



The incremental validity of a computerised assessment added to clinical rating scales to differentiate adult ADHD from autism spectrum disorder

Madeleine J. Groom^a, Zoe Young^{a,d}, Charlotte L. Hall^{a,b,*}, Alinda Gillott^c, Chris Hollis^{a,b,d}

^a Division of Psychiatry and Applied Psychology, Institute of Mental Health, University of Nottingham, Triumph Road, Nottingham NG7 2TU, UK

^b CLAHRC-EM, Division of Psychiatry and Applied Psychology, Institute of Mental Health, University of Nottingham, Triumph Road, Nottingham NG7 2TU, UK

^c Intellectual and Developmental Disabilities Service, Nottinghamshire Healthcare NHS Trust, Nottingham, UK

^d NIHR MindTech Healthcare Technology Co-operative, Institute of Mental Health and Nottinghamshire Healthcare NHS Trust, Nottingham, UK

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ABSTRACT

There is a clinical need for objective evidence-based measures that are sensitive and specific to ADHD when compared with other neurodevelopmental disorders. This study evaluated the incremental validity of adding an objective measure of activity and computerised cognitive assessment to clinical rating scales to differentiate adult ADHD from Autism spectrum disorders (ASD).

Adults with ADHD ($n=33$) or ASD ($n=25$) performed the QbTest, comprising a Continuous Performance Test with motion-tracker to record physical activity. QbTest parameters measuring inattention, impulsivity and hyperactivity were combined to provide a summary score ('QbTotal'). Binary stepwise logistic regression measured the probability of assignment to the ADHD or ASD group based on scores on the Conners Adult ADHD Rating Scale–subscale E (CAARS-E) and Autism Quotient (AQ10) in the first step and then QbTotal added in the second step. The model fit was significant at step 1 (CAARS-E, AQ10) with good group classification accuracy. These predictors were retained and QbTotal was added, resulting in a significant improvement in model fit and group classification accuracy. All predictors were significant. ROC curves indicated superior specificity of QbTotal. The findings present preliminary evidence that adding QbTest to clinical rating scales may improve the differentiation of ADHD and ASD in adults.

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1. Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is characterised by core symptoms of inattention, hyperactivity and impulsivity and is increasingly recognised as a condition that affects adults as well as children (Faraone et al., 2006; Fayyad et al., 2007). The clinician's judgment is the most widely accepted method of ADHD assessment in children, integrating parent, teacher and patient reports with direct clinical observation. Applying this approach to adults has proved more difficult, however as there may be fewer informants (parents, teachers) available and recent evidence suggests clinical rating scales for adults such as the Conners' Adult ADHD Rating Scale (CAARS) are not as well validated as their child counterparts (Van Voorhees et al., 2011). In addition, such rating scales may be relatively insensitive to key clinical features such as physical over-activity (Lis et al., 2010) and rely on self-

evaluation skills and retrospective recall that may be unreliable. These difficulties mean that the clinician may have less information available when trying to reach a diagnosis and are further exacerbated when ADHD presents with overlapping symptoms of other psychiatric diagnoses (Davidson, 2007; Van Voorhees et al., 2011).

Autism is a pervasive developmental disorder encompassing social and communication difficulties and stereotyped repetitive behaviours (American Psychiatric Association, 2013) prevalent in about 1% of the adult population (Brugha et al., 2011). ADHD and Autism Spectrum Disorders (ASD) often co-occur (Rommelse et al., 2011) and exhibit overlapping difficulties in social interaction and communication (Geurts et al., 2004a), inattention and hyperactivity (Frazier et al., 2001), language delay (Hagberg et al., 2010) and executive function deficits (Geurts et al., 2004b). These phenotypic similarities may lead both to potential 'double-counting' of symptoms with the result of falsely inflated diagnostic co-morbidity between the two conditions and patients misclassified into the incorrect diagnostic category. As such, there is a need for more objective and reliable methods to accurately differentiate ADHD and ASD.

* Correspondence to: Institute of Mental Health, Innovation Park, University of Nottingham, Triumph Road, Nottingham NG7 2TU, UK.

E-mail address: charlotte.hall@nottingham.ac.uk (C.L. Hall).

Cognitive tests allow specific aspects of cognition to be measured and isolated from one another (such as sustained attention versus inhibitory control) and may provide access to cognitive features which show 'double dissociation' and allow better distinction between conditions than self-report measures. They may also provide additional information to help differentiate between neurodevelopmental disorders by measuring cognitive features that are specific to one condition. The tool that has perhaps most frequently been used with this aim in ADHD is the Continuous Performance Test (CPT), a measure of sustained attention and inhibitory control in which participants monitor a continuous stream of stimuli to report the presentation of a target stimulus. There has been some success using the CPT to differentiate ADHD from typically developing children (Epstein et al., 2003) and adults (Schoechlin and Engel, 2005) but the results are less compelling when differentiating ADHD from other psychiatric groups (Riccio and Reynolds, 2001; Solanto et al., 2004), perhaps because impairments in attention and executive functions are shared by a number of neuropsychiatric disorders. The studies conducted to date primarily addressed the question of whether the CPT could be used in isolation to differentiate ADHD from healthy individuals or those with other disorders. A more pragmatic and clinically relevant question is whether such tests can be used alongside other clinical information to improve assessment of ADHD (Roth and Saykin, 2004). Furthermore, the CPT measures attention and inhibitory control but has the limitation of not assessing motor activity, a cardinal feature of ADHD.

The Quantified behaviour Test (QbTest; Qbtech Ltd., www.qbtech.com) is a cognitive assessment tool developed specifically to measure the core symptoms of ADHD in conjunction with clinical interview measures and rating scales; not as a stand-alone diagnostic tool. The test combines a computerised CPT designed to measure inattention and impulsivity with a motion-tracking infrared camera to measure activity (hyperactivity) during test completion. Sensitivity of the measures to ADHD has been reported in affected individuals (Edebol et al., 2013) and at-risk siblings (Reh et al., 2014) and there is also evidence of sensitivity to medication response in adults (Bijlenga et al., 2015). However no research has investigated the specificity of the test in adult ADHD when compared with adult ASD. It is important to investigate the potential clinical utility and incremental validity of QbTest because, despite a weak evidence base, it has already been introduced into clinical practice in a number of healthcare clinics in the United Kingdom (U.K.) and Europe. Further research is therefore urgently needed to evaluate the utility of QbTest as an aid to diagnostic decision-making in the assessment of ADHD.

The aim of the present study was to determine whether QbTest aids the differentiation of adult ADHD from ASD when combined with brief, standardised clinical rating scales, as part of a full clinical assessment. We predicted that adding QbTest to brief clinical rating scales for ADHD (CAARS) and autism (AQ10) would show incremental validity with significantly improved distinction between ADHD and ASD, and compared with using clinical rating scales alone.

2. Methods

2.1. Participants

Thirty-seven adults aged 18–60 years with a DSM-IV diagnosis of ADHD (24 males; mean age $30.46 \pm \text{SD } 10$) years and 25 adults aged 19–47 years with a ICD10 diagnosis of Asperger's Syndrome (19 males, mean age $33.22 \pm \text{SD } 11.74$ years) were recruited to the study. Participation in the study was voluntary and signed consent was obtained for all participants. Ethical approval for the study was granted by the local Research Ethics Committee and Research and Development Department of Nottinghamshire Healthcare NHS Trust. The groups were matched on age, gender ratio, and socio-economic status (see Table 1). Socio-economic status was estimated for each participant using the Index of Multiple Deprivation (Department for Communities and Local Government, 2015) which categorises English postal districts according to several indices of deprivation. The categories are decile ranks where low ranks (1–3) represent high levels of deprivation and high ranks (8–10) represent low levels of deprivation.

The ADHD sample was recruited from a specialist adult ADHD clinic in Nottingham, U.K. All were interviewed by a psychiatrist with expertise in adult ADHD using the Diagnostic Interview for ADHD in Adults (Kooij and Francken, 2010) to establish current and lifetime DSM-5 ADHD diagnosis, in addition to self- and observer-reported symptom ratings using the Conners Adult ADHD Rating Scale (CAARS) (Conners et al., 1999), Autism Quotient (Baron-Cohen et al., 2001) (further information on these measures are given below) and Adult ADHD Rating Scale (Kessler et al., 2005). Fifty participants were approached to take part and gave consent. Of these, 3 were excluded as an ADHD diagnosis was not established, 3 were excluded due to non-completion of the test and 2 were excluded as they did not stop their ADHD medication prior to the test as requested. A further 5 participants with a dual diagnosis of ADHD and ASD were excluded, and AQ10 scores were unavailable for 4, leaving a final sample of 33. Of the final sample,

Table 1
Group Comparisons on QbTest Measures and Rating Scales.

	ADHD (n=32)	ASD (n=25)	Group comparison
Gender (% male)	63	76	$\chi^2 = 1.18$, ns
Age	31.64 (10.17)	33.22 (11.74)	$t = .55$, ns
Socio-economic status (IMD) (% Low, High, Mid)	50, 32, 18	64, 24, 12	$\chi^2 = 1.16$, ns
Q-Activity	2.81 (1.09)	1.10 (1.45)	$F = 25.80$, $p < .001$, $\eta^2 = .32$
Q-Impulsivity	1.45 (1.17)	.58 (1.08)	$F = 8.30$, $p < .01$, $\eta^2 = .13$
Q-Inattention	1.76 (1.24)	.43 (1.07)	$F = 18.13$, $p < .001$, $\eta^2 = .25$
CAARS-A Inattention	72.88 (9.78)	66.48 (12.38)	$F = 4.76$, $p < .05$, $\eta^2 = .08$
CAARS-B Hyp/Rest	68.47 (6.41)	54.20 (11.79)	$F = 34.09$, $p < .001$, $\eta^2 = .38$
CAARS-C Impulsivity	69.16 (9.99)	58.72 (8.68)	$F = 17.16$, $p < .001$, $\eta^2 = .24$
CAARS-D Self Concept	63.94 (11.64)	62.96 (11.74)	$F = 1.00$, ns
CAARS-E ADHD	75.69 (8.63)	64.32 (12.38)	$F = 16.67$, $p < .001$, $\eta^2 = .23$
AQ10	5.44 (1.81)	7.36 (2.33)	$F = 2.32$, $p < .001$, $\eta^2 = .18$

'Q' = q-score measure from QbTest.

CAARS = Conners Adult ADHD Rating Scale.

AQ10 = Autism Quotient 10-item version.

IMD = Index of Multiple Deprivation: Low = decile ranks 1–3 representing high deprivation; mid = decile ranks 4–7; High = decile ranks 8–10 representing low deprivation.

25 were diagnosed ADHD-Combined, 3 ADHD-Predominantly Inattentive and 1 ADHD-Predominantly Hyperactive/Impulsive; sub-type information was unavailable for 3 participants.

The ASD sample was recruited from a specialist service for adults with Asperger syndrome in Nottingham, U.K. All were assessed by an experienced multidisciplinary team using the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al., 1994) and the Autism Diagnostic Observation Schedule (ADOS) (Gotham et al., 2007) to establish ICD10 diagnosis of Asperger's Syndrome. Of 34 service-users who consented to participate, 1 failed to complete the QbTest and 8 were excluded due to comorbid ADHD, leaving a final sample of 25 participants.

All diagnoses used ICD-10 criteria other than for ADHD where DSM-5 criteria were used, as is accepted practice in the UK. Comorbid diagnoses in the ADHD group included ICD-10 diagnoses of depression (2), anxiety disorder (2) and emotionally unstable personality disorder (equivalent to DSM-5 borderline personality disorder) (2). Within the ASD group, ICD-10 comorbid diagnoses included anxiety (4), depression (2), anxiety and depression (1), bipolar disorder (1) and substance misuse (1). Any participants taking prescribed psychostimulant medication were asked to abstain for 24 h before assessment as these medications would ameliorate performance deficits on QbTest.

2.2. Measures

2.2.1. Self-report clinical measures

The CAARS (Conners et al., 1999) is an 18-item questionnaire with a 5-point rating scale to measure ADHD symptoms over the preceding 6 months. It comprises 5 sub-scales: A-Inattention/Memory; B-Hyperactivity/Restlessness, C-Impulsivity/Emotional Lability, D-Self-Concept, E-ADHD Index. The scale is used extensively in clinical practice and research and has good test-re-test reliability and high sensitivity and specificity (Erhardt et al., 1999).

The Autism Quotient-10 (AQ-10; Allison et al., 2012; Baron-Cohen et al., 2001) is a ten-item self-report questionnaire with the purpose of screening for possible autism spectrum disorders. Responses are made on a scale and a total score is yielded. A score of 6 or above is potentially indicative of ASD. The scale has high sensitivity and specificity (Allison et al., 2012).

2.2.2. QbTest

The QbTest is a computerised CPT coupled with an infra-red motion tracking system. There are two versions of the test: QbTest (6–12) and QbTest (12+) with the latter designed specifically to avoid potential ceiling effects in adolescents and adults (ages 12+). The CPT for ages 12+ was used in the present study. The test comprises 600 stimuli presented sequentially and centrally on a computer screen in pseudorandom order for 200 ms each with an inter stimulus interval (ISI) of 2000 ms. Stimuli are blue or red squares and circles. Participants are required to press a hand-held responder button when an on-screen stimulus matches in colour (blue or red) and shape (square or circle) with the previous stimulus (targets) and to withhold the response when the stimuli do not match. Of the total presented stimuli 150 (25%) are targets. Speed and accuracy are equally encouraged. The task lasts approximately 20 min and is preceded by a 5-min practice session which includes standardised on-screen instructions. Measurement of hit rate (proportion of correctly responded to targets), Reaction Time (RT) to targets and RT variability (standard deviation of RT) give an index of attention while the proportion of commission errors (incorrect responses to non-targets) gives an index of impulsivity. The motion-tracking system is an infra-red camera placed 1 m from the participant which captures movement by tracking a reflective headband worn by the participant. Activity is recorded throughout the CPT by recording the location of the

marker on the headband on x-y co-ordinates, at a frequency of 50 samples per second and with a spatial resolution of 1/27 mm per infra-red camera unit. Summary scores ('q-scores') in each of these domains (labelled Q-Activity, Q-Inattention, Q-Impulsivity) are obtained for each individual by transforming the raw data into units of standard deviation from the mean of an age- and gender-stratified normative sample, after correcting for skew. Q-scores are therefore equivalent to z-scores (Ulberstad, 2012) and higher Q-scores indicate greater risk of ADHD. To provide an index equivalent to the CAARS-E ADHD Index and to reduce the number of variables entered into regression analysis (see Section 2.4) a composite QbTest measure (QbTotal) was computed by calculating the mean of the 3 'cardinal' Q-score parameters.

2.3. Procedure

The QbTest took place in each clinic and was conducted by a fully trained research assistant (ZY). All participants watched a short instruction video. The researcher checked their understanding of the test verbally and by monitoring performance during the standardised practice test. All participants completed the CAARS, AQ10 and QbTest immediately before their clinic appointment.

2.4. Data analysis

To provide an overview of group differences on the QbTest, CAARS and ASD, the ADHD and ASD groups were compared on each of the QbTest cardinal parameters (Q-Activity, Q-Inattention, Q-Impulsivity), QbTotal, the 5 CAARS sub-scales (A to E) and the AQ10 using univariate ANOVA. To reduce type 1 error rate a Bonferroni corrected p-value of .005 ($\alpha = .05/10$) was applied.

To determine whether QbTest improves the differentiation of ADHD from ASD when added to CAARS and AQ10, binary logistic regression was performed to measure the probability of assignment to the ADHD or ASD group (dependent variable), based on scores on the CAARS-E, AQ10 and QbTest (predictor variables). To ensure a good case variable ratio given the total sample size, the CAARS-E subscale ('ADHD Index') was used rather than all sub-scales and the QbTest composite score, QbTotal, was used as an equivalent to CAARS-E. Composite measures also offer greater practical value in a clinical setting by providing a simple summary score. These variables were entered into logistic regression in two steps with CAARS-E and AQ10 entered simultaneously in the first step and QbTotal entered into the second step. This order was chosen as the most sensible to address the question of whether QbTest improves the sensitivity and specificity afforded by brief clinical rating scales. At each step, the goodness of fit of the model was evaluated with chi-square with a significance threshold of .05. In addition, the percentage of participants correctly assigned to the ADHD group and to the ASD group was evaluated to determine the sensitivity and specificity of the model. Tolerance statistics indicated no multi-collinearity between the variables included in the model. After examining leverage values one participant in the ADHD group was excluded from the analysis. To determine whether the model was robust to the order in which the individual predictors were entered, the order of entry of the predictors was reversed and resulted in the same final classification.

Receiver Operating Characteristic (ROC) curves were calculated for each predictor variable related to ADHD diagnosis (CAARS-E, QbTotal) to determine which offered the best sensitivity and specificity to ADHD and to identify associated cut-off scores on each measure.

3. Results

As shown in Table 1, the ADHD and ASD groups were well-matched on age and gender distribution. Q-scores (reflecting deviation from a normative sample in standardised units) were significantly greater in the ADHD than ASD group on all QbTest cardinal parameters but Q-Impulsivity did not meet the Bonferroni-corrected threshold. The groups also differed significantly on all sub-scales of the CAARS except CAARS-D (Self-Concept), although the difference on CAARS-A Inattention/Memory did not survive correction. The ASD group scored significantly higher on the AQ10.

To determine whether adding QbTotal enhanced the sensitivity and specificity of identifying ADHD when combined with the CAARS-E ADHD Index and AQ10 alone, these variables were entered, stepwise, into binary logistic regression with Group (ADHD, ASD) as the dependent variable. The goodness of fit of the model at the first step with CAARS-E and AQ10 entered as predictors was highly significant ($\chi^2=31.59$, $p<.001$) yielding group classification accuracy of 81% (84% sensitivity, 76% specificity, see Table 2) and explaining 57% of variance in the data (Nagelkerke $R^2=.57$). CAARS-E (Wald=11.21, $p<.01$; Exp (β)=1.19, 95% CI=1.07, 1.32) and AQ10 were both significant predictors (Wald=9.78, $p<.01$; Exp (β)=.46, 95% CI=.28, .75).

In step 2 QbTotal was added to the model and led to a highly significant improvement in model fit (Step $\chi^2=14.11$, $p<.001$, Model $\chi^2=45.69$, $p<.001$) with 74% of variance in the data explained (Nagelkerke $R^2=.74$) and overall classification accuracy of 90% (94% sensitivity, 84% specificity). CAARS-E (Wald=6.21, $p<.05$, Exp (β)=1.18, 95% CI=1.04, 1.33) and AQ10 (Wald=9.26, $p<.01$, Exp (β)=.42, 95% CI=.24, .74) remained significant and QbTotal was also significant (Wald=8.95, $p<.01$, Exp (β)=6.50, 95% CI=1.91, 22.17). Detailed figures on the assignment of participants to either the ADHD or ASD groups at each step of the analysis are shown in Table 2.

ROC curves were computed for CAARS-E and QbTotal and the Area Under the Curve (AUC) was calculated. As shown in Fig. 1, QbTotal yielded the highest AUC value, .87 (classified as 'good') while the value for CAARS-E was .77 ('fair'). The ROCs indicate that at equivalent sensitivity of around .8, QbTotal demonstrates superior specificity compared with CAARS-E. On the CAARS-E, sensitivity of .84 and specificity of .60 corresponds to a T-score of 69. On QbTotal, sensitivity of .84 and specificity of .80 corresponds to a Q-score of 1.12.

Table 2
Participant Assignment to the ADHD or ASD Group at Each Step of the Model.

	Predicted Group Membership		
	ADHD	ASD	Correct (%)
Step 1 (CAARS-E, AQ10)			
ADHD (N=32)	27	5	84
ASD (N=25)	6	19	76
Step 2 (+ QbTotal)			
ADHD (N=32)	30	2	94
ASD (N=25)	4	21	84

At each step the row for each group shows the numbers predicted by the model to belong to the ADHD group (first column) and to the ASD group (second column). The final column shows the accuracy of the step for each group.

CAARS-E=Conners Adult ADHD Rating Scale – subscale E (ADHD Index).

AQ10=Autism Quotient 10-item version.

QbTotal=index of activity on QbTest-plus, created by averaging the Q-scores for Q-Activity, Q-Impulsivity and Q-Inattention.

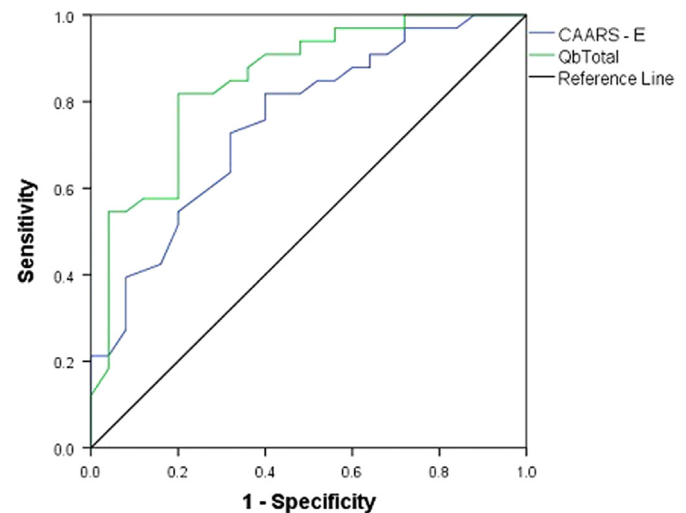


Fig. 1. ROC Curve of CAARS-E and QbTotal. Sensitivity (y-axis) and specificity (x-axis) are shown for CAARS-E (blue line) and QbTotal (green line) predicting ADHD group membership. The diagonal line (black) shows the reference point of 0 sensitivity and specificity. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

4. Discussion

The aim of this study was to determine whether QbTest improved the classification of adults with ADHD or ASD when added to brief standardised rating scales that are frequently used in clinical practice. The results confirm our predicted effects; QbTest significantly improved classification accuracy when combined with two rating scales designed to assess ADHD (CAARS-E) and ASD (AQ10) compared with using the rating scales alone. This suggests it may provide a useful, additional source of information when used as part of a full clinical assessment for ADHD in adults.

One previous study reported good sensitivity and specificity differentiating adult ADHD from healthy controls using QbTest (Edebol et al., 2013). Uniquely, we demonstrate that QbTest can be used to aid the differentiation of adults with ADHD from adults with ASD. Logistic regression revealed that the combination of CAARS-E and AQ10 successfully classified 81% of participants but 16% of the ADHD sample were mis-classified as 'ASD' and 24% of the ASD sample as 'ADHD'. The further addition of the composite measure from the QbTest improved the classification accuracy to 90%; this was a statistically significant improvement from the previous model comprising only the clinical rating scales and only two individuals with ADHD (6%) and four with ASD (16%) were incorrectly assigned. Thus, high scores on QbTotal improved correct assignment to the ADHD group, but also low scores on QbTotal improved correct assignment to the ASD group, thereby aiding differential diagnosis. The results provide some preliminary support for adding QbTest to standard clinical rating scales to aid differentiation of ADHD from ASD in adults. In addition, we identified a Q-score of 1.12 associated with 84% sensitivity and 80% specificity to ADHD, suggesting that this may be a useful cut-off predictive of ADHD when the sample comprises individuals with ADHD and ASD diagnoses.

It should be noted that although statistically significant, the improvements in the model with QbTest added are fairly modest and do not yield perfect results. Thus, although these findings offer some promise for the use of a computerised cognitive test to augment routine clinical diagnostic assessment, future research is needed to assess their reliability and generalisability and to determine the stability of the putative cut-off score for ADHD. In particular, further evidence is needed to help clinicians and healthcare service managers decide whether adding QbTest to

clinical assessment of ADHD is cost effective. A recent audit reported that adding QbTest to ADHD assessment in a child and adolescent service reduced time to diagnosis and resulted in cost savings (Hall et al., 2016). Although these results offer some promise, further research is needed to determine how best to implement the test to enhance diagnostic decision-making in a cost-effective way.

It is noteworthy that the univariate group ANOVA effects for Q-Impulsivity and CAARS-Inattention failed to reach statistical significance after correction for multiple comparisons. This suggests that these measures perform less well in differentiating between ADHD and ASD than the other parameters. Furthermore, the mean Q-Activity score of 2.81 in the ADHD group indicates significant rates of activity in this adult group. This is consistent with previous evidence (Lis et al., 2010) and suggests that when compared against a large normative database (Ulberstad, 2012), hyperactivity is still present in adulthood in ADHD. The relatively small sample size of the present study prevented inclusion of the individual QbTest parameters and CAARS subscales in logistic regression. A further question leading on from the present findings is therefore whether the individual parameters on QbTest offer greater sensitivity and specificity compared with the composite measures used here. In particular, it would be useful to determine whether the Q-Activity parameter is effective in differentiating the Combined and Inattentive ADHD sub-types. The present study sample comprised mostly adults with the Combined sub-type and so this important question could not be addressed here. Further research could also examine relationships between the movement and attention parameters recorded by QbTest as there is evidence to suggest that increases in activity may be intimately related to fluctuations in attention (Licht and Tryon, 2009).

Certain limitations should be considered when interpreting the results. Firstly, the research was limited to two specialist adult neurodevelopmental clinics in Nottinghamshire, U.K. Although there is no reason to consider the participants or clinics were not representative of other specialist ADHD or Asperger's clinics, care should be taken when generalising these findings to other sectors of the ADHD or ASD populations. In particular, all those in the ASD group were diagnosed with Asperger's Syndrome and were therefore relatively high functioning and in the ADHD group, the majority were combined sub-type. Secondly, in this study, we first sought to see if QbTest could aid the differentiation of two neurodevelopmental diagnoses. In real-world clinical practice however, differential diagnoses with adult ADHD are often complex with other co-occurring disorders being considered (e.g. bipolar disorder or antisocial personality disorder). One previous study suggests QbTest may fare less well when samples are more heterogeneous (Söderström et al., 2014). It will also be important to determine whether the impressive sensitivity and specificity parameters reported here are upheld in a sample that includes comorbid ADHD/ASD cases.

To conclude, the findings presented here suggest that adding a computerised cognitive assessment to frequently used standard clinical rating scales of ADHD and ASD improves correct diagnostic classification of these two neurodevelopmental disorders in adults. Further work is needed to replicate these findings in larger, more diverse samples and to evaluate the benefits and costs of including QbTest in clinical assessment. It will be important to further establish an evidence base for this measure which has already been introduced into some clinics.

Conflicts of interest

The National Institute of Health Research (NIHR) funded the study with a contribution from Qbtech Ltd. paid to the University

of Nottingham. The study design, analysis and conclusions are the sole responsibility of the authors and independent of Qbtech. The funding sources did not play any role in the collection, analysis or interpretation of data; in the writing of the report; and in the decision to submit the article for publication. None of the authors have received personal financial support from Qbtech and have no financial stake in the company. CH receives financial support from the National Institute of Health Research (NIHR) paid to the University of Nottingham.

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