggest that informant, age, gender and culture have only small effects on ratings of ADHD symptoms. Nevertheless, it is of interest that a quantitative genetic twin study identified that parents and teachers report different psychopathological phenomena (Arnett et al., 2015). Whether the discrepancies are real or arising from methodological differences across these studies remains untested.

To our knowledge, this work is novel in terms of assessing all these factors together, in the same sample, examining individual symptoms as well as the combination of information

using the ‘and’ versus ‘or’ rules.

The objectives of this study are as follows:

1. Is the probability of endorsing a symptom dependent on parent- or teacher-assessment results? Do the different INFAs describe the same phenomena/behaviour?
2. Are some symptoms more likely to be endorsed due to a child’s age, gender and/or effects of co-occurring diagnoses?
3. How is potential measurement non-invariance (MNI) reflected in combined-information items, using, ‘and’ versus ‘or’ rules?

Methods

In 2003, the International Multicenter ADHD Gene (IMAGE) project funded by National Institute of Mental Health (NIMH) was launched in Europe. The IMAGE project is an international collaborative study that aims to identify genes that increase the risk for ADHD using QTL linkage and association strategies. Ethical approval for the study was obtained from Ethical Review Boards within each country and informed consent obtained for the use of the samples for analyses relating to the genetic investigation of ADHD. More details can be found in Chen et al. (2008); Müller et al. (2011a), Müller et al. (2011b) and Garcia Rosales et al. (2015).

Instruments

Parental Account of Clinical Symptoms (PACS). PACS (Chen and Taylor, 2006) has been used as the research diagnostic instrument for the probands and affected siblings. PACS is a standardized investigator-based research diagnostic interview, designed to capture accurately and systematically the clinical phenotypes relating to hyperactivity, especially ADHD and Hyperkinetic Disorder along with other related childhood psychiatric disorders. The philosophy of PACS is very much similar to that of the Autism Diagnostic Interview, in which the interviewer endeavours to obtain an objective “fly on the wall” description of behaviour from the parents and establishes the ratings of severity and frequency. An algorithm was used to translate PACS ratings into DSM-IV criteria (Curran et al., 2000). In the inattentive behaviour section, all the DSM-IV criteria exploring IA are reviewed. In the hyperactivity/impulsivity section of PACS, behaviour is rated in different day-to-day situation using behavioural counts.

The structure and administration techniques of PACS have been designed to minimise opportunities for introducing responders' and raters' bias. Inter-rater reliability has been reported as adequate in several samples and reliability checks were maintained during the project.

Conners Teacher Rating Scale: Revised-Long (CTRS:R-L)

This is a validated and widely used questionnaire in the field of ADHD (Collett et al., 2003) based on DSM-IV, with an important research base. It is also commonly used in routine clinical practice.

Informant Assessment (INFA)

Parents and teachers report on the presence or absence of a symptom, using PACS and Conners respectively. NICE guidelines regard a detailed parental interview and a teacher rating as the key measures; PACS is a standardised and quantified parent interview; Conners scales are widely used and can be seen as the field standard. Therefore, our invariance evaluation incorporates not only any rater differences but also the scale (assessment medium) differences. Hence, our invariance evaluation does not separate between the variability due to the informant and the informant assessment tool employed. Therefore our focus is not at the properties of a certain assessment tool but on the measurement outcome itself. That is, with the cost of not being able to separate the effect of the role (parent/teacher) from the effect of the corresponding technical tool we achieve measuring potential bias at the final "symptom present/symptom

absent” judgements made by each type of informant using the best tool available in each case. All other types of invariance have been conducted twice (per informant and therefore per assessment tool) and therefore there are separate reports for PACS and Conners and inevitably separate reports for parents and teachers. This is also consistent with the ADHD diagnostic algorithm used in the IMAGE project where items from PACS completed by parents and teacher Conners information are combined.

Hypescheme. The Hypescheme (Curran et al., 2000) was used to yield a categorical diagnosis of ADHD and comorbid disorders. The Hypescheme is an operational criteria checklist and minimum dataset for the research diagnoses of ADHD. The full algorithm is available on request; it follows the criteria and instructions of DSM-IV.

Participants

All children (probands and siblings) were aged 5 to 17 years, had an $IQ \geq 70$, and were of European Caucasian descent. Probands were recruited when referred for psychiatric evaluation aged 5 to 17, had at least one sibling, received an expert clinician’s diagnosis of ADHD and met Hypescheme criteria. There was access to at least one biological parent for DNA collection. Exclusion criteria for probands and siblings include IQ below 70, of non-European Caucasian descent, free of other brain disorders, and any genetic or medical disorder associated with externalizing behaviours that might mimic ADHD.

Statistical analyses

Item factor analysis (IFA) model. Factor analysis is the statistical tool which allows the identification and measurement of one or more latent traits (symptom dimensions, factors) from a set of observed variables (indicators, symptoms, items). In the current work the indicators are binary (presence/absence of a symptom) and therefore we used the item factor analysis model for categorical data (IFA; Mislevy, 1986; Muthén, 1989a; Wirth and Edwards, 2007). The item factor analysis model is summarised as follows:

$$\Phi^{-1}[\Pr(Y_i=1|\theta)] = -\tau_i + \lambda_i\theta, \quad (1)$$

where Φ^{-1} stands for the probit link¹ function, $\Pr(Y_i=1|\theta)$ is the probability of the symptom i to be present conditional on the latent trait θ (here either IA or HI), and τ_i , λ_i are the threshold and the loading of the item Y_i , respectively

The **threshold** parameter corresponds to the severity of a symptom (*location* or *difficulty* parameter). The smaller the threshold parameter, the more easily a symptom is endorsed (less difficult, less severe), the **loading** parameter parallels the change in the probability of a positive response (symptom endorsement) as the level of the trait changes (*slope* or *discrimination* parameter). The larger the loading parameter, the more related to the latent continuum a symptom is (the more discriminative). The model (1) suggests that the item probability depends both on the items' characteristics (τ_i , λ_i) and on the distribution of the individuals' latent trait (θ). Note that the threshold of the item analysis model equals minus the difficulty ($-\tau_i = a_i$) parameter of the analogue item response theory, and in the special case of binary data there is a one to one correspondence between the item factor analysis model used here and the two parameter logistic item response theory model.

MI definitions. *Measurement non-invariance* refers to differences in the parameters (loadings and thresholds) of the IFA model. Such differences may occur a) between several groups assessed synchronously, b) at the same group assessed in different conditions, and/or c) due to the effect of a covariate (age for instance) and raise concerns of bias in the measurement. To be able to compare the scores (here number of symptoms endorsed) across groups or conditions, full or at least partial MI needs to be established. Assuming that the same model applies in all groups or conditions (that is the model under consideration fits well in the data for each group or condition - ie configural invariance), MI requires both equal loadings (metric invariance) and equal thresholds (scalar invariance), across groups or conditions¹. That is, to establish MI, we first tested if the loadings of the items on the latent traits are invariant across groups or conditions (weak, metric or loadings invariance). If the loadings were equal, then we proceeded with testing the equality of the thresholds (scalar or strong invariance). The items with both equal loadings and thresholds across groups and conditions are hereafter referred to as measurement invariant (MI items). If all items were invariant, then full MI was assumed² (MI for all items). Frequently, not all items satisfied both the metric and the scalar invariance steps. In this case we established partial, rather than full MI. For example, if the loading of one item differed significantly across groups or conditions, then the procedure ended for this item. The procedure however continued for the rest of the items, to test for scalar invariance since metric invariance could be established. The items with either unequal loadings and/or unequal thresholds across groups and conditions are referred to hereafter as measurement non-invariant (MNI items). Depending upon the potential source of non-invariance considered, different statistical models were used. Figure 1 depicts the three different model settings (based on the

basic IFA model) used here, namely a) the multiple group IFA model (MIFA; Muthén and Christoffersson, 1981), b) the longitudinal IFA model (LIFA; Muthén, 1996), and c) the multiple indicators multiple causes model (MIMIC; Muthén, 1979, 1989b).

Multiple group IFA (MIFA). MIFA was used to assess the gender differences in the IFA models, for the IA and HI traits separately. In categorical items some authors suggest that the loadings and the thresholds of the indicators should be freed or relaxed in tandem, since together they form the item characteristic curve (Muthén & Muthén, 1998-2012), meaning that the metric invariance stage is omitted. Other authors disagree (Millsap, 2011). We present both steps for completeness and to match the DIF definitions under the IRT framework. (see Table 1).

A series of three models were fitted, from the least restricted (configural invariance) to the most restricted model (threshold invariance) and are summarised in Table 1. Specifically, in M_1 all loadings and thresholds were freely estimated. In M_2 , the loadings are restricted to be equal across genders, for the metric invariance evaluation. In M_3 , in addition to the loadings, the thresholds were also restricted to be equal across genders, for the scalar invariance evaluation. For the identification of the model, additional constraints are required. To set the metric of the scale, either the latent factor is assumed to follow a standard normal distribution (mean zero and variance one) or, alternatively, one item per factor needs to be constrained. Depending upon the model tested in each case and its constraints, we adjusted our choices of model identification constraints accordingly (see Table 1). The residual (error) variances were also constrained to unity, to have a unique solution for the model parameters (identified model).

<< Table 1 about here >>

Longitudinal IFA (LIFA). The dependencies introduced in the model by rating the same sample twice, can be accounted for by the LIFA model (for instance see Liu et al., 2017). Parent and teacher INFA ratings refer to the exact same children (dependent samples), as opposed to the independent samples studied in MIFA (e.g. boys versus girls responses). Thus, MIFA should not be used in this comparison as it fails to take under consideration these dependencies of the observations. In the LIFA model, the latent trait (IA or HI) was formed twice within the same model (dual factors); once derived from parent-INFA and the other from teacher-INFA. The steps described for the MIFA model and summarised in Table 1, were repeated for the LIFA model. To reflect the dependencies in the responses, the pairs of indicators which corresponded to the same symptom and the dual factors (parent-INFA – teacher-INFA) were set to co-vary (all covariances are denoted by double-headed, curved arrows in Figure 1).

A limitation of the method is that homogeneity is assumed within teacher and parent groups. That is, it is assumed that the informant-related variability is due to the type of the informant (between parents and teachers) rather than due to individual differences (within parents' and teachers' groups). To be able to account for the variability within each informant group, the number of children of each parent should run into several tens if not hundreds (depending upon the magnitude of the effect as in any statistical test), which is not feasible here. This limitation was therefore considered acceptable within the scope of this work.

MIMIC model. The MIMIC model is essentially an IFA model with covariates. Similarly to regression, the MIMIC model considers the effect of a covariate (gender, age or comorbidity) onto the latent trait (indirect effect) and the additional effect (direct effect) the covariate(s) might have on the selected item(s). If the direct effect of a covariate on an item (symptom) is significant, then MNI due to the covariate is evident for that item.

The MIMIC model is most often implemented to test invariance in the case of a numerical covariate or in the presence of multiple covariates. Here, it was used to evaluate MI due to age, as well as due to comorbidity, adjusted at the same time for age and gender. In all cases, the direct effects were constrained initially to zero and, based on the improvement of the model fit, the equality constraints were relaxed gradually. The model that included only significant direct effects was considered as the final model, in all cases. The limitation of the MIMIC model is that it evaluates directly the scalar invariance but, unlike MIFA, it can be used for continuous covariates.

All analyses were conducted in Mplus (Muthén and Muthén, 1998-2012) using the theta parametrization (Muthén and Asparouhov, 2002, for details). The estimator used the analysis was the robust weighted least squares estimator (Muthén, du Toit, & Spisic, 1997).

Goodness of fit. MIFA and LIFA invariance testing were conducted by fitting a series of nested models (with and without equality/invariance constraints) and evaluating the difference in their fit via a chi-square test (often referred to as the DIFTEST, Muthén & Muthén, 1998-2012). For the model fit assessment we used the relative chi-square (relative χ^2 : values close to 2 indicate close fit; Hoelter, 1983), the Root Mean Square Error of

Approximation (RMSEA, values less than 0.8 are required for an adequate fit; Browne & Cudeck, 1993), the Taylor-Lewis Index (TLI, values higher than 0.9 are required for close fit; Bentler & Bonett, 1980) and the Comparative Fit Index (CFI, values higher than 0.9 are required for close fit; Bentler, 1990).

Results

Demographic characteristics

The initial sample consisted of 3229 participants, of whom 1788 had complete ADHD ratings by parents and teachers. Among those, 1383 children were randomly selected for this study ensuring at the same time that only one child per family would be included (siblings have been prioritized). In the final sample, there were 247 females (17.9%) and 1136 males, aged from 4 to 19 years (mean=10.9, sd=2.9 years). According to the t-test, the genders did not differ with respect to age ($t=1.125$, $df=1358$, $p=0.261$).

MI across informants (LIFA)

Inattention. In the case of the IA items, the fit of the (LIFA-dual) model was satisfactory (relative $\chi^2=3.8$, CFI=0.97, TLI=0.96, RMSEA=0.046). Partial metric invariance held for the symptoms *listens*, *instructions*, *disorganised*, *unmotivated* and *distracted* ($\chi^2=8.5$, $df=4$, $p=0.075$) indicating that the symptoms were related to IA equivalently for parents and teachers. Partial scalar invariance however held only for the *disorganised* and *unmotivated* items ($\chi^2=2.7$, $df=1$, $p=0.100$).

Our results suggest that for the same absolute levels of IA, the two types of INFAs had the same expected response (probability of endorsing) in the cases of two criteria only:

disorganised and *unmotivated* (Table 2). The parents were more likely than teachers to endorse *careless*, *listens*, *loses*, *distracted*, and *forgetful* (smaller threshold parameter). The teachers were more likely than parents to endorse *attention* and *distracted*. In summary, MNI was evident in seven out of nine IA symptom criteria.

Hyperactivity. With respect to the HI, the fit of the (LIFA-dual) model was also satisfactory (relative $\chi^2=3.8$, CFI=0.97, TLI=0.96, RMSEA=0.046). Partial metric invariance held for the symptoms *fidgets*, *seat* and *talks* ($\chi^2=5.297$, df=2, p=0.071). Partial scalar invariance also held for these three symptoms only ($\chi^2=2.274$, df=2, p=0.321).

Both INFA ratings concur with the same probability of endorsing the symptoms *fidgets*, *seat* and *talks* (Table 2), indexing the same absolute levels of HI. However, teachers were more likely than parents to endorse *quiet*, *motor*, *blurts*, and *wait* as present. Parents were more likely than teachers to endorse the symptoms *forgetful* and *listens*. In summary, MNI was evident in 6/9 HI symptom criteria.

Table 2 presents the estimated item parameters and the (tetrachoric) correlations between the same symptom indicators for the final models. It is striking that, MI could not be established for both loadings and thresholds for most of the ADHD symptom criteria. If both INFAs essentially measured the same underlying concept, we would expect to find more concurrence with regard to thresholds and loadings across the 18 items. This result provides evidence that parent and teacher-INFAs essentially do not measure the same underlying concept. Moreover, the correlations were strikingly low and non-significant, which further confirms the conceptual discrepancies between INFAs.

<<Table 2 about here>>

MI across genders (MIFA)

Do boys and girls with the same absolute levels of the traits (IA or HI) have the same probability of symptom endorsement, according to a) parental assessment, b) teacher assessment, c) combining ratings using the ‘and-rule’, and d) combining ratings using the ‘or-rule’? Detailed results are presented in Table 3.

a) Parental assessment

IA: Metric invariance was present for all symptom criteria, indicating that all symptoms were equally related to IA across genders. Scalar invariance was established for all symptoms apart from *unmotivated* and *loses*. The parents endorsed *unmotivated* more easily in boys compared to girls (unstandardized thresholds: -0.8 for boys and -0.6 for girls). The opposite occurred for *loses* (unstandardized thresholds: 0 versus -0.4, for boys and girls respectively).

HI: metric invariance held for all symptom criteria, and scalar invariance was established for all symptoms apart from *talks*. The parents endorsed *talks* more easily in boys compared to girls (unstandardized thresholds: -1 for boys and -0.6 for girls).

In summary, MI was evident in the parent-INFA ratings in 7/9 symptoms of IA, and in 8/9 of HI. That is, parent-INFA ratings were invariant with respect to gender in more than 80% of the ADHD symptoms, and we conclude that the child’s gender did not bias notably the parent-INFA ratings.

b) Teacher assessment

IA: full metric invariance was present, and scalar invariance was evident for all symptoms apart from *forgetful*. The teachers endorsed *forgetful* more easily in girls than in boys (unstandardized thresholds: 0.8 for boys and 0.4 for girls).

HI: full metric invariance was also present, and scalar invariance was evident for all symptoms apart from *talks*, as in the case of parents' ratings. Like the parents, the teachers endorsed *talks* more easily in girls than in boys (unstandardized thresholds: 0.5 for boys and 0.9 for girls).

In summary, teacher-INFA ratings were invariant (non-biased) with respect to gender in 90% of the ADHD symptoms, and we conclude that the child's gender did not bias notably the teacher-INFAs ratings.

c) combining ratings using the 'and-rule'

When the 'and-rule' was used to combine the information from parents and teacher-INFAs in IA, full MI was established (full metric and scalar invariance for all symptom criteria). In HI, full metric invariance also held but scalar invariance was evident in all items apart from *talks*. When the 'and-rule' is employed, the probability of symptom *talks* endorsement was higher in girls than in boys (unstandardized thresholds: 0.8 for boys and 1.2 for girls).

In summary, 'and-rule' combined-information ratings were invariant with respect to gender in seventeen out of the eighteen ADHD symptoms, and we conclude that the child's gender did not bias these ratings.

d) combining ratings using the 'or-rule'

Full metric invariance was established in the case of the 'or-rule' combined-information

items for both IA and HI. With respect to scalar invariance, partial invariance was established for all symptoms apart from the *forgetful* and *loses* criteria for IA, and *talks* for HI. The endorsement probability for both symptoms *forgetful* and *loses* were higher in girls than in boys (unstandardized thresholds: *forgetful*: -0.8 for boys and -0.4 for girls; *loses*: -0.8 for boys and -0.4 for girls). The probability of symptom *talks* endorsement was higher in girls than in boys (unstandardized thresholds: -1.4 for boys and -0.9 for girls).

In summary, the ‘or-rule’ combined-information ratings were invariant with respect to gender in fifteen out of the eighteen ADHD symptoms, and we conclude that the child’s gender did not bias notably these ratings.

Age invariance

When a significant direct effect is positive, the symptom is expected to be endorsed more often for each unit of age increase and for the same absolute levels of the trait. Conversely, if the effect is negative, this probability decreases. Significant direct age effects are reported in Table 4.

IA. The probability of endorsing *unmotivated* increased with age, both in the parent ratings and the ‘and-rule’ combined-information ratings. Age affected positively the endorsement of *forgetful* for teachers (higher probability of endorsing the symptom as age increases, for the same absolute values of IA). Negative effects were present when the ‘or-rule’ combined-information ratings were considered in the endorsement of *listens* and *distracted* (lower probability of endorsing the symptoms as age increases, for the same absolute values of IA). All direct effects were however very low in magnitude (<0.1 in absolute value), indicating

that age does not notably bias the IA ratings.

HI. A larger number of significant direct effects emerged, compared to IA. The older the child, the less likely it was for parents to endorse *runs/climbs*. On the contrary, the older the child, the more likely it was for parents to endorse *motor* and *blurts*. The same effects were evidenced when the combined-information ratings were considered. Additionally, significant positive direct effects were present in the teachers' INFA ratings for *talks*, *waits*, *blurts* and *interrupts* and significant negative effects were present in the 'or-rule' combined ratings for *seat*.

Among those significant direct effects, only the positive effect of age on the parent-INFAs endorsement of *motor* was of low to moderate magnitude (0.25). All direct effects were very low in magnitude (<0.1 in absolute value), indicating that age does not notably bias the HI ratings.

Co-occurring diagnoses invariance

In this section we investigate whether the probability of endorsing a symptom is affected (biased) by co-occurring diagnoses, adjusted for age and gender, and IA or HI. Significant direct effects are presented in Table 5.

Co-occurring AD

IA: Co-occurring AD increased the probability of endorsement of *attention* and *unmotivated* in the parents' ratings. There was no effect on the teacher-INFA or the combined information ratings.

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HI: co-occurring AD had no effect on either the parents' or the teachers' ratings. When the ratings were combined, co-occurring AD decreased the probability of endorsement for *runs/climbs* in the 'and-rule' ratings and the probability of endorsement of *blurts* in the 'or-rule' ratings. We will only report positive or negative significant effects, for conciseness.

Based on our results, co-occurring AD does not notably bias the symptom criteria endorsement of ADHD.

Co-occurring CD

IA: Co-occurring CD increased the probability of endorsement of *attention*, *unmotivated*, and *loses* in the parent-INFAs ratings. Similarly, co-occurring CD increased the probability of endorsement of *attention* and *loses* in the 'and-rule' combined-information ratings.

HI: Co-occurring CD decreased the probability of endorsement of *talks* and *blurts* in the parent-INFAs ratings. Similarly, co-occurring CD decreased the probability of endorsement of *seat* on the teachers' ratings but increased the probability of endorsing *interrupts*. In the combined-information ratings, co-occurring CD decreased the probability of endorsing *talks* on the 'or-rule' ratings but increased the probability of endorsing *motor* on the 'and-rule' ratings.

In summary, co-occurring CD only affected the probability of endorsement of the IA criteria in parent-INFA ratings. Also, co-occurring CD affected the probability of endorsement to some of the HI symptom criteria, which were different depending on INFA.

Co-occurring ODD

IA: Co-occurring ODD increased the probability of endorsement of *attention* and *unmotivated* in the parents' ratings. With respect to the combined information ratings, co-occurring ODD also increased the probability of endorsing *unmotivated* in both combined ratings. Additionally, co-occurring ODD also increased the probability of endorsing *attention* and *loses* in the 'and-rule' items.

HI: Co-occurring ODD influenced four symptom criteria, in relation to parent-INFAs ratings. Specifically, when ODD was present, the probability of the parents endorsing *fidgets* and *seat* was increased, whereas the probability of endorsing *wait* and *interrupts* was increased. In the 'and-rule' ratings, the endorsement probability of *quiet* was increased and *runs/climbs* was decreased; in contrast *runs/climbs* was increased in the 'or-rule' ratings. With respect to teachers' ratings, when ODD was present, only the probability of endorsing *runs/climbs* was decreased. The probability of endorsing *runs/climbs* was also increased with the presence of ODD in the 'or-rule combined-information ratings but decreased when the 'and-rule' was used. Finally, the probability of endorsing *quiet* was increased with the presence of ODD when the 'and-rule' was used.

Based on our results, co-occurring ODD does not notably bias the symptom criteria endorsement of ADHD. In summary, co-occurring ODD affected the probability of endorsement of ADHD symptom criteria in parent-INFA.

Discussion

In this work we examined the potential influence (measurement bias) introduced in the ratings of the ADHD symptom criteria due to INFAs, gender, age, co-occurring diagnoses (AD, CD, and ODD in particular), and the rule to combine INFA ratings. Our results indicate substantial MNI between parents' and teachers' ratings (i.e. 7/9 IA and 6/9 HI items), implicating that they capture different aspects of children's behaviour. Second, within informant, age and gender did not markedly affect symptom endorsement probabilities. Third, with respect to co-occurring diagnoses, teacher-INFA ratings were essentially uninfluenced by the presence of AD, CD, and ODD. On the other hand, the parents' endorsement probabilities were mildly influenced by AD, and more notably influenced by ODD. Fourth, 17 out of 18 items were invariant using the 'and' rule to combine INFA ratings; 15 of 18 items were invariant using the 'or' rule. Our findings suggest a general robustness of DSM ADHD diagnostic items in relation to the potential influences of the factors examined. Parents and teachers appear to capture different patterns of behaviours, which may reflect different expressions of a trait or different underlying traits; the 'or' rule may capture a richer picture of a child's ADHD phenomenology.

The differences between INFAs can be partially attributed to the differences between the children's behaviours at school and at home. A quantitative genetic twin study identified that the information provided by parents and teachers is different and that they report different psychopathological phenomena (Arnett et al., 2015). Furthermore, Hartman et al. (2007) found in their twin modelling study that the best fit model of their data includes unique genetic contributions from parent and teachers. Parent and teacher-INFAs may validly describe different aspects of behaviour. They should be seen as different sources of information to be

combined by the expert clinician, in the context of a holistic biopsychosocial psychiatric assessment.

MI in relation to **gender** was evident. The symptoms related to the trait in a similar manner for both genders; there is no evidence for the same behaviours are being assessed differently across genders. Thresholds differed for only four items. Standard methods can therefore be used to assess the differences in the total number of symptoms between genders. This is consistent with the literature reviewed in this paper.

Similarly, **age** affected the endorsement only of *unmotivated* (parents) and *forgetful* (teachers). Even for HI symptoms the effect sizes of the estimates were very low, and unlikely to have any notable impact in clinical settings.

None of the **co-occurring diagnoses** influenced the teachers' probability of endorsing the IA items. With respect to HI, AD did not affect the teacher-INFAs probability of endorsing any of the symptoms; ODD reduced the probability of endorsing only in one symptom (*runs/climbs*); and CD affected the teacher-INFA probability of endorsing in two symptoms (negatively *seat* and positively *interrupts*). Based on these results we conclude that the teachers' ratings are not markedly biased in the presence of co-occurring diagnosis.

For parent-INFAs IA ratings, *attention* and *unmotivated* endorsements were positively affected in all cases (ODD, CD and AD); and *loses* only in the case of co-occurring CD. With respect to HI, AD did not affect the parent-INFAs probability of endorsing any of the symptoms; CD reduced the probability of endorsing two symptoms (*talks, blurts*); and ODD reduced the probability of endorsing two symptoms (*seat, fidgets*) and increased the probability

of endorsement in two more (*wait, interrupts*). Based on these results we conclude that parents' ratings are influenced by the presence of ODD, in particular, the measurement of the HI items.

In addition to age, gender, and comorbidity effects on informant ratings, we also evaluated the invariance when the ratings are **combined** by using either the 'or' and the 'and' rules. The 'and' rule captures pervasiveness of symptomatology and potentially severity. As recognized in DMS-5, "manifestations of the disorder have to be present in more than one setting". The combined-information items reflect invariances present on INFA' ratings or cancel those invariances out. Interestingly, there were fewer MNI symptoms using the 'and-rule' than when using the 'or-rule', in terms of gender (Table 3) and age (Table 4), (apart from the direct effects of age in IA). That is, the 'and-rule' was less prone to invariance due to gender and age. The reverse held with respect to co-occurring diagnosis (Table 5); there were more measurement invariant symptoms using the 'and-rule' than when using the 'or-rule'. Overall, there is no substantial difference between the two methods in terms of invariance.

Our study further develops the idea of 'situational/informant specificity' of certain ADHD symptoms: this means that the rating differences between parents and teachers may also be influenced by age and gender. Rucklidge (2010) suggested that the reported male preponderance might be attributable to referral bias leading to under-identification of ADHD in young females. Genetic model fitting of population twin samples have also identified differences between parent and teacher ratings. Nikolas & Burt (2009) reviewed the pattern of genetic and environmental influences on ADHD symptom dimensions and found that the genetic contribution to mothers' ratings included as dominant genetic factors for inattentiveness (25%); in contrast, 77% of the variance in ADHD as defined by teacher ratings was attributable

to additive genetic factors for both hyperactivity and inattentiveness with no significant contributions from dominant genetic factors (0%).

Sex-specific genetic dominant genetic influences in boys have been suggested (Nikolas and Burt, 2009). Those findings are consistent with the idea posited by Rucklidge (2010) that symptom thresholds should be adjusted for gender and that separate standards of measurement should be used according to gender. Overall our findings do not support gender-specificity like those of Monuteaux (2010) and Gomez (2011, 2012, 2016). Clinicians might note a few gender-specific items (*unmotivated* and *talks* for boys and *loses* for girls, as rated by parents; and *forgetful* in boys and *talks* for girl, as rated by teachers).

HI items are associated with age, as rated by teacher-INFAs. Parent-INFAs appear to rate certain items differently in the presence of comorbidity whereas teachers seem less susceptible. It may also be that teacher-INFAs are better at differentiating one comorbid disorder from another thus avoiding the potential conflation, as expressed as cross-loading.

Our study is novel in four aspects. To our knowledge this is the first study to evaluate MI within the same data regarding ADHD symptoms (i) in relation to age, gender, and co-occurring diagnosis using naturalistic parent and teacher assessments in keeping with NICE guidance and routine clinical practice; and (ii) between INFAs. It is also novel in assessing MI and its implication in combining parent and teacher INFAs using the 'and' and 'or' rules. If our findings were replicated by future studies, the findings could potentially have significant implications on the diagnostic criteria adopted by future classification systems, with regard to the item calibration, gender specificity and the source of information (i.e. parent or teacher

INFAs). Clinicians' understanding of problems of impulsiveness and attention in classrooms might need some further conceptual development in terms of the impact of ADHD features in the classroom.

Our sample consisted of participants recruited from different centres located in different European countries, Müller et al. (2011a) have demonstrated the multi-level nature of our data with potential factors influencing symptom levels as well as age and gender effects across centres and countries inherent in most multicentre studies. Our focus is not on the properties of certain assessment tools but on the measurement outcome itself, in a naturalistic setting, in keeping with the NICE Guidance for ADHD (2018). Given the cross-sectional design of the IMAGE study, the effects of developmental trajectories could not be modelled. The IMAGE data were collected based on DSM-IV criteria. The key changes in DSM5 include 'threshold criteria relating to age', 'pervasiveness' and the combination of dimensionality with category. As there is no substantial change in the wording of the ADHD criteria between DSM-IV and DSM5, our findings would at large be relevant to clinical practice and research using the DSM5 system. However, our findings must therefore be considered as preliminary and should be interpreted with caution pending further investigations.

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Table 1: Successive models and constraints implemented in the evaluation of invariance across groups or conditions.

| | M₁ (Configural) | | M₂ (Metric) | | M₃ (Scalar) | |
|--|---|---------------------|---|---------------------|---|---------------------|
| Group (or Condition) * | A | B | A | B | A | B |
| loadings | freely estimated | freely estimated | constrained⁺ to be equal | | constrained⁺ to be equal | |
| thresholds | freely estimated | freely estimated | freely estimated | freely estimated | constrained⁺ to be equal | |
| residual variances | 1 | 1 | 1 | 1 | 1 | 1 |
| factor means | 0 | 0 | 0 | 0 | 0 | freely estimated |
| factor variance | 1 | 1 | 1 | freely estimated | 1 | freely estimated |
| <p>[*]In MIFA A: males, B: females. In LIFA A: parents, B: teachers. B is the reference group.</p> <p>⁺In the case of partial rather than full MI, the constraints for the MNI items were relaxed.</p> | | | | | | |

Table 2: Unstandardised item parameters[†] and correlations between same symptom indicators, for the most constraint models (invariant coefficients are denoted with bold)– LIFA model.

| <i>Item</i> | Inattention | | | <i>Item</i> | Hyperactivity/Impulsivity | | |
|-------------------------|--------------------|-------------------|---------------------|--------------------------|----------------------------------|-------------------|---------------------|
| | <i>Loadings</i> | <i>Thresholds</i> | <i>Correlations</i> | | <i>Loadings</i> | <i>Thresholds</i> | <i>Correlations</i> |
| <i>Careless</i> | 2.63 (0.69) | -3.72 (-1.14) | *0.11 | <i>Fidgets</i> | 1.41 | -1.56 | 0.28 |
| <i>Attention</i> | 0.34 (0.80) | 0.28 (-1.39) | *0.00 | <i>Seat</i> | 1.20 | -0.78 | *-0.04 |
| <i>Listens</i> | 0.52 | -0.73 (-0.53) | *-0.04 | <i>Runs/climbs</i> | 1.69 (1.50) | -1.71 (-0.48) | 0.34 |
| <i>Instructions</i> | 0.64 | -0.34 (-0.49) | -0.17 | <i>Quiet</i> | 1.04 (0.99) | 0.01 (-0.56) | *-0.07 |
| <i>Disorganised</i> | 0.89 | -1.34 | 0.23 | <i>Motor</i> | 1.62 (1.71) | -0.62 (-1.65) | *-0.21 |
| <i>Unmotivated</i> | 0.74 | -0.95 | *0.14 | <i>Talks</i> | 1.10 | -1.03 | 0.19 |
| <i>Loses</i> | 1.14 (0.56) | -0.44 (-0.26) | 0.18 | <i>Blurts</i> | 0.58 (1.36) | -0.29 (-1.19) | 0.19 |
| <i>Distracted</i> | 0.84 | -2.41 (-1.86) | *0.15 | <i>Wait</i> | 0.86 (1.90) | -0.66 (-1.94) | 0.27 |
| <i>Forgetful</i> | 1.01 (0.45) | -0.44 (*0.03) | *-0.10 | <i>Interrupts</i> | 0.92 (1.64) | -2.06 (-1.61) | *-0.02 |

[†] In the presence of non-invariance the parents' coefficients are presented with teachers' coefficients within brackets.
* Not significantly different than zero.
negative thresholds indicate that the 50% chance of endorsing is located below the average trait (0)
positive thresholds indicate that the 50% chance of endorsing is located above the average trait (0)

Table 3: Gender non-invariant items and difference in the model fit (DIFFTEST), per trait and per type of items – MIFA model.

| Invariance | | Inattention | | | | Hyperactivity/Impulsivity | | | |
|------------|---------------|--------------------|----------|----|-------|---------------------------|----------|----|-------|
| ratings | type | MNI items* | χ^2 | df | p | MNI items* | χ^2 | df | p |
| Parents | <i>metric</i> | - | 10.73 | 8 | 0.218 | - | 7.92 | 8 | 0.441 |
| | <i>scalar</i> | unmotivated, loses | 9.97 | 7 | 0.126 | talks | 11.74 | 7 | 0.110 |
| Teachers | <i>metric</i> | - | 5.76 | 8 | 0.674 | - | 3.75 | 8 | 0.879 |
| | <i>scalar</i> | forgetful | 5.23 | 7 | 0.631 | talks | 13.75 | 7 | 0.056 |
| And-rule | <i>metric</i> | - | 14.14 | 8 | 0.078 | - | 2.73 | 8 | 0.950 |
| | <i>scalar</i> | - | 8.80 | 8 | 0.360 | talks | 12.25 | 7 | 0.093 |
| Or-rule | <i>metric</i> | - | 12.83 | 8 | 0.118 | - | 6.86 | 8 | 0.552 |
| | <i>scalar</i> | loses, forgetful | 11.79 | 6 | 0.067 | talks | 12.05 | 7 | 0.099 |

**Indicates measurement non-invariant symptom criteria ratings*

Table 4: Significant direct effects of age, per trait and per type of items - MIMIC model.

| | Inattention | | | | | | | |
|---------------------|---------------------------|---------|----------|---------|----------|---------|---------|---------|
| | Parents | | Teachers | | And-rule | | Or-rule | |
| | effect | p-value | effect | p-value | effect | p-value | effect | p-value |
| <i>Careless</i> | | | | | | | | |
| <i>Attention</i> | | | | | | | | |
| <i>Listen</i> | | | | | -0.03 | 0.026 | | |
| <i>Instructions</i> | | | | | | | | |
| <i>Disorganised</i> | | | | | | | | |
| <i>Unmotivated</i> | 0.06 | <0.001 | | | | | 0.06 | 0.001 |
| <i>Loses</i> | | | | | | | | |
| <i>Distractions</i> | | | | | -0.04 | 0.020 | | |
| <i>Forgetful</i> | | | 0.03 | 0.036 | | | | |
| | Hyperactivity/Impulsivity | | | | | | | |
| | Parents | | Teachers | | And-rule | | Or-rule | |
| | effect | p-value | effect | p-value | effect | p-value | effect | p-value |
| <i>Fidgets</i> | | | | | | | | |
| <i>Seat</i> | | | | | | | -0.04 | 0.019 |
| <i>Runs/climbs</i> | -0.11 | <0.001 | | | -0.05 | 0.003 | -0.08 | <0.001 |
| <i>Quiet</i> | | | | | | | | |
| <i>Motor</i> | 0.25 | <0.001 | | | 0.07 | <0.001 | 0.12 | <0.001 |
| <i>Talks</i> | | | 0.06 | <0.001 | | | | |
| <i>Blurts</i> | 0.04 | 0.002 | 0.06 | 0.001 | 0.04 | 0.006 | 0.04 | 0.013 |
| <i>Wait</i> | | | 0.05 | 0.013 | | | | |
| <i>Interrupts</i> | | | 0.04 | 0.021 | | | -0.07 | 0.032 |

Table 5: Significant direct effects for each co-occurring diagnosis, separately per trait and per type of rating (p-value within parenthesis) - MIMIC models are adjusted for age and gender.

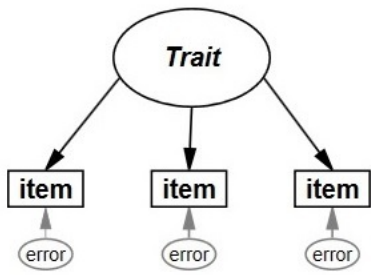
| | Inattention | | | | | |
|---------------------|----------------------------------|------------------|-------------------------|------------------|--------------------------------------|------------------|
| | Anxiety Disorder | | Conduct Disorder | | Oppositional Defiant Disorder | |
| | <i>parents</i> | <i>teachers</i> | <i>parents</i> | <i>teachers</i> | <i>parents</i> | <i>teachers</i> |
| <i>Careless</i> | | | | | | |
| <i>Attention</i> | 0.18 (0.020) | | 0.47 (<0.001) | | 0.27 (0.001) | |
| <i>Listen</i> | | | | | | |
| <i>Instructions</i> | | | | | | |
| <i>Disorganised</i> | | | | | | |
| <i>Unmotivated</i> | 0.23 (0.022) | | 0.55 (<0.001) | | 0.39 (<0.001) | |
| <i>Loses</i> | | | 0.34 (0.020) | | | |
| <i>Distracted</i> | | | | | | |
| <i>Forgetful</i> | | | | | | |
| | | | | | | |
| | <i>'and-rule'</i> | <i>'or-rule'</i> | <i>'and-rule'</i> | <i>'or-rule'</i> | <i>'and-rule'</i> | <i>'or-rule'</i> |
| <i>Careless</i> | | | | | | |
| <i>Attention</i> | | | 0.34 (<0.001) | | 0.21 (0.011) | |
| <i>Listen</i> | | | | | | |
| <i>Instructions</i> | | | | | | |
| <i>Disorganised</i> | | | | | | |
| <i>Unmotivated</i> | | | | | 0.23 (0.013) | 0.29 (0.024) |
| <i>Loses</i> | | | 0.24 (0.018) | | 0.20 (0.026) | |
| <i>Distracted</i> | | | | | | |
| <i>Forgetful</i> | | | | | | |
| | | | | | | |
| | Hyperactivity/Impulsivity | | | | | |
| | Anxiety Disorder | | Conduct Disorder | | Oppositional Defiant Disorder | |
| | <i>parents</i> | <i>teachers</i> | <i>parents</i> | <i>teachers</i> | <i>parents</i> | <i>teachers</i> |
| <i>Fidgets</i> | | | | | -0.30 (0.019) | |
| <i>Seat</i> | | | | -0.23 (0.045) | -0.36 (0.001) | |
| <i>Runs/climbs</i> | | | | | | -0.24 (0.025) |
| <i>Quiet</i> | | | | | | |
| <i>Motor</i> | | | | | | |
| <i>Talks</i> | | | -0.41 (0.002) | | | |
| <i>Blurts</i> | | | -0.21 (0.036) | | | |
| <i>Wait</i> | | | | | 0.18 (0.039) | |
| <i>Interrupts</i> | | | | 0.28 (0.016) | 0.39 (0.015) | |
| | | | | | | |
| | <i>'and-rule'</i> | <i>'or-rule'</i> | <i>'and-rule'</i> | <i>'or-rule'</i> | <i>'and-rule'</i> | <i>'or-rule'</i> |
| <i>Fidgets</i> | | | | | | |
| <i>Seat</i> | | | | | | |
| <i>Runs/climbs</i> | -0.49 (0.005) | | | | -0.34 (0.001) | 0.46 (0.001) |
| <i>Quiet</i> | | | | | 0.25 (0.008) | |
| <i>Motor</i> | | | 0.28 (0.019) | | | |
| <i>Talks</i> | | | | -0.34 (0.018) | | |
| <i>Blurts</i> | | -0.24 (0.010) | | | | |

| | | | | | | | |
|-------------------|--|--|--|--|--|--|--|
| <i>Wait</i> | | | | | | | |
| <i>Interrupts</i> | | | | | | | |

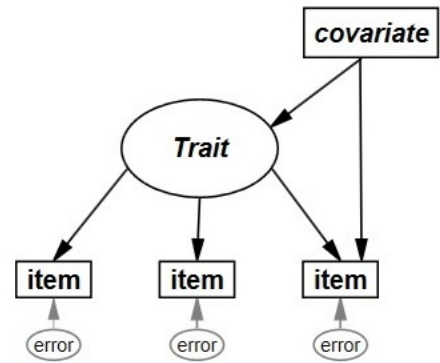
Figure 1: Model specifications (Trait: here IA or HI; Item: here symptom criterion; Error: residual variances; Group: here gender; Covariate: here age or co-occurring diagnoses; Cond. 1 and 2: here informants. Black arrows denote loadings and grey curved arrows denote correlations)

¹A fourth step is to test if the variability of the symptom endorsement not accounted for by the latent trait (specificity) is equal across groups or conditions. This is the residual invariance and it is established if the residual variances (that is, variability not explained by the latent trait) of a given item in (1) are equal across groups or conditions. However, in binary items, the residuals are required to be equal across genders and conditions for the identification of the model, and thus this type of invariance was not examined.

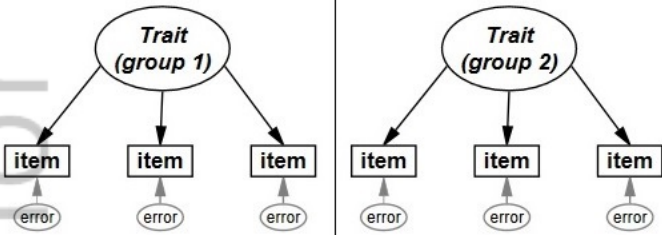
²The probit function Φ is the inverse of the cumulative distribution function of the standard normal distribution



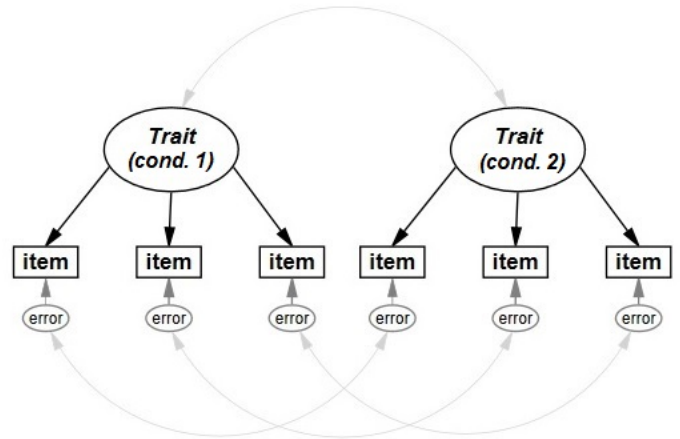
IFA



MIMIC



MIFA



LIFA

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