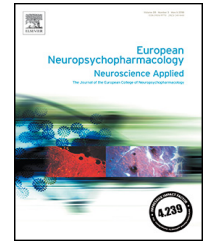




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Visual and auditory emotion recognition problems as familial cross-disorder phenomenon in ASD and ADHD

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Received 21 August 2017; received in revised form 9 May 2018; accepted 25 June 2018

Available online xxx

KEYWORDS

Autism spectrum disorder;
Attention-deficit/hyperactivity disorder;
Auditory emotion recognition;
Visual emotion recognition;
Factor analysis;
Endophenotype

Abstract

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are frequently comorbid disorders. Emotion recognition problems are considered an important familial deficit in ASD, but this is unknown in ADHD. Very few studies have directly compared emotion recognition performance of youth with ASD and/or ADHD and of their unaffected siblings across age to quantify the contribution of emotion recognition problems to the ADHD phenotype. We therefore devised a study of 64 ASD+ADHD participants, 89 ASD-only participants, 111 ADHD-only participants, 122 unaffected ASD(+ADHD) siblings, 69 unaffected ADHD-only siblings and 220 controls aged 7-18 years, who had completed two tasks assessing auditory and visual emotion recognition. Factor analysis was used to detect underlying dimensions of emotion recognition capacity. Linear mixed models were used to compare performance across groups and to assess age effects. The factor-analysis revealed four factors separating speed and accuracy regarding visual and auditory emotion recognition. ASD+ADHD, ASD-only, and ADHD-only participants all performed worse than controls. ASD+ADHD, ASD-only, and ADHD-only participants

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<https://doi.org/10.1016/j.euroneuro.2018.06.009>

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Please cite this article as: F. Waddington et al., Visual and auditory emotion recognition problems as familial cross-disorder phenomenon in ASD and ADHD, European Neuropsychopharmacology (2018), <https://doi.org/10.1016/j.euroneuro.2018.06.009>

did not differ in the severity of their emotion recognition problems. Both unaffected sibling groups performed intermediate between patients and controls. For ASD+ADHD and ADHD-only participants, group differences were more marked in adolescence than childhood, whereas in ASD participants this was not observed. We conclude that emotion recognition problems are a familial deficit in ADHD to a similar extent as in ASD. Emotion recognition problems specifically - and social cognition problems more generally - should be assessed in clinical practice for ADHD.

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1. Introduction

Impairments in social cognition are considered a primary deficit in autism spectrum disorder (ASD; [American Psychiatric Association, 2000](#); [American Psychiatric Association, 2013](#)). Social cognition refers to “the ability to recognize, manipulate, and behave with respect to socially relevant information” ([Adolphs, 2001](#)). Subsequently, emotion recognition (the ability to identify emotional facial expressions and emotional prosody; (see [Adolphs, 2001](#); [Adolphs, 2003](#); [Bänziger, Grandjean & Scherer, 2009](#)) is an essential component to social cognition. Poorer emotion recognition capacities have been shown to be an important feature for understanding ASD (for reviews see [Harms, Martin & Wallace, 2010](#); [Uljarevic and Hamilton, 2013](#)), although results for recognition abilities of specific types of emotions have been inconsistent ([Bal et al., 2010](#); [Gebauer, Skewes, Horlyck & Vuust, 2014](#); [Leung et al., 2015](#); [Oerlemans et al., 2014](#); [Wallace et al., 2011](#)). Emotion recognition problems potentially aggravate with increasing age ([Lozier, Vanmeter & Marsh, 2014](#); [Xavier et al., 2015](#)). Furthermore, they are likely to constitute a familial vulnerability trait (i.e. endophenotype) for ASD, as less severe but significant emotion recognition deficits have also been described in unaffected relatives of patients with ASD ([Neves et al., 2011](#); [Oerlemans et al., 2014](#); [Spencer et al., 2011](#)).

In comparison to ASD, much less is known regarding the contribution of emotion recognition problems to attention-deficit/hyperactivity disorder (ADHD) (see [Collin, Bindra, Raju, Gillberg & Minnis, 2013](#) for a review). Impaired executive functions are generally considered to be essential in understanding ADHD, as much as social cognition is considered essential for understanding ASD. Studies examining the association between ADHD and executive functions far outnumber those examining the association between ADHD and emotion recognition (>5-fold, Pubmed search July 2018). This is surprising, because ASD and ADHD are frequently comorbid, possibly due to overlapping etiological factors ([Lichtenstein, Carlstrom, Ramstam, Gillberg & Ankarster, 2010](#); [Musser et al., 2014](#); [Rommelse et al., 2011](#)). The comorbidity and overlap in etiological mechanisms has been the basis for the gradient overarching disorder hypothesis, stating that ASD and ADHD may be seen as different manifestations of one overarching disorder, with ADHD being the milder expression compared to ASD ([Rommelse et al., 2011](#); [Taurines et al., 2012](#)). Emotion recognition

problems are then to be expected in patients with ADHD also.

Studies having examined emotion recognition abilities in individuals with ADHD have mainly concentrated on visual emotion recognition ([Aspan et al., 2014](#); [Bora & Pantellis, 2016](#); [Chronaki et al., 2015](#); [Collin et al., 2013](#); [Da Fonseca, Segulier, Santos, Poinso & Deruelle, 2009](#); [Demopoulos, Hopkins & Davis, 2013](#); [Greenbaum, Stevens, Nash, Koren & Rovet, 2009](#); [Sinzig, Morsch & Lehmkuhl, 2008](#); [Uekermann et al., 2010](#); [Yuill & Lyon, 2007](#)). These studies suggest that there is an emotion processing deficit in ADHD, but which facial expressions are in particular poorly recognised remains inconclusive. Some of these studies report difficulties accurately identifying negative emotional expressions whereas others find general emotion recognition problems, including difficulties using contextual information to identify emotions. Only a few studies have investigated affective prosody ([Chronaki et al., 2015](#); [Demopoulos et al., 2013](#); [Greenbaum et al., 2009](#)), and these report conflicting results. The first study by [Greenbaum et al. \(2009\)](#) did not find a significant difference between children with ADHD and controls. [Demopoulos and colleagues \(2013\)](#), in contrast, found that children with ADHD were poor at affective prosody recognition overall, although not as poor as children with ASD. Lastly, [Chronaki et al. \(2015\)](#) found that children with ADHD have more difficulty than healthy controls in specifically recognising angry voices. They also found accuracy of recognising prosody to be negatively correlated with hyperactivity. Although there are only a few studies of affective prosody in ADHD, these results mimic those found for facial affect recognition. Consequently, it is clear that emotion recognition and likely social cognition in general warrants further investigation in ADHD, particularly in relation to the symptoms of ADHD and comorbid disorders.

In a recent meta-analysis on visual emotion recognition and theory of mind in ADHD, it was concluded that impairments in these domains may be more severe in ASD than in ADHD, but that there is significant overlap in the extent to which people with these disorders experience social cognition problems in general, and emotion recognition problems in particular ([Bora & Pantellis, 2016](#)). Age appeared to attenuate social cognition problems more so in ADHD than in ASD ([Bora & Pantellis, 2016](#)), but it should also be noted that, in addition to emotion recognition deficits, there may be additional reasons or contributing factors that affect the manifestation of social cognition problems in the two disorders, such as lack of social motivation ([Demurie, Royers, Baeyen & Sonuga-Barke, 2012](#); [Golan et al., 2010](#)) and

peer rejection (Kuusikko et al 2009; Wehmeier, Schacht & Barkley, 2010). There is also the possibility that executive dysfunction contributes to emotion recognition problems, particularly in ADHD, as attention and inhibition have been shown to be correlated with the ability to recognise emotions from faces (Sinzig et al., 2008).

In general, conclusions about (dis)similarities in emotion recognition performance in ASD and ADHD so far were only based on visual -and not auditory- emotion recognition and mostly derived from indirect comparisons between participants with ADHD and ASD. Studies reporting on direct comparisons regarding the severity and type of emotion recognition problems across age in probands with ASD, ADHD, and comorbid diagnoses are sparse, preventing firm conclusions regarding (dis)similarities of impairments in this vital domain.

Given the lack of studies in this area and subsequently the poor insight into familial deficits of emotion recognition across ASD and ADHD, we aimed to directly compare visual and auditory emotion recognition abilities across age (cross-sectional) in a large sample of youth with ASD+ADHD, ASD-only, ADHD-only, and their unaffected siblings. Since emotion recognition problems seem to occur across different types of emotion (i.e. sad, happy, angry, fearful) as well across sensory domains (i.e. auditory versus visual; Lozier et al., 2014; Uekermann et al., 2010), instead of performing emotion-specific analyses for each sensory domain individually, we investigated all domains and types of emotions by subjecting them to a factor-analysis; this enabled us to reduce variables and to detect underlying dimensions of emotion recognition capacity (Cattell, 2012). By including unaffected siblings of youth with each of the disorders or their combination, we were able to investigate to what extent these features can be seen as endophenotypes (Gottesman & Gould, 2003) in ASD and ADHD. In the context of this study, one of the criteria for endophenotypes can be assessed, namely if unaffected siblings demonstrate emotion recognition abilities at an intermediate level between probands and controls. This study builds upon previous work reporting on a smaller, overlapping sample of participants with ASD and their unaffected siblings (Oerlemans et al., 2014). To our knowledge, it is the first study of emotion recognition in unaffected siblings of individuals with ADHD and the first one to directly compare patients with ASD, ADHD, and ASD+ADHD, as well as controls across age.

2. Experimental procedures

2.1. Participants

The data used in this study came from two cohorts, the NeuroIMAGE study, which is a follow-up (2009-2012) of the Dutch part of the International Multicenter ADHD Genetics (IMAGE) study performed between 2003-2006 (Müller et al, 2011a,b; Nijmeijer et al., 2009; Rommelse et al., 2008) and the Biological Origins of Autism (BOA) study (van Steijn et al., 2012), which was modelled after (Neuro)IMAGE. Recruited families were included if (1) they had one child with a clinical diagnosis of ADHD (NeuroIMAGE) or ASD (BOA) and (2) at least one biological sibling (regardless of possible clinical diagnosis) willing to participate. Healthy control youth

had no formal or suspected ADHD or ASD or any first-degree relatives with a suspected or formal diagnosis. All participants were of European Caucasian descent. Exclusion criteria were an IQ <70, a diagnosis of epilepsy, known genetic disorders (e.g. Down-syndrome or Fragile-X-syndrome), or a clinical diagnosis of autistic disorder or Asperger disorder (NeuroIMAGE). The NeuroIMAGE and BOA cohorts have different age ranges and therefore for the current study, a subsample of the younger participants from BOA and older participants from NeuroIMAGE were selected to ensure these cohorts were matched on mean age ($M=12.6$ years, $SD=2.4$, age range from 7-18 years) (Table 1). Due to the individually relatively limited number of comorbid ASD+ADHD unaffected siblings, these were grouped together with the ASD unaffected siblings. In total, 89 participants with ASD (further mentioned as ASD-only probands), 64 participants with comorbid ASD+ADHD (further mentioned as ASD+ADHD probands), 122 of their unaffected siblings, 111 patients with ADHD (further mentioned as ADHD-only probands), 69 unaffected siblings, and 220 controls were included.

All participants were phenotyped for ASD and ADHD using validated and standardised questionnaires and diagnostic interviews. Briefly, youth already clinically diagnosed with ASD and/or ADHD, their siblings, and the control youth were screened for the presence of ASD and ADHD symptoms using the parent-reported Social Communication Questionnaire (SCQ; Rutter, Bailey & Lord, 2003) and the parent- and teacher-reported Conners Rating Scales-Revised (CPRS; CTRS), respectively (Conners, 1997). Raw scores of ≥ 10 on the SCQ Total score and T-scores ≥ 63 on the Conners DSM-IV Inattention, Hyperactivity-Impulsivity, or Combined scales were considered as potential clinical cases. All youth scoring above cut-off on any of the screening questionnaires underwent full clinical assessment using the Parental Account of Childhood Symptoms ADHD subversion (PACS) for ADHD (BOA cohort; Taylor, Sandberg, Thorley & Giles, 1991) or Schedule for Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime Version (K-SADS; Kaufman et al., 1997; in NeuroIMAGE). Clinical assessment for ASD was performed using the Autism Diagnostic Interview-Revised (ADI-R) structured interview for ASD (Le Couteur, Lord & Rutter, 2003; in BOA-cohort). Youth with a confirmed diagnosis of ASD were excluded from the NeuroIMAGE cohort, whereas those with a suspected diagnosis of ADHD were not excluded from the BOA cohort. Control youth were required to obtain non-clinical scores (i.e. a raw score <10 on the SCQ and T-score <63 on both CPRS and CTRS) to qualify for this study. For siblings to be classified as unaffected, they were also required to obtain non-clinical scores (further details in Supplement).

2.2. Measures

2.2.1. Emotion recognition

Speed (mean reaction time) and accuracy (percentage of errors) of visual and auditory emotion recognition were measured using the Identification of Facial Emotions (IFE) task and the Affective Prosody (AP) task from the battery of the Amsterdam Neuropsychological Tasks (ANT; De Sonneville, 1999). In the IFE task, participants viewed individual photos of facial expressions and indicated by clicking a yes or no

Table 1 Sample characteristics, including z-scores of diagnostic criteria.

	1. ASD+ADHD probandsN=64	2. ASD- only probands N=89	3. ADHD- only probandsN=111	4. ASD Unaf- fected SiblingsN=122	5. ADHD Unaf- fected SiblingsN=69	6. ControlsN=220	Group Contrasts
Age (M/SD)	12.14 2.79	12.32 2.48	12.67 1.71	11.77 2.79	12.81 1.63	13.11 2.35	1 = 2 = 3 > 4 < 5 = 6
IQ (M/SD)	102.36 13.15	101.51 14.67	99.49 14.13	105.73 12.63	99.61 14.42	105.15 12.42	1 = 2 = 3 < 4 > 5 < 6
Male (%)	87.5	77.5	51.4	43.4	37.7	50	3 = 1 > 2 = 6 = 4 = 5
DSM ADHD	0.92 0.59	0.57 0.64	0.92 0.80	-0.33 0.81	-0.22 0.71	-0.69 0.70	3 = 2 > 1 > 5 4 > 6
Inatten- tion z-score							
DSM ADHD	0.99 0.56	0.63 0.67	0.84 0.80	-0.29 0.74	-0.32 0.68	-0.66 0.59	3 = 2 > 1 > 4 = 5 5 > 6
Hyperac- tivity z-score							
Conners Teacher's Inatten- tion z-score	1.09 0.74	-0.001 0.88	0.63 0.93	-0.28 0.86	-0.16 0.54	-0.46 0.81	3 > 2 > 1 = 5 5 = 4 4 > 6
Conners Teacher's Hyperac- tivity z-score	0.84 0.77	0.15 0.87	0.71 1.0	-0.29 0.91	-0.15 0.72	-0.43 0.79	3 = 2 > 1 > 5 5 = 4 > 6
CSBQ ASD core items z-score	1.02 0.75	1.07 0.67	0.50 0.61	-0.15 0.68	-0.27 0.63	-0.65 0.60	1 = 3 > 2 > 4 = 5 > 6

N.B. ASD-only= Autism Spectrum Disorders; ADHD-only= Attention Deficit/Hyperactivity Disorder; M= Mean; SD= Standard Deviation; IQ=Intelligence Quotient; DSM= Diagnostic Statistics Manual; CSBQ= Children's Social Behaviour Questionnaire.

button if they saw or did not see the target emotion (happy, fearful, or angry) in these photos (Fig. S3). In the AP task, participants listened to sentences of neutral content that differed in prosody. The participants had to verbally identify the emotion (happy, fearful, sad, or angry) of the voice they heard. Both tasks are fully described elsewhere (Oerlemans et al., 2014).

2.2.2. Intelligence

An estimate of the Full Scale Intelligence Quotient (FSIQ) was derived from two subtests of the Wechsler Intelligence Scale for Children version III (WISC-III; Wechsler, 2002), for participants younger than 16 years, or the Wechsler Adult Intelligence Scale version III (WAIS-III; Wechsler, 2005) Vocabulary (Vo) and Block Design (BD), for participants 16 years or older.

2.3. Procedure

The tasks described were part of the broader assessment batteries used in the BOA and NeuroIMAGE cohorts. Testing was conducted in quiet rooms with minimal distractions. Participants were asked to withhold use of psychoactive drugs for at least 24 hours before measurement. During the testing day, participants were motivated with short breaks and at the end of the day, the participants were rewarded. Both studies were approved by the appropriate medical ethics boards. Written informed consent was obtained from all participants and their parents (parents signed informed consent for participants under 12 years of age).

2.4. Statistical analyses

SPSS version 22 was used for the analysis of the data. Less than 5% of the data was missing. Data was imputed for each cohort separately using SPSS based on the data from the IFE and AP tasks as well as gender, age, IQ, family and diagnostic status. The measures for both cohorts together were normalised and standardized using Van der Waerden transformation, and the IQ scoring was reversed. Consequently, all of the variables had scores on the same z-scale, with lower scores implying better performance (fewer errors, faster reaction times, and a higher IQ).

An exploratory factor analysis on the 14 dependent measures (mean reaction time and percentage of errors of the administered emotions of the IFE and AP tasks, as applied in previous studies: (Oerlemans et al., 2014; De Sonnevile et al., 2002; Njokiktjen et al., 2001) in the first cohort (NeuroIMAGE) was performed using MPlus version 6 (Muthén & Muthén, 2010) to examine the underlying dimensions of emotion recognition performance. Robustness of this factor structure was then tested using Confirmatory Factor Analysis (CFA) in the second cohort (BOA). When the CFA provided an adequate fit, further analyses were performed combining both cohorts. In all models, family was included as a random effect in order to account for familial relatedness of participants. For both EFA and CFA, model fit was assessed on the basis of Akaike Information Criteria (AIC), Bayesian Information Criteria (BIC), Satorra-Bentler adjusted Chi-square

p-value, Root Mean Square Error of Approximation (RMSEA), Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI).

Linear mixed models including diagnosis, age, and diagnosis \times age fixed effects were used to assess the differences between the diagnostic groups (with age) on emotion recognition factor scores. Effects of gender and IQ were examined. Multiple comparisons were corrected for using the false discovery rate (FDR) controlling procedure, with the *q*-value set at .05. Post-hoc contrasts were performed on factors with significant diagnosis \times age interactions. Median split was used to define groups of younger and older children.

3. Results

3.1. Descriptives

Table 1 shows the characteristics of the participants analysed in the current study. There were no significant differences in the mean age ($F(5, 653.38)=0.33, p = .57$), but there were significant differences in IQ ($F(5, 663.44)=62.18, p < .001$) and proportion of males ($\chi^2(5)=63.32, p < .001$) between the six groups (see Table 1). Therefore, results are presented with and without accounting for effects of sex, IQ, and age.

Emotion-specific analyses were not the main aim of this study, but were performed for reference purposes, and results are shown and described in the Supplement.

3.2. Underlying factor structure of emotion recognition

The EFA in the first cohort (NeuroIMAGE) indicated that a four-factor solution provided a good fit, and this was confirmed using a CFA in the second (BOA) cohort (see Tables S2 and S3). The four factors represented (1) accuracy of identification of facial emotional expressions, (2) speed of identification of facial emotional expressions, (3) accuracy of auditory emotion recognition, and (4) speed of auditory emotion recognition. These emotion recognition factors formed the basis for a comparison of the performance ASD, ADHD, and ASD+ADHD probands, the unaffected siblings, and the controls.

3.2.1. Group differences regarding underlying dimensions of emotion recognition performance

Please see Fig. 1 for the results. An overall linear effect of diagnosis was present on three out of four factors (speed of visual emotion recognition $F(5, 594.78) = 3.41, p = .007, d = 0.23$; accuracy of visual emotion recognition $F(5, 558.40)=4.57, p < .001, d=0.27$; speed of auditory emotion recognition $F(5, 592.00) = 10.24, p < .001, d = 0.52$; accuracy of auditory emotion recognition $F(5, 590.58) = 1.23, p = .29, d = 0.05$). Pairwise comparisons (shown in Table S5) indicated that the ASD-only, ADHD-only, and ASD+ADHD probands performed similarly on the individual emotion recognition factors (*p*'s = .09-.91, *d*'s = 0.02-0.27). The ASD+ADHD probands were found to perform significantly worse than the controls on three out of four factors (speed of visual emotion recognition $p=.007, d = 0.39$;

Group Performance on Emotion Recognition Factors

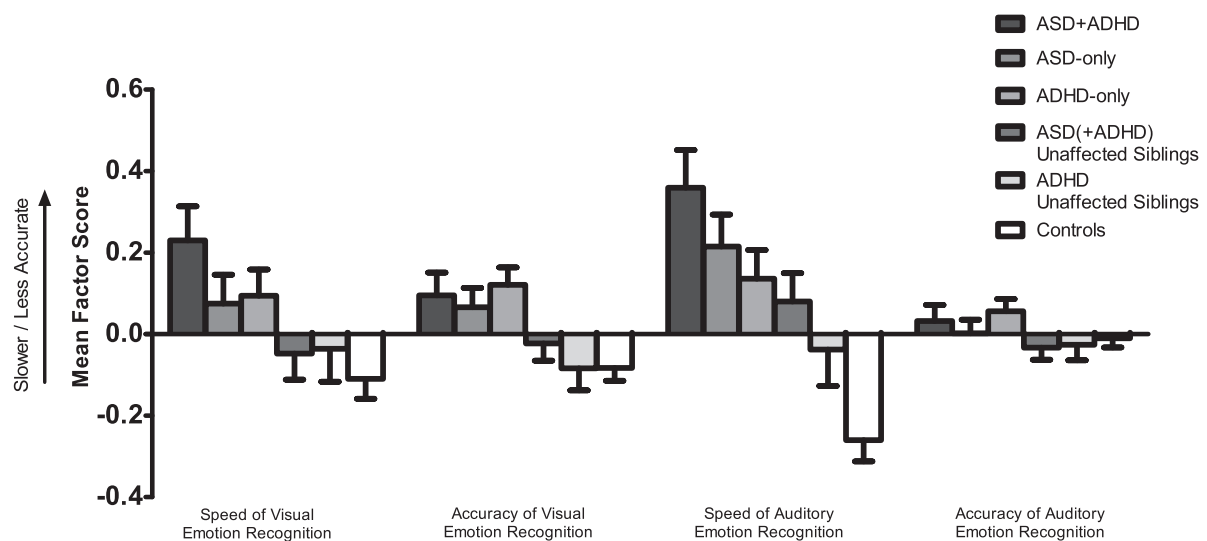


Fig. 1 Group performance on the emotion recognition factors. Mean factor scores (– SE) for each emotion recognition factor. Values are means corrected for age and within family correlations.

accuracy of visual emotion recognition $p = .03$, $d = 0.31$; speed of auditory emotion recognition $p < .001$, $d = 0.77$; accuracy of auditory emotion recognition $p = .75$, $d = .05$. However, when the effects of sex and IQ were accounted for, the effect of accuracy of visual recognition was no longer significant ($p = .33$, $d = 0.14$), whereas the other factor effects (speed of visual emotion recognition and speed and accuracy of auditory emotion recognition) remained significant. The ASD-only probands were found to perform significantly worse than the controls on accuracy of visual emotion recognition and speed of auditory emotion recognition (p 's $\leq .034$, d 's = 0.23–0.59), but not for speed of visual recognition (p 's = .10, d 's = 0.21) and accuracy of auditory recognition ($p = .81$, $d = 0.03$). Furthermore, when the effects of sex and IQ were accounted for, the effect of accuracy of visual recognition was no longer significant ($p = .33$, d 's = 0.12). The ADHD-only probands were found to perform significantly worse than the controls on accuracy of visual recognition ($p = .002$, $d = 0.36$) and speed of auditory recognition ($p < .001$, $d = 0.49$), regardless of co-varying for sex and IQ.

The ASD(+ADHD) unaffected siblings group's performance was between ASD-only probands and controls, not differing significantly from ASD-only probands on any of the factors (p 's = .25–.79, d 's = 0.04–0.16) nor from controls on three out of four factors (p 's = .30–.79, d 's = 0.03–0.12), except for speed of auditory recognition ($p < .001$, $d = 0.40$). None of these results changed, when sex and IQ were accounted for. ASD+ADHD probands and ASD(+ADHD) unaffected siblings were only significantly different on accuracy of auditory recognition ($p = .035$, $d = 0.33$). However, this effect was not significant when sex and IQ were accounted for. Similarly, the ADHD-only unaffected siblings group's performance was in between that of the ADHD-only probands

and controls, not differing from ADHD-only probands on three out of four factors (p 's = .18–.44, d 's = 0.12–0.21), except for accuracy of visual recognition ($p = .023$, $d = 0.19$), and not differing from controls on any of the four factors (p 's = .06–1, d 's = 0–0.26). Neither of these results changed when sex and IQ were accounted for. The performance of the ASD(+ADHD) and ADHD-only unaffected sibling groups also did not significantly differ on any factor (p 's = .34–.91, d 's = 0.02–0.14), regardless of co-varying for sex and IQ.

An age \times diagnosis interaction was found for speed of visual recognition ($F(5, 655.33) = 3.51$, $p = .016$, $d = 0.24$), but not for any of the other factors (accuracy of visual recognition ($F(5, 663.23) = 1.00$, $p = .54$, $d = 0.12$); speed of auditory recognition ($F(5, 669.98) = 1.12$, $p = .54$, $d = 0.17$); accuracy of auditory recognition ($F(5, 660.71) = 0.82$, $p = .54$, $d = 0.04$); see Fig. 2).

Post-hoc analyses of speed of visual recognition were carried out with age groups based on a median split. These indicated that both ASD+ADHD probands and ADHD-only probands versus controls contrasts were larger for adolescents (≥ 13 years: ASD+ADHD probands ($n = 25$) versus controls ($n = 125$), $p < .001$; ADHD-only probands ($n = 56$) versus controls, $p = .001$) than for children (< 13 years: ASD+ADHD probands ($n = 39$) versus controls ($n = 95$), $p = .07$; ADHD-only probands ($n = 55$) versus controls, $p = .77$; see Fig. 2). The ASD-only probands did not show significant differences in contrasts compared to controls (ASD-only children ($n = 55$): $p = .06$; ASD-only adolescents ($n = 34$): $p = .20$) nor ADHD-only probands (children: $p = .15$; adolescents: $p = .16$). Furthermore, only adolescent ASD-only and ASD+ADHD probands differed significantly (children: $p = .53$; adolescents: $p = .042$). However, ADHD-only and ASD+ADHD probands were not significantly different (children: $p = .50$; adolescents: $p = .33$).

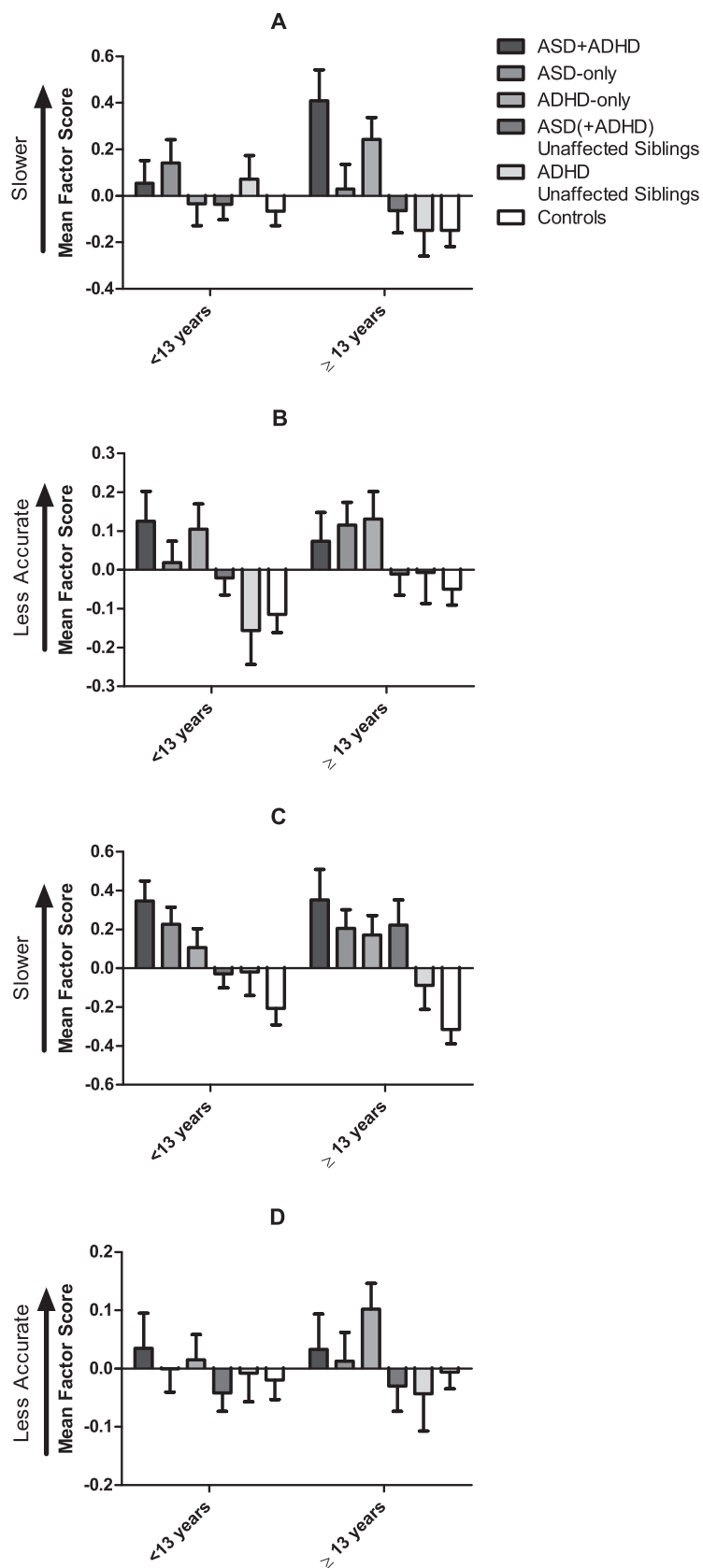


Fig. 2 Effect of age on visual and auditory emotion recognition abilities across childhood (participants <13 years old) and adolescence (participants ≥13 years old). Mean factor scores (– SE) for **A**= speed of visual emotion recognition; **B**= accuracy of visual emotion recognition; **C**= speed of auditory emotion recognition; **D**= accuracy of auditory emotion recognition.

3.2.2. Relationship between behaviour and emotion recognition factors

Correlation analyses between the emotion recognition factors and behavioural symptoms (ASD, ADHD, and comorbidities) were performed. For the ASD core items on the CSBQ, we found speed and accuracy of visual emotion recognition as well as speed and accuracy of auditory emotion recognition to have positive correlations with symptom levels (Visual Speed: $r = .18$, $p < .001$; Visual Accuracy: $r = .15$, $p < .001$; Auditory Speed: $r = .23$, $p < .001$; Auditory Accuracy: $r = .11$; $p = .008$).

For the Conners Parents (CPRS) and Teachers (CTRS) scales, accuracy of visual and auditory emotion recognition correlated positively with hyperactivity and inattention levels (Visual Accuracy - Hyperactivity CPRS: $r = 0.17$, $p < .001$; Hyperactivity CTRS: $r = 0.10$, $p = .015$; Inattention CPRS: $r = 0.14$, $p < .001$; Inattention CTRS: $r = 0.14$, $p = .001$; Auditory Accuracy - Hyperactivity CPRS: $r = 0.12$, $p = .004$; Hyperactivity CTRS: $r = 0.10$, $p = .02$; Inattention CPRS: $r = 0.10$, $p = .01$; Inattention CTRS: $r = 0.10$, $p = .02$). Speed of visual and auditory emotion recognition positively correlated with hyperactivity and inattention on the CPRS only (Visual Speed - Hyperactivity CPRS: $r = 0.12$, $p = .004$; Inattention CPRS: $r = 0.13$, $p = .002$; Auditory Speed - Hyperactivity CPRS: $r = 0.17$, $p < .001$; Inattention CPRS: $r = 0.17$, $p < .001$), and speed of auditory emotion recognition positively correlated with inattention on the CTRS only ($r = 0.13$, $p = .002$).

Anxiety levels and oppositional behaviour from CPRS and CTRS did correlate positively with the accuracy of visual emotion recognition (Anxiety CPRS: $r = 0.08$, $p = .03$; CTRS: $r = 0.09$, $p = .02$; Oppositional behaviour CPRS: $r = 0.16$, $p < .001$; CTRS: $r = 0.10$, $p = .01$). Speed of visual emotion recognition positively correlated with anxiety only (CPRS: $r = 0.11$, $p = .004$). Speed of auditory emotion recognition positively correlated with anxiety and oppositional behaviour (CPRS - Anxiety: $r = 0.18$, $p < .001$; Oppositional behaviour: $r = 0.12$, $p = .002$), whereas the accuracy of auditory emotion recognition did not correlate with either anxiety or oppositional symptom levels (Anxiety CPRS: $r = 0.04$, $p = .27$; CTRS: $r = 0.03$, $p = .39$; Oppositional behaviour CPRS: $r = 0.06$, $p = .14$; CTRS: $r = 0.07$, $p = .12$).

4. Discussion

The current study is the first to directly compare visual and auditory emotion recognition performance in a large sample of children and adolescents with pure and comorbid ASD and ADHD and in their unaffected siblings. This study also extends previous work by determining underlying dimensions of emotion recognition abilities. Further, by including unaffected siblings of youth with ADHD and youth with ASD, the extent to which these features can be seen as familial vulnerability traits (endophenotypes) was investigated. Results revealed a clear factor structure in both investigated cohorts, indicating that emotion recognition is best understood in terms of speed and accuracy in the visual and auditory domain. Results further indicated that emotion recognition problems of youth with ADHD-only are as severe as those observed in youth with ASD-only with both ASD and ADHD symptoms correlating with this deficit. This

illustrates that emotion recognition problems are as integral to ADHD as they are to ASD. Observed group differences were not moderated by age, except for speed of visual emotion recognition, where emotion recognition problems were -unexpectedly- somewhat more pronounced in adolescents than in children with ADHD-only and ASD+ADHD, but not ASD-only probands. Unaffected siblings of ASD(+ADHD) and ADHD-only probands performed intermediate between probands and controls.

The ASD+ADHD, ASD-only, and ADHD-only groups did not significantly differ from each other on emotion recognition factors, but the ASD+ADHD more strongly deviated from the controls than the non-comorbid groups. This - to some extent - corroborates previous findings that ASD+ADHD probands have greater emotion recognition problems than ASD-only or ADHD-only probands (Oerlemans et al., 2014; Sinzig et al., 2008; Van der Meer et al., 2012). Moreover, the results are also in line with a recent meta-analysis describing facial emotion recognition problems in ADHD (Bora & Pantellis, 2016). Our study adds to these findings by showing the importance of speed of emotion recognition in ASD and ADHD: in comparison to controls, probands had more pronounced impairments in regard to speed of identifying visual and auditory emotions, rather than accuracy. This potentially has clinical relevance in that the social interactions of patients may be significantly hampered by their inability to quickly identify emotions. Moreover, we demonstrate that both facial and auditory emotion recognition problems are present in ADHD, and that these do not seem to attenuate with age in ADHD, as was previously suggested (Bora & Pantellis, 2016). If anything, emotion recognition problems appeared most pronounced in adolescents with ASD+ADHD or ADHD-only. This may suggest that ADHD symptoms are contributing to emotion recognition problems in ASD+ADHD more than ASD symptoms. However, it is plausible that in our sample the children with ADHD did not display emotion recognition deficits as strong as the adolescents with ADHD, which creates the impression that emotion recognition deficits worsen from childhood to adolescence. Nonetheless, if emotion recognition problems do not attenuate during adolescence in ADHD or ASD+ADHD as seems to be the case for probands with ASD, this would tentatively suggest that there is a difference in the developmental trajectory of emotion recognition problems in ASD versus ADHD. However, our study is cross-sectional and therefore firm conclusions regarding the effects of age should await validation from longitudinal studies.

Whether emotion recognition deficits are cause or consequence in ASD and ADHD needs to be determined. Many studies have highlighted links of hyperactivity and inattention with social cognition problems in ADHD and ASD (Bora & Pantellis, 2016; Chronaki et al., 2015; Demopoulos et al., 2013; Oerlemans et al., 2014; Sinzig et al., 2008). The current study extends on these findings by demonstrating that both speed and accuracy of visual and auditory emotion recognition is positively -albeit modestly- correlated with hyperactivity, inattention and ASD symptoms. The relatively small correlations likely illustrate the heterogeneity of emotion recognition difficulties in relation to ASD and ADHD symptoms. Previous studies have also demonstrated that there is a functional dependency between the development of executive functioning and social interaction: the

development of executive functioning facilitates the maturation of cognitive skills that are important for social interaction, and probably also vice versa (Baribeau et al., 2015; Hartman, Geurts, Franke, Buitelaar & Rommelse, 2016; Van der Meer et al., 2012). This illustrates that problems may result from impairments in executive functioning and social cognition, and that there are multiple ways as to how executive functioning and social cognition impairments may link to the behaviours that define both ASD and ADHD. We hypothesize that this association is bi-directional, such that symptoms of ASD and ADHD also hinder the development of emotion recognition. Consequently, emotion recognition may be more important to our understanding of ADHD than previously considered.

The current study supports the notion that emotion recognition problems can be seen as a familial vulnerability marker (i.e. endophenotype) for ASD and ADHD and their comorbidity. The unaffected sibling groups performed intermediate between their relatives with the full disorder and control participants. These findings are in line with previous behavioural and neuroimaging studies. In ASD, studies have demonstrated that unaffected relatives of ASD probands have difficulties recognising emotions (Wallace, Sebastian, Pellicano, Parr & Bailey, 2010) and display activation patterns during emotion recognition tasks (Spencer et al., 2011). Although emotion recognition studies of ADHD and their unaffected relatives are lacking, there are studies investigating other domains relevant to social cognition, such as response inhibition, that have found ADHD probands and their unaffected siblings to demonstrate poor response inhibition (Schachar et al., 2005; Slaats-Willemse et al., 2003) and atypical neural activation patterns in the prefrontal cortex and the cerebellum during go/no-go tasks (Mulder et al., 2008). Combining the evidence suggests that emotion recognition ability is a familial (potentially heritable) vulnerability trait that could increase the risk of developing a neurodevelopmental disorder of any type. Notably though, the unaffected siblings of ASD(+ADHD) probands were significantly slower at auditory emotion recognition than controls, whereas the unaffected siblings of ADHD-only probands did not differ from controls. This may indicate that ADHD is a milder expression of a similar overarching disorder as proposed by the overarching disorder hypothesis (Rommelse et al., 2011; Taurines et al., 2012; Van der Meer et al., 2012). Alternatively, the aetiology of this deficit may not only differ in ASD and ADHD, but comorbid ASD+ADHD may also have a different aetiology relative to the pure disorders, though further studies with genetic or longitudinal designs are required to further understand the aetiology. This may also suggest that emotion recognition problems are causal in ASD, yet more a consequence in ADHD. To ascertain this, a more detailed study of the developmental trajectory of emotion recognition in these disorders is necessary. For example, the symptoms of ASD and ADHD, and emotion recognition problems could be studied in children from early childhood to young adulthood at multiple time points to ascertain when symptoms or emotion recognition deficits are first present as well as how the symptoms and emotion recognition problems may interact overtime and if these trajectories differ for children who are given a diagnosis of ASD, ADHD and ASD+ADHD during their childhood.

The results of the emotion-specific analyses were not disparate to those of the factor analysis. The ASD and/or ADHD probands had difficulties in quickly and accurately identifying all emotions and were not dissimilar in these deficits. As expected, the controls were accurate in the identification of emotional expressions and prosody. On average, ASD and/or ADHD probands were slower than controls in recognising prosody, with the exception of fear. This suggests general, rather than emotion-specific, deficits being present, which further strengthens the value of utilising factor analysis.

Further strengths of the study are the large sample size for each group, the well-phenotyped groups, the direct comparison between probands with ASD-only, ADHD-only, and ASD+ADHD, the inclusion of unaffected siblings, the inclusions of children as well as adolescents, and the assessment of emotion recognition problems across various emotions and sensory domains. Limitations of the current study include the exclusion of low functioning individuals with ASD or ADHD (IQ lower limit was set at 70), thereby preventing generalisation of the results to the lower end of the IQ spectrum. Furthermore, data on recognition of sad facial expressions was not collected due to time limitations. However, this is unlikely to have negatively impacted the study results, as the identified factors were not emotion-specific. Finally, only group averages were presented, thereby ignoring the heterogeneity within groups. However, the main aim of this study was to examine the overall association between ADHD and emotion recognition problems in comparison to those found in ASD. Other methods, like factor mixture modelling, will allow more insight to be gained into inter-individual variability in the future.

Over the last decade the classification of ASD and ADHD has been debated and their comorbidity has now been acknowledged in the DSM5 (Casey, Oliveri & Insel, 2014). An alternative to this categorical system is the Research Domains Criteria (RDoC) approach (Insel et al., 2010). This approach promotes the use of dimension-based taxonomy rather than the current categorical systems, which may be arbitrary and hindering our knowledge of the psychopathology of these disorders. Such a dimensional system is also thought to provide greater insight into brain-behaviour associations throughout typical and atypical development (Casey, Oliveri & Insel, 2014). The current study also has implications for the diagnosis of ASD, ADHD and their comorbidity. Although emotion recognition is not the sole defining feature of either ASD nor ADHD, the presence of this deficit across both disorders and the declining trend of emotion recognition problems from probands, to unaffected siblings and controls suggests that this is a dimensional feature that could provide insight into our understanding of these disorders.

4.1. Conclusion

The current study emphasises that emotion recognition problems are as integral to ADHD as they are to ASD, that they form a familial cognitive deficit in ADHD and do not appear to attenuate in adolescence. As these findings suggest that emotion recognition is an overlapping feature for ASD and ADHD, this supports the RDoC approach and the

potential to develop a dimension-based taxonomy. A direct clinical implication of this study is that emotion recognition problems specifically -and social cognition problems more generally- should also be assessed in clinical practice for ADHD and treatment plans developed accordingly. For further insight, longitudinal studies assessing emotion recognition, executive functions, and heterogeneous ASD and ADHD symptoms levels throughout development are necessary. If (partly) causal to ADHD/ASD symptoms, changes in emotion recognition will have an impact on the co-occurrence patterns of ADHD and ASD across the lifespan (Hartman et al., 2016).

Acknowledgements

The authors would like to thank all the parents, teachers and children, who kindly participated.

Role of the funding source

This project was supported by the European Community's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement #643051 (MiND). The study was also partly funded by grants assigned to Dr. Rommelse by the Netherlands Organisation for Scientific Research (NWO grant #91610024) and to Dr. Buitelaar (NWO Large grant #1750102007010). Dr. Franke is supported by a Vici grant from NWO (grant # 016-130-669) and by the European Community's Seventh Framework Program (FP7) under grant agreement #278948 (TACTICS), the Innovative Medicines Initiative Joint Undertaking under grant agreement #115300 (EU-AIMS), resources of which are composed of financial contribution from the European Union's Seventh Framework Program (FP7/2007-2013) and the European Federation of Pharmaceutical Industries and Associations (EFPIA) companies' in kind contribution, and the European Community's Horizon 2020 Program grant #642996 (BRAINVIEW). Funding agencies had no role in study design, data collection, interpretation nor influence on writing.

Conflict of interest declaration

Waddington, Hartman, de Bruijn, Lappenschaar, Oerlemans and Rommelse have no conflict of interest to disclose. In the past 4 years Buitelaar has been a consultant to/member of advisory board of/and/or speaker for Janssen Cilag BV, Eli Lilly, Bristol-Myer Squibb, Organon/Shering Plough, UCB, Shire, Medice and Servier. Franke has received educational speaking fees from Merz and Shire.

Author contribution

FW, NR and BF were responsible for the study concept and design. AMO and YGdB contributed to the acquisition of data in BOA. FW performed the analyses. ML assisted with data analysis. NR assisted with the interpretation of findings. FW drafted the manuscript. NR, BF, JKB, CAH and AMO provided critical revision of the manuscript for important intellec-

tual content. All authors critically reviewed content and approved the final version for publication.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.euroneuro.2018.06.009](https://doi.org/10.1016/j.euroneuro.2018.06.009).

References

- Adolphs, R., 2001. The neurobiology of social cognition. *Curr. Opin. Neurobiol.* 11, 231-239.
- Adolphs, R., 2003. Cognitive neuroscience of human social behaviour. *Nat. Rev. Neurosci.*, 4, 165-178.
- Aspan, N., Bozsik, C., Gadoros, J., Nagy, P., Inantsy-Pap, J., Vida, P., Halasz, J., 2014. Emotion recognition pattern in adolescent boys with attention-deficit/hyperactivity disorder. *Biomed. Res. Int.* 1-8.
- Bal, E., Harden, E., Lamb, D., Van Hecke, A.V., Denver, J.W., Porges, S.W., 2010. Emotion recognition in children with autism spectrum disorders: relations to eye gaze and autonomic state. *J. Autism Dev. Disord.* 40, 358-370.
- Bänziger, T., Grandjean, D., Scherer, K.R., 2009. Emotion recognition from expressions in face, voice, and body: the Multimodal Emotion Recognition Test (MERT). *Emotion* 9, 691-704 (Washington, D.C.).
- Baribeau, D.A., Doyle-Thomas, K.A., Dupuis, A., Iaboni, A., Crosbie, J., McGinn, H., Nicolson, R., 2015. Examining and comparing social perception abilities across childhood-onset neurodevelopmental disorders. *J. Am. Acad. Child Adolesc. Psychiatry* 54, 479-486 e471.
- Bora, E., Pantelis, C., 2016. Meta-analysis of social cognition in attention-deficit/hyperactivity disorder (ADHD): comparison with healthy controls and autistic spectrum disorder. *Psychol. Med.* 46, 699-716.
- Casey, B.J., Oliveri, M.E., Insel, T., 2014. A neurodevelopmental perspective on the research domain criteria (RDoC) framework. *Biol. Psychiatry* 76, 350-353.
- Cattell, R., 2012. *The Scientific Use of Factor Analysis in Behavioral and Life Sciences*. Springer Science & Business Media.
- Chronaki, G., Garner, M., Hadwin, J.A., Thompson, M.J.J., Chin, C.Y., Sonuga-Barke, E.J.S., 2015. Emotion-recognition abilities and behavior problem dimensions in preschoolers: Evidence for a specific role for childhood hyperactivity. *Child Neuropsychol.* 21, 25-40.
- Collin, L., Bindra, J., Raju, M., Gillberg, C., Minnis, H., 2013. Facial emotion recognition in child psychiatry: a systematic review. *Res. Dev. Disabil.* 34, 1505-1520.
- Conners, C.K., 1997. *Conners' Parent Rating Scale-Revised (L)*. Multi-Health Systems North Tonawanda, NY.
- Diagnostic and Statistical Manual of Mental Disorders, 2000, Fourth edition American Psychiatric Association (APA) Washington.
- Diagnostic and Statistical Manual of Mental Disorders, 2013, Fifth edition American Psychiatric Association (APA) Washington.
- Da Fonseca, D., Seguier, V., Santos, A., Poinso, F., Deruelle, C., 2009. Emotion understanding in children with ADHD. *Child Psychiatry Hum. Dev.* 40, 111-121.
- Demurie, E., Roeyers, H., Baeyens, D., Sonuga-Barke, E., 2012. The effects of monetary and social rewards on task performance in children and adolescents: liking is not enough. *Int. J. Methods Psychiatric Res.* 21, 301-310.
- De Sonneville, L.M.J., 1999. Amsterdam neuropsychological tasks: a computer-aided assessment program. *Comput. Psychol.* 6, 187-203.

- De Sonnevile, L.M.J., Verschoor, C.A., Njokiktjen, C., Op het Veld, V., Toorenaar, N., Vranken, M., 2002. Facial identity and facial emotions: speed, accuracy, and processing strategies in children and adults. *J. Clin. Exp. Neuropsychol.* 24, 200-213.
- Demopoulos, C., Hopkins, J., Davis, A., 2013. A comparison of social cognitive profiles in children with autism spectrum disorders and attention-deficit/hyperactivity disorder: a matter of quantitative but not qualitative difference. *J. Autism Dev. Disord.* 43, 1157-1170.
- Gebauer, L., Skewes, J., Horlyck, L., Vuust, P., 2014. Atypical perception of affective prosody in Autism Spectrum Disorder. *Neuroimage Clin.* 6, 370-378.
- Gottesman, I.I., Gould, T.D., 2003. The endophenotype concept in psychiatry: etymology and strategic intentions. *Am. J. Psychiatry* 160, 636-645.
- Golan, O., Ashwin, E., Granader, Y., McClintock, S., Day, K., Leggett, V., Baron-Cohen, S., 2010. Enhancing emotion recognition in children with autism spectrum conditions: an intervention using animated vehicles with real emotional faces. *J. Autism Dev. Disorders* 40, 269-279.
- Greenbaum, R.L., Stevens, S.A., Nash, K., Koren, G., Rovet, J., 2009. Social cognitive and emotion processing abilities of children with fetal alcohol spectrum disorders: a comparison with attention deficit hyperactivity disorder. *Alcohol Clin. Exp. Res.* 33, 1656-1670.
- Harms, M.B., Martin, A., Wallace, G.L., 2010. Facial emotion recognition in autism spectrum disorders: a review of behavioral and neuroimaging studies. *Neuropsychol. Rev.* 20, 290-322.
- Hartman, C.A., Geurts, H.M., Franke, B., Buitelaar, J.K., Rommelse, N.N., 2016. Changing ASD-ADHD symptom co-occurrence across the lifespan with adolescence as crucial time window: illustrating the need to go beyond childhood. *Neurosci. Biobehav. Rev.* 71, 529-541.
- Insel, T., Cuthbert, B., Garvey, M., Heinssen, R., Pine, D.S., Quinn, K., Wang, P., 2010. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. *Am. J. Psychiatry* 167, 748-751.
- Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Ryan, N., 1997. Schedule for affective disorders and schizophrenia for school-age children present and lifetime version (K-SAD-S-PL): initial reliability and validity data. *J. Am. Acad. Child Adolesc. Psychiatry* 36, 980-988.
- Kuusikko, S., Haapsamo, H., Jansson-Verkasalo, E., Hurtig, T., Mattila, M.L., Ebeling, H., Moilanen, I., 2009. Emotion recognition in children and adolescents with autism spectrum disorders. *J. Autism Dev. Disord.* 39, 938-945.
- Le Couteur, A., Lord, C., Rutter, M., 2003. The autism diagnostic interview-revised (ADI-R). Western Psychological Services, Los Angeles, CA.
- Leung, R.C., Pang, E.W., Cassel, D., Brian, J.A., Smith, M.L., Taylor, M.J., 2015. Early neural activation during facial affect processing in adolescents with Autism Spectrum Disorder. *Neuroimage Clin.* 7, 203-212.
- Lichtenstein, P., Carlstrom, E., Rastam, M., Gillberg, C., Anckarsater, H., 2010. The genetics of autism spectrum disorders and related neuropsychiatric disorders in childhood. *Am. J. Psychiatry* 167, 1357-1363.
- Lozier, L.M., Vanmeter, J.W., Marsh, A.A., 2014. Impairments in facial affect recognition associated with autism spectrum disorders: a meta-analysis. *Dev. Psychopathol.* 26, 933-945.
- Mulder, M.J., Baeyens, D., Davidson, M.C., Casey, B.J., Van Den Ban, E., Van Engeland, H., Durston, S., 2008. Familial vulnerability to ADHD affects activity in the cerebellum in addition to the prefrontal systems. *J. Am. Acad. Child Adolesc. Psychiatry* 47, 68-75.
- Müller, U.C., Asherson, P., Banaschewski, T., Buitelaar, J.K., Ebstein, R.P., Eisenberg, J., Roeyers, H., 2011a. The impact of study design and diagnostic approach in a large multi-centre ADHD study. Part 1: ADHD symptom patterns. *BMC Psychiatry* 11, 54.
- Müller, U.C., Asherson, P., Banaschewski, T., Buitelaar, J.K., Ebstein, R.P., Eisenberg, J., Steinhausen, H.C., 2011b. The impact of study design and diagnostic approach in a large multi-centre ADHD study: part 2: Dimensional measures of psychopathology and intelligence. *BMC Psychiatry* 11, 55.
- Musser, E.D., Hawkey, E., Kachan-Liu, S.S., Lees, P., Roullet, J.B., Goddard, K., Nigg, J.T., 2014. Shared familial transmission of autism spectrum and attention-deficit/hyperactivity disorders. *J. Child Psychol. Psychiatry* 55, 819-827.
- Muthén, L.K., Muthén, B.O., 2010. 1998-2010 Mplus user's guide. Muthén and Muthén. Los Angeles, pp. 39-49.
- Neves Mde, C., Tremeau, F., Nicolato, R., Lauer, H., Romano-Silva, M.A., Correa, H., 2011. Facial emotion recognition deficits in relatives of children with autism are not associated with 5HTTLPR. *Rev. Bras. Psiquiatr.* 33, 261-267.
- Nijmeijer, J.S., Hoekstra, P.J., Minderaa, R.B., Buitelaar, J.K., Alting, M.E., Buschgens, C.J.M., Hartman, C.A., 2009. PDD Symptoms in ADHD, an Independent Familial Trait. *J. Abnorm. Child Psychol.* 37, 443-453.
- Njokiktjen, C., Verschoor, A., De Sonnevile, L., Huyser, C., het Veld, V.O., Toorenaar, N., 2001. Disordered recognition of facial identity and emotions in three Asperger type autists. *Eur. Child Adolesc. Psychiatry* 10, 79-90.
- Oerlemans, A.M., van der Meer, J.M.J., van Steijn, D.J., de Rutter, S.W., de Bruijn, Y.G.E., de Sonnevile, L.M.J., Rommelse, N.N.J., 2014. Recognition of facial emotion and affective prosody in children with ASD (plus ADHD) and their unaffected siblings. *Eur. Child Adolesc. Psychiatry* 23, 257-271.
- Rommelse, N.N.J., Alting, M.E., Oosterlaan, J., Buschgens, C.J.M., Buitelaar, J., Sergeant, J.A., 2008. Support for an independent familial segregation of executive and intelligence endophenotypes in ADHD families. *Psychol. Med.* 38, 1595-1606.
- Rommelse, N.N.J., Geurts, H.M., Franke, B., Buitelaar, J.K., Hartman, C.A., 2011. A review on cognitive and brain endophenotypes that may be common in autism spectrum disorder and attention-deficit/hyperactivity disorder and facilitate the search for pleiotropic genes. *Neurosci. Biobehav. Rev.* 35, 1363-1396.
- Rutter, M., Bailey, A., Lord, C., 2003. The social communication questionnaire: Manual. Western Psychological Services. Los Angeles.
- Schachar, R.J., Crosbie, J., Barr, C.L., Ornstein, T.J., Kennedy, J., Malone, M., Pathare, T., 2005. Inhibition of motor responses in siblings concordant and discordant for attention deficit hyperactivity disorder. *Am. J. Psychiatry* 162, 1076-1082.
- Sinzig, J., Morsch, D., Lehmkuhl, G., 2008. Do hyperactivity, impulsivity and inattention have an impact on the ability of facial affect recognition in children with autism and ADHD. *Eur. Child Adolesc. Psychiatry* 17, 63-72.
- Slaats-Willems, D., Swaab-Barneveld, H., De Sonnevile, L., Van Der Meulen, E., Buitelaar, J.A.N., 2003. Deficient response inhibition as a cognitive endophenotype of ADHD. *J. Am. Acad. Child Adolesc. Psychiatry* 42, 1242-1248.
- Spencer, M.D., Holt, R.J., Chura, L.R., Suckling, J., Calder, A.J., Bullmore, E.T., Baron-Cohen, S., 2011. A novel functional brain imaging endophenotype of autism: the neural response to facial expression of emotion. *Transl. Psychiatry* 1, e19.
- Taurines, R., Schwenck, C., Westerwald, E., Sachse, M., Siniatchkin, M., Freitag, C., 2012. ADHD and autism: differential diagnosis or overlapping traits? A selective review. *ADHD Atten. Def. Hyp. Disord* 4, 115-139.
- Taylor, E., Sandberg, S., Thorley, G., Giles, S., 1991. The Epidemiology of Childhood Hyperactivity. Oxford University Press, New York.
- Uekermann, J., Kraemer, M., Abdel-Hamid, M., Schimmelmann, B.G., Hebebrand, J., Daum, I., Kis, B., 2010. Social cognition in attention-deficit hyperactivity disorder (ADHD). *Neurosci. Biobehav. Rev.* 34, 734-743.

- Uljarevic, M., Hamilton, A., 2013. Recognition of emotions in autism: a formal meta-analysis. *J. Autism Dev. Disord.* 43, 1517-1526.
- van der Meer, J.M., Oerlemans, A.M., van Steijn, D.J., Lapenschaar, M.G., de Sonnevile, L.M., Buitelaar, J.K., Rommelse, N.N., 2012. Are autism spectrum disorder and attention-deficit/hyperactivity disorder different manifestations of one overarching disorder? Cognitive and symptom evidence from a clinical and population-based sample. *J. Am. Acad. Child Adolesc. Psychiatry* 51, 1160-1172 e1163.
- van Steijn, D.J., Richards, J.S., Oerlemans, A.M., de Ruiter, S.W., van Aken, M.A.G., Franke, B., Rommelse, N.N.J., 2012. The co-occurrence of autism spectrum disorder and attention-deficit/hyperactivity disorder symptoms in parents of children with ASD or ASD with ADHD. *J. Child Psychol. Psychiatry* 53, 954-963.
- Wallace, G.L., Case, L.K., Harms, M.B., Silvers, J.A., Kenworthy, L., Martin, A., 2011. Diminished SENSITIVITY TO SAD FACIAL EXPRESSIONS IN HIGH FUNCTIONING AUTISM SPECTRUM DISORDERS IS ASSOCIATED WITH SYMPTOMATOLOGY AND ADAPTIVE FUNCTIONING. *J. Autism Dev. Disord.* 41, 1475-1486.
- Wallace, S., Sebastian, C., Pellicano, E., Parr, J., Bailey, A., 2010. Face processing abilities in relatives of individuals with ASD. *Autism Res.* 3, 345-349.
- Wechsler, D., 2002. WISC-III Handleiding. The Psychological Corporation, London.
- Wechsler, D., 2005. WAIS-III-NL: Nederlandstalige bewerking: Technische handleiding (herziene uitgave). Pearson Assessment and Information BV, Amsterdam.
- Wehmeier, P.M., Schacht, A., Barkley, R.A., 2010. Social and emotional impairment in children and adolescents with ADHD and the impact on quality of life. *J. Adolesc. Health* 46, 209-217.
- Xavier, J., Vignaud, V., Ruggiero, R., Bodeau, N., Cohen, D., Chaby, L., 2015. A multidimensional approach to the study of emotion recognition in autism spectrum disorders. *Front Psychol.* 6, 1954.
- Yuill, N., Lyon, J., 2007. Selective difficulty in recognising facial expressions of emotion in boys with ADHD. *Eur. Child Adolesc. Psychiatry* 16, 398-404.