Attention and inhibition in children with ASD, ADHD and comorbid ASD+ADHD: an event-related potential study

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[ABSTRACT]

Background: Substantial overlap has been reported between attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). Deficits in executive function are characteristic of both disorders but these impairments have not been directly compared across pure and comorbid cases using event-related potentials (ERPs).

Methods: Behavioural parameters and ERPs were recorded during a flankered cued-continuous performance task (CPT-OX) administered to 8-13 year old boys with ASD (n=19), ADHD (n=18), comorbid ASD+ADHD (n=29) and typically developing (TD) controls (n=26). Preparatory processing (contingent negative variation; CNV) and attentional orienting (Cue-P3) at cues, response execution at targets (Go-P3), inhibitory processing at non-targets (NoGo-P3) and conflict monitoring between target and non-target trials (Go-N2 vs NoGo-N2) were examined.

Results: Categorical diagnoses and quantitative trait measures indicated that participants with ADHD (ADHD/ASD+ADHD) made more omission errors and exhibited increased reaction-time variability and reduced amplitude of the Cue-P3 and NoGo-P3, compared to TD/ASD participants. Participants with ASD (ASD/ASD+ADHD) demonstrated reduced N2 enhancement from Go to NoGo trials compared to TD/ADHD participants. Participants with ASD-only displayed enhanced CNV amplitude compared to ASD+ADHD and TD participants.

Conclusions: Children with ADHD show deficits in attentional orienting and inhibitory control, while children with ASD show abnormalities in conflict monitoring and response preparation. Children with comorbid ASD+ADHD present as an additive co-occurrence with deficits of both disorders, although non-additive effects are suggested for response preparation. Measuring ERPs that index attention and inhibition is useful in disentangling cognitive markers of ASD and ADHD and elucidating the basis of co-occurring ASD+ADHD to guide clinical assessment.
Background

Attention deficit hyperactivity disorder (ADHD) is a childhood disorder characterised by developmentally inappropriate and impairing levels of inattentiveness, hyperactivity and impulsivity (American Psychiatric Association, 2000), with prevalence in school-aged children around 5% (Polanczyk et al., 2007, Polanczyk and Jensen, 2008). Although current diagnostic criteria preclude a co-diagnosis (DSM-IV), epidemiological studies suggest comorbid ADHD symptomatology is demonstrated in 30% of children with autism spectrum disorder (ASD), a disorder characterised by abnormalities in social interaction, communication and restricted/repetitive behaviours (Simonoff et al., 2008). In addition, a substantial proportion of overlap between ADHD and ASD is attributable to shared genetic influences (Rommelse et al., 2009). It is under discussion whether this common co-occurrence reflects an additive comorbidity as supported in the upcoming DSM-V, rather than a separate condition with distinct impairments (Taurines et al., 2012). One approach to distinguish between the different comorbidity models is to evaluate underlying pathophysiological mechanisms associated with ASD and ADHD in the comorbid ASD+ADHD group.

One domain of shared impairment between ASD and ADHD is executive function (EF; Rommelse et al., 2011). Specifically, substantial overlap is evident for inhibition, verbal fluency and spatial working memory with subtle differences in severity between the disorders (Corbett et al., 2009, Geurts et al., 2004, Goldberg et al., 2005, Nyden et al., 1999, Ozonoff et al., 2004, Verte et al., 2006). Other studies, however, suggest the disorders can be dissociated on the basis of, for example, intact inhibitory control and more severe impairments in cognitive flexibility and planning in ASD (Geurts et al., 2004, Happé et al., 2006a, Ozonoff and Jensen, 1999, Verte et al., 2006). There are few and inconsistent findings from EF studies that include individuals with comorbid ASD+ADHD to delineate this phenotypic variability. Inhibitory deficits similar to ADHD have been reported for comorbid ASD+ADHD, while other studies demonstrate reduced cognitive flexibility compared to ASD (Bühler et al., 2011, Sinzig et al., 2008). Conversely, relatively intact performance (number of errors) on a continuous performance test (CPT) has been shown in ASD+ADHD compared to ADHD (Nyden et al., 2010), which suggests that these impairments are not necessarily an additive effect of the pure disorders.
Evidence for an inhibitory deficit in ADHD is supported by event-related potential (ERP) studies that allow sensitive measurement of distinct temporal stages in overt and covert cognitive processing (McLoughlin et al., 2005). Several studies have demonstrated, using a cued-CPT, a reduced fronto-central NoGo-P3 component in response to non-target stimuli as an index of response inhibition (Banaschewski et al., 2004, Doehnert et al., 2010, Fallgatter et al., 2004, Valko et al., 2009). Importantly, however, this deficit is typically preceded by attenuated electrophysiological responses to cues, as indexed by the parietal Cue-P3 and the subsequent central contingent negative variation (CNV; Albrecht et al., 2005, Banaschewski et al., 2003, Banaschewski et al., 2004, Brandeis et al., 2002, Doehnert et al., 2010, Valko et al., 2009, Van Leeuwen et al., 1998). Notably, the Cue-P3 and the CNV index covert processing since these deficits occur without concurrent responses or performance errors and predict subsequent performance (Banaschewski et al., 2003, Banaschewski et al., 2004, Van Leeuwen et al., 1998). In addition, N2 enhancement from Go to NoGo trials, an index of conflict monitoring (Yeung and Cohen, 2006), is reduced in ADHD during the Stop Signal Task (Pliszka et al., 2000), although case-control differences are not reported in the CPT-OX (Banaschewski et al., 2004, Fallgatter et al., 2004, Overtoom et al., 1998) unless ADHD has co-occurring oppositional defiant disorder (Overtoom et al., 1998). These impairments are seen in ADHD during childhood, adolescence (Doehnert et al., 2010, Spronk et al., 2008, Valko et al., 2009) and adulthood (McLoughlin et al., 2010). These parameters also share familial influences with ADHD in children (Albrecht et al., in press) and adults (McLoughlin et al., 2011), which combined with limited evidence of shared environmental effects on ADHD (Burt et al., 2012, Burt, 2009, Faraone et al., 2005, Wood et al., 2010) suggests that they are a marker of genetic risk in ADHD (Tye et al., 2011).

Despite consistent evidence for attention deficits in ASD (Sanders et al., 2008), there is limited neurophysiological research on these processes (Jeste and Nelson, 2009). In visual oddball tasks and variants thereof, which involve response to rare targets among frequently occurring stimuli, longer latencies of the P3 and N2, and larger amplitude of the P3 to target stimuli have been reported in ASD (Kemner et al., 1999, Sokhadze et al., 2009, Strandburg et al., 1993, Tsai et al., 2011). These findings may suggest inefficient categorization and processing of attentional stimuli. Nevertheless, the direction of effects is not consistent (Courchesne et al., 1989, Hoeksma et al., 2006, Pritchard et al., 1987, Townsend et al., 2001, Tsai et al., 2011, Verbaten et al., 1991) and null findings are also reported (Courchesne et al., 1989, Hoeksma et al., 2006, Pritchard et al., 1987, Tsai et al., 2011). In
addition, no ERP study has utilised a paradigm that directly measures attentional orienting and inhibitory control in ASD, and there has been no comparison of these attention processes at the neurophysiological level with comorbid ASD+ADHD cases.

Very few previous cognitive-electrophysiological studies of ASD and ADHD include either a comparison group of the other disorder or a separate comorbid group (although see e.g. Clarke et al., 2011, Groen et al., 2008), and many studies do not measure the possibility of co-occurring symptoms. Not only does this introduce ‘blurring’ of diagnostic groups, but also limits any conclusions being made about the nature of deficits in the comorbid group. In combination with the inconsistent findings on EF at the behavioural level, little is known about the mode of co-occurrence between ASD and ADHD at the neural level. The aim of this study was therefore to investigate whether ERP abnormalities associated with ADHD are also found in ASD and comorbid ASD+ADHD, following in-depth diagnostic assessments that minimise misspecification in group allocation. Due to the lack of previous studies that have investigated these constructs, this analysis is exploratory and thus limited hypotheses are made: (1) children with ADHD would demonstrated reduced inhibitory processing; (2) children with ASD would show reduced conflict monitoring (due to its close association with shifting strategy) and (3) children with ASD+ADHD would show both of these deficits, but would not necessarily present as an additive co-occurrence, based on the limited studies of all three conditions.

Methods and Materials

Sample

Nineteen participants with ASD, 18 with ADHD, 29 with ASD and ADHD, and 26 typically developing controls (TD) took part in the study. Only males were included in the study to reduce sample heterogeneity and due to the higher ratio of males diagnosed with ASD compared to females (Elsabbagh et al., 2012, Polanczyk et al., 2007). The age range was 8-13 years, with a mean overall age of 10.77 years (SD=1.80) and there was no significant difference in age between groups (Table 1). All participants were required to have an IQ>70, normal or corrected-to-normal vision, and not to be taking any medication except for stimulants, which had to be interrupted 48h prior to testing sessions. Within the sample, 6 participants with ADHD were taking medication (1 Equasym, 3 Concerta, 1 Equasym and Concerta, 1 unspecified) and 6 participants with ASD+ADHD were taking medication (5 Concerta, 1 dexamphetamine). Exclusion criteria included non-fluent English, specific
medical disorders, other comorbid psychiatric disorder (not including ODD), history of traumatic brain injury and a diagnosis of epilepsy.

The participants were recruited from out-patient neurodevelopmental clinics and local parent support groups in southeast London. All participants had a clinical diagnosis made according to ICD-10 criteria (autism, Aspergers syndrome, ADHD combined type) and then underwent systematic and rigorous clinical assessment to confirm pure or comorbid research diagnosis (Figure 1). All cases were initially evaluated with Conners 3rd Edition Parent Rating Scale short form (Conners, 2008) and Social Communication Questionnaire (SCQ) (Berument et al., 1999, Rutter et al., 2003). Cases of ASD were diagnosed using the Autism Diagnostic Interview−Revised (ADI−R) (Lord et al., 1994) using modified criteria (IMGSAC, 1998) and the Autism Diagnostic Observation Schedule (ADOS-G) (Gotham et al., 2007). Cases of ADHD were diagnosed using Parent Account of Childhood Symptoms (PACS) (Taylor et al., 1986), which has been extensively used by the IMAGE consortium (Chen et al., 2008). Co−morbid ASD+ADHD cases met full diagnostic criteria for ASD and full diagnostic criteria for ADHD using the ADI−R/ADOS-G and PACS. Questionnaire measures confirmed that participants with ASD+ADHD and ADHD had a higher number of ADHD symptoms and also lower full-scale IQ compared to both ASD and TD. Participants with ASD+ADHD followed by ASD had the highest number of autism symptoms, compared to ADHD and TD (see Table 1).

The TD group consisted of children recruited through local schools and forums. Children were not included if they had any psychiatric diagnosis and were assessed with the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997), SCQ and Conners’ questionnaires. Ten TD participants scored above threshold on the Conners’. Further assessment of 8 of these children with the PACS interview confirmed that these children did not reach a diagnosis of ADHD and thus were retained in the study.1 In addition, participants who had a sibling with a diagnosis of ASD and/or ADHD were not included. The study protocol was approved by a medical ethics committee. Written parental consent was given before the experiment began.

1 Although not reaching the diagnostic threshold, four of these subjects had a high score of above 5 on one or both domains of the PACS interview. It was not possible to conduct the PACS interview on the remaining two subjects who scored above threshold on the Conners. We therefore also applied a more stringent approach to control selection (excluding these 2 subjects who could not be contacted for PACS assessment and those scoring 5 or above on either domain of the PACS interview), which did not affect any of the results. We also conducted univariate analysis of variance (ANOVA) that confirmed these children did not differ from controls on any performance or ERP parameter. In addition, the retention of these control subjects in comparison of the 4 groups works against any hypotheses predicting changes in results and thus the inclusion of these subjects only strengthens the findings.
Tasks and stimuli

The cued-CPT (flanker version; (Doehnert et al., 2008, McLoughlin et al., 2010, McLoughlin et al., 2011, Valko et al., 2010) consists of a black letter array formed of a centre letter flanked on each side by distractor letters, presented in four identical blocks of 100 letter arrays each. Participants were instructed to ignore the distractor letters and attend only to the centre letter. There were 11 different centre letters (O, X, H, B, C, D, E, F, G, J and L) subtending approximately 0.5 degrees. Target centre letters ‘X’ and ‘O’ were flanked by the incompatible letter ‘O’ or ‘X’ and distractor letters were flanked by either ‘X’ or ‘O’. The letter arrays were presented briefly (150ms) every 1.65s in a pseudo-random sequence at the centre of a computer monitor at the viewing distance of 120cm. The 80 cues (XOX) initiated 40 cue-target (XOX-OXO) and 40 cue non-target sequences (XOX-XDX). In 40 cases, a distractor-X letter array (OXO) was not preceded by the cue and had to be ignored, as well as any other irrelevant letters. Participants were instructed to respond only to cue-target sequences (XOX-OXO) by pressing a button as quickly as possible with the index finger of their preferred hand (Table 1). The task was practised (24 trials including 3 cue-target and 2 cue-non target sequences) and comprehension ascertained based on correct performance prior to task onset. The duration of the task was 11 minutes. Participants were seated on a height-adjustable chair in a video-monitored testing cubicle. The flankered CPT-OX was administered after 6 minutes of resting EEG data recording as part of a larger test battery (not presented here) with a total duration of 70 minutes. Presentation of the tasks was ordered in the same way for each group to control for effects of practice and fatigue. IQ was assessed using four subtests of the Wechsler Abbreviated Scale of Intelligence (WASI; (Wechsler, 1999) (Block Design, Vocabulary, Matrix Reasoning and Similarities) and took 45 minutes to complete.

Cognitive performance

Performance measures in the flankered CPT-OX task included mean reaction time to target stimuli (MRT, mean latency of responding in ms after target onset), within-subject variability in reaction times (SD-RT, within-subject variability in RTs in milliseconds), and the coefficient of reaction time variability (CV, SD-RT/MRT), calculated across correctly answered target-OXOs that were detected between
200-1500msec post-stimulus. Errors were broken down into subcategories (omission errors, total commission errors, and O-not-X commission errors).

**Electrophysiological recording and analysis**

EEG was recorded using a 62 active electrode recording system (ActiCap, Brain Products, Munich, Germany; extended 10-20 montage). The recording reference electrode was positioned at FCz. Vertical and horizontal electrooculograms (EOGs) were simultaneously recorded from electrodes above and below the left eye and at the outer canthi. The signal was digitized at 500Hz sampling rate, stored and analyzed offline.

Data were analysed in Brain Vision Analyzer (2.0; Brain Products, Munich, Germany). The signal was re-referenced offline to the average reference and downsampled to 256Hz. We applied 0.1-30Hz (24dB/Oct) Butterworth filters. Ocular artifacts were removed from the data using biased infomax independent component analysis (Jung et al., 2000). The extracted independent components were manually inspected and ocular artifacts were removed by back-projection of all but those components. Remaining artifacts exceeding 200μV peak-to-peak in any channel were rejected from the data. Baseline correction was performed using a 200msec prestimulus reference period. Stimulus-locked epochs (peristimulus window from −200 to 1650 ms) were averaged for the following trial types: cue (trials to letter XOX); go (trials to OXOs preceded by XOX); no-go (trials to random target letters e.g., ODO following XOX). Averages contained at least 19 segments (Supplementary Material S1), only included trials with correct responses (Go) or correctly rejected trials (NoGo, Cue), and were free from residual artifacts.

ERP amplitudes were restricted to leads for which effects were expected to be largest, based on previous studies (Banaschewski et al., 2003, Banaschewski et al., 2004, Jonkman, 2006, Valko et al., 2009). The P3 was calculated as the mean amplitude in a 400-700msec latency window, because the activity within this time window occurred over a long period making it difficult to identify one peak, as has been done in previous similar studies (Groom et al., 2010). The Cue-P3 and Go-P3 were measured at Pz, and the NoGo-P3 was measured at Cz, Cpx and Pz due to increased anteriorisation with increasing age (Jonkman, 2006, Valko et al., 2009). This is supported by our topographical maps (Figure 3). The N2 was scored as the maximal negative peak at Fz between 170-400msec. The CNV was calculated as the mean area at Cz between 1300-1650msec. Due to potential effects of the CNV
on the baseline of subsequent ERPs (target and non-target stimuli), the ERP data were analysed with an additional longer baseline of -350ms, which did not change the results (data available upon request).

**Statistical analysis**

Six children were excluded from performance and ERP analysis on the basis of extreme omission errors (>70%, upper 5% of sample) indicating a lack of attention to task and/or poor understanding of task instructions that limited the number of segments for reliable ERP analysis (ADHD n=2; ASD+ADHD n=4). One TD participant was removed from analysis due to technical difficulties during recording and two additional ASD+ADHD participants were removed from the Go condition due to insufficient segments. Outliers were removed (±3.5 SD; n=1 ASD from CNV analysis). Clinical and demographic characteristics excluding these participants remained the same, although the difference in full scale IQ between ADHD (103) and ASD (117) became significant (p=.03; see below). Excluded participants were significantly younger (9.08 years) than included participants (10.92 years; p=.01) and had higher inattention symptom scores (t score=83 vs. 71, p=.03).

Errors and SD-RT were non-normally distributed (indicated by sktest command in Stata; Stata Corp, College Station, Texas) and were therefore square-root transformed (indicated by ladder command in Stata). The NoGo-P3 at the three scalp locations was entered into a MANOVA with Tamhane correction that caters for unequal variance. The N2 was entered into a repeated-measures ANOVA with condition (Go vs NoGo) as the within-subjects factor. For other performance and ERP measures (Cue-P3, Go-P3, CNV) the groups were compared for differences using separate univariate ANOVAs. Sidak correction was used to correct for multiple testing, unless otherwise stated. In order to evaluate the utility of this method to dissociate clinical groups and elucidate the basis of comorbidity, the between-subjects factor was defined in two ways: (1) a comparison of 4 groups of ASD-only, ADHD-only, ASD+ADHD and TD to assess differences between pure and comorbid groups; (2) 2x2 comparisons with ADHD (ADHD/ASD+ADHD) and ASD (ASD/ASD+ADHD) to examine the interaction between the disorders. A non-significant interaction between the disorders is compatible with an additive model.

Correlations between IQ and age and each of the dependent variables were calculated across the whole sample (and verified within each diagnostic group), due to differences in IQ between
groups and developmental effects on these parameters. When these correlations were significant, analyses of covariance (ANCOVAs) were conducted or for correlations age-corrected residuals were calculated to analyze whether group differences were influenced by IQ and/or age. Where significant group differences were found, correlations were calculated between ERP parameters and cognitive performance. A difference score calculated for the N2 ERP amplitude between Go and NoGo conditions and a calculated average across the three electrode locations for the NoGo-P3 ERP amplitude were entered into the correlation analysis. Main effects and interactions at a significance level of $p < .05$ (two-tailed) and trends ($p<.1$) were followed up with further analysis.

**Results**

**CPT performance**

The CPT performance data are summarized by group in Table 2 and Table 3. IQ had no significant effects on performance measures (all $p>.5$). Age was a significant covariate for MRT, SD-RT and omission errors and therefore was retained in these analyses. There was a significant effect of group on the number of omission errors [$F (3, 80) =2.89, p=.04$]. Post-hoc analyses revealed significantly higher number of errors made by ASD+ADHD participants ($p=.04$, $d=0.81$). Significant main effects of group were found on CV [$F (3, 81) =3.26, p=.03$] and post-hoc analyses revealed that the ADHD-only group had more variable reaction times than the TD group ($p=.03$, $d=0.80$). No significant effects were found for MRT, SD-RT, commission errors or O-not-X commission errors (all $p>.1$).

Combining participants with ADHD diagnosis (ADHD-only and ASD+ADHD) revealed increased variability as indexed by SD-RT [$F (1, 80) =4.31, p=.04, d=0.59$], and CV [$F (1, 81) =6.06, p=.02, d=0.53$] and more omission errors [$F (1, 80) =6.54, p=.01, d=0.55$], compared to participants with no ADHD symptoms (ASD-only and TD). Comparisons of participants with ASD diagnosis (ASD-only and ASD+ADHD) and without ASD diagnosis (ADHD-only and TD) were not significantly different on any performance measures (all $p>.05$). The interaction between ADHD and ASD was non-significant for SD-RT [$F (1, 80) =0.55, p=.46$] and omission errors [$F (1, 80) =0.38, p=.54$], suggesting additive effects. There was, however, a trend towards an interaction for CV [$F (1, 81) =3.34, p=.07$].

[TABLE 2: Descriptive Data for Behavioural Measures and ERP Amplitudes]

[TABLE 3: Summary of Main Behavioural and ERP findings for TD versus each clinical group]
**ERP parameters**

The ERP data is summarised by group in Table 2 and Table 3. Age and IQ were not significant as covariates for any of the ERP measures (all *p* > 0.5). Noted correlations between ERP parameters and behavioural measures across the whole sample are shown in Table 4.

**Cue-P3**

ERP grand averages and maps of all four groups are illustrated in Figure 2. A significant main effect of group on amplitude of the Cue-P3 emerged \([F(3, 81) = 4.79, p = .004]\). Post-hoc analyses indicated attenuated Cue-P3 in ASD+ADHD \((p = .002, d = 1.16)\) compared to the TD group. Participants with ADHD diagnosis (ADHD/ASD+ADHD) \([F(1, 81) = 7.81, p = .01, d = 0.68]\) were driving the attenuation of the Cue-P3 with a trend for participants with ASD diagnosis (ASD/ASD+ADHD) \([F(1, 81) = 3.71, p = .06, d = 0.52]\). The interaction between ADHD and ASD was non-significant suggesting additive effects \([F(1, 81) = 0.52, p = .48]\). Across the whole sample, the Cue-P3 amplitude was associated with ADHD symptoms \((r = -.19, p = .07;\) Hyperactivity-Impulsivity: \(r = -.23, p = .03)\) and not ASD symptoms \((r = -.15, p = .18)\). Attenuated Cue-P3 was correlated with poor task performance \((SD\text{-}RT: r = -.25, p = .02; CV: r = -.29, p = .01;\) omission errors: \(r = -.36, p = .001)\) and attenuated NoGo-P3 \((r = .50, p < .001)\).

**Go-P3**

There was no main effect of group on the amplitude of the Go-P3 \([F(3, 79) = 1.91, p = .13]\). When combined by the presence of ADHD diagnosis there was a trend towards attenuated Go-P3 amplitude \([F(1, 79) = 3.68, p = .06, d = 0.47]\), which was not shown when combined by ASD diagnosis \([F(1, 79) = 1.14, p = .29, d = 0.31]\). There was no significant interaction between ASD and ADHD \([F(1, 79) = 0.10, p = .75]\).

**NoGo-P3**

ERP grand averages and maps of all four groups are illustrated in Figure 3. A significant multivariate effect on group emerged for the NoGo-P3 \([F(9, 237) = 2.19, p = .02;\) Pillai’s trace = .23]. Univariate testing indicated a significant effect of group at CPz using a Bonferroni adjusted alpha level of .017 \([F
Post-hoc analyses revealed the ASD+ADHD group displayed significantly attenuated NoGo-P3 at CPz compared to TD (p=.01, d=1.04) with a trend compared to ASD-only participants (p=.08, d=0.86). When combined by ADHD diagnosis (ADHD/ ASD+ADHD), a multivariate effect of group emerged [F (3,77) =4.35, p=.02, d=0.69; Pillai’s trace=.14], indicating significantly attenuated NoGo-P3 in ADHD/ASD+ADHD. Univariate analyses revealed reduced amplitude at each scalp location, reaching Bonferroni-corrected significance at CPz [F (1,79) =12.82, p=.001, d=0.79] and uncorrected significance at Cz [F (1,79) =5.15, p=.02, d=.053] and Pz [F (1, 79) =5.88, p=.03, d=0.52] compared to participants without ADHD (TD/ASD). There was no effect of the presence of ASD diagnosis (ASD/ASD+ADHD; all p>.05), supported by correlations with symptom scores (Inattention: r=-.23, p=.03; Hyperactivity-Impulsivity: r=-.25, p=.02; SCQ: r=-.01, p=.93). There was no significant interaction between ASD and ADHD suggesting additive effects [F (3, 77) =1.08, p=.36]. The amplitude of the NoGo-P3 was associated with response variability (SD-RT: r=-.29, p=.01; CV: r=-.23, p=.03).

N2

A main effect of condition emerged showing enhanced amplitude in the NoGo condition [F (1, 79) =7.66, p=.01]. A main effect of group on N2 amplitude across both conditions emerged [F (3, 79) =5.83, p=.001], with post-hoc analyses revealing the N2 was significantly attenuated in the ASD+ADHD group compared to the TD group (p=.001, d=1.12) and the ASD-only group (p=.04, d=0.90). When grouped according to symptoms, both ADHD diagnosis (ADHD/ASD+ADHD: F (1, 79) =11.25, p=.001, d=0.73) and a trend for ASD diagnosis (ASD/ASD+ADHD: F (1, 79) =3.55, p=.06, d=0.46) were associated with reduced N2 amplitude.

A significant interaction between group and condition emerged [F (3, 79) =3.69, p=.02]. Post-hoc analyses revealed that compared to TD participants with ASD-only demonstrated significantly reduced N2 amplitude enhancement in the NoGo condition (p=.02, d=0.80), with a trend emerging for ASD+ADHD participants (p=.08, d=0.73). An ASD diagnosis (ASD/ASD+ADHD) appeared to account for this deficit [F (1, 79) =4.51, p=.04, d=0.53] and there was no effect of ADHD diagnosis (ADHD/ASD+ADHD: F (1, 79) =1.27, p=.26, d=0.30), supported by correlations with symptom scores (Inattention: r=-.00, p=.99; Hyperactivity: r=.11, p=.34; SCQ: r=.24, p=.03). There was a trend towards
an interaction between ASD and ADHD and condition $[F (1, 79) = 3.89, p = .05]$. N2 amplitude enhancement was associated with response variability on the task (CV: $r = -.23$, $p = .04$).

**CNV**

ERP grand averages and maps of all four groups are illustrated in Figure 3. Analyses indicated a significant main effect of group on amplitude of the CNV $[F (3, 80) = 4.10, p = .01]$. Post-hoc analyses revealed that participants with ASD-only had significantly greater amplitude compared to the TD group ($p = .04$, $d = .083$) and the ASD+ADHD group ($p = .01$, $d = .90$). When combining the groups by the presence of ASD (ASD/ASD+ADHD) or ADHD (ADHD/ASD+ADHD) there were no significant group differences ($p > .1$), suggesting an enhanced CNV is specific to ASD-only. The interaction term between ASD and ADHD was significant suggesting non-additive effects $[F (1, 80) = 10.11, p = .002]$. In order to examine the potential contribution of developmental effects to this finding, we ran the analyses excluding the youngest third of participants (age < 9.82), revealing a trend level effect of group on CNV amplitude $[F (3, 54) = 2.37, p = .08]$, with no significant post-hoc differences between groups. Enhanced amplitude of the CNV was associated with enhanced NoGo-P3 amplitude ($r = -.27$, $p = .01$) and reduced response variability on the task (SD-RT: $r = .24$, $p = .03$).

**Discussion**

This novel study investigated (1) differences in the neurophysiological correlates of attention and inhibition in strictly-defined cases of ASD and ADHD and (2) whether these markers were shared or distinct in comorbid ASD+ADHD, using an ERP paradigm that has been used in previous studies of ADHD. Findings from group differences for diagnostic status and correlations between quantitative
trait measures converge to suggest unique deficits across the two disorders. For the majority of findings, children with comorbid ASD+ADHD display deficits of both disorders suggestive of an additive co-occurrence, rather than a separate condition with a distinct pattern of deficits.

The attenuation of the NoGo-P3 in both ADHD groups supports previous studies that indicate abnormal inhibitory processing in children with ADHD (Banaschewski et al., 2004, Doehnert et al., 2010, Fallgatter et al., 2004, Valko et al., 2009). Notably, these deficits were demonstrated in ADHD and not in ASD, which is in line with previous cognitive research (Bühler et al., 2011, Happé et al., 2006b). In addition, both ADHD groups displayed reduced amplitude of the Cue-P3, in agreement with previous studies (Banaschewski et al., 2003, Banaschewski et al., 2004, Doehnert et al., 2010, Van Leeuwen et al., 1998). The non-significant effect for ASD-only and ASD-related symptoms implies attentional orienting impairments may be specific to ADHD, which may suggest reported deficits in attentional orienting in ASD are due to undetected ADHD symptoms (Sanders et al., 2008, Tsai et al., 2011). The trend for reduced Cue-P3 in the ASD groups suggests, however, that attentional orienting might be impaired in ASD in a larger sample. Given that the Cue-P3 also correlated with poor task performance associated with ADHD, this finding may indicate less effective recruitment of cognitive resources to process subsequent stimuli, and suggests behavioural impairments are temporally or causally preceded by neuronal deficits in covert processes (Spronk et al., 2008).

Attenuated N2 amplitude across both conditions was found in children with ASD+ADHD, suggesting this group displays the most severe abnormalities. Reduced or absent N2 amplitude enhancement from Go to NoGo trials was only found in the ASD groups. This complements previous work in ASD reporting problems in shifting from one response to another (Hill, 2004, Sanders et al., 2008). The intact N2 amplitude enhancement in ADHD is in line with previous studies using the CPT-OX that did not find case-control differences (Banaschewski et al., 2004, Fallgatter et al., 2004, Overtoom et al., 1998). Differences have been found in other more demanding tasks, such as the Stop task (Albrecht et al., 2005) and the Eriksen flanker task (Albrecht et al., 2008, McLoughlin et al., 2009), which may suggest that reduced N2 in ADHD is task-dependent. These findings suggest impaired conflict monitoring is related to ASD symptoms and as children with ASD-only appear to present with the greatest deficits, investigation of a continuum of ASD severity increasing with impairment is warranted in this domain.
Children with ASD-only had enhanced CNV amplitude compared to TD and ASD+ADHD children. This may indicate that children with ASD+ADHD have impaired preparatory processes compared to ASD-only children, and further that ASD-only children allocate more cognitive resources to prepare for the upcoming stimulus compared to ASD+ADHD and TD children. This is supported by associations between the CNV and the NoGo-P3, suggestive of a compensatory strategy or alternative mechanism to strengthen typical inhibitory control that is present in the ASD-only group (O’Hearn et al., 2008). This finding also points toward syndrome-specific abnormalities in pure and complex cases of ASD. The lack of significant abnormality in ADHD-only participants is inconsistent with previous work (Banaschewski et al., 2004, Valko et al., 2009) although not all have reported differences (Van Leeuwen et al., 1998). This may be due to developmental changes in the CNV (Klein and Feige, 2005); studies of ADHD show an enhanced late CNV in occipital regions at 5-7 years of age (Spronk et al., 2008) with a trend reported at 6-12 years (Hennighausen et al., 2000). The non-significant finding may therefore be due to varying stages of development in the sample, as supported by additional analyses revealing limited group effects when excluding younger participants.

In support of previous research using the same task, there was limited evidence of impaired response execution processes as indexed by the Go-P3 (Banaschewski et al., 2004, Van Leeuwen et al., 1998). As these impairments in target detection are more apparent in slow conditions (Wiersema et al., 2006), this might suggest these deficits in ADHD are related to suboptimal arousal, and further that they can be reduced by valid cues as used in the present task (McLoughlin et al., 2010), which may also explain typical Go-P3 amplitude in ASD contrary to some previous work (Townsend et al., 2001).

Task performance was impaired in both ADHD groups, shown by increased response variability and reduced accuracy, supporting previous findings (Klein et al., 2006, Kuntsi et al., 2010, Willcutt et al., 2005), and suggesting increased variability is not shown in ASD (Johnson et al., 2007). The lack of further group differences in performance is likely to be due to the use of the flanker version of the CPT-OX which was not specifically designed to optimally measure task performance. The larger effect sizes for neurophysiological markers in comparison to task performance highlight the greater sensitivity of ERP measures to detect differences in inhibitory measures between diagnostic groups.
Taken together, the findings indicate neurophysiological abnormalities in response preparation and conflict monitoring in ASD, which is in line with theoretical accounts that propose children with ASD have behavioural difficulties in the ability to flexibly shift to different cognitive demands (Hill, 2004) and disengage attention ("sticky attention"; e.g. (Holmboe et al., 2010)). Children with ADHD display neurophysiological abnormalities in attentional orienting, inhibitory processing and behavioural deficits in task performance, suggestive of specific deficits compared to ASD as well as widespread attentional dyscontrol. According to cognitive energetic models suboptimal arousal may be the basis of these varied deficits, due to problems in cognitive resource allocation to activation and arousal systems (Sergeant, 2000). The findings provide insight into the pathophysiological basis of the comorbidity between ADHD and ASD and are generally compatible with an additive co-occurrence demonstrating deficits of both disorders, supporting findings from twin studies (Ronald et al., 2008). This is of particular interest as the association between ASD and ADHD traits is proposed to be the result of genetic overlap with attention problems (Polderman et al., in press). Because the deficits are most apparent in the comorbid group for inhibitory processing and attentional orienting, the specificity of ADHD correlates may be dependent on the presence or absence of comorbid disorders. Nevertheless, the significant interaction between ASD and ADHD on CNV amplitude as well as on response variability as indexed by the CV suggests non-additive effects and the conceptualization of the comorbid condition as a distinct condition. An examination of face and gaze processing deficits in the same sample, however, demonstrates gaze processing abnormalities in the ASD and comorbid group that were not shown in the ADHD group, supporting an additive model (Tye et al., in press). The highly heterogeneous nature of all clinical groups is likely to give rise to various models of comorbidity across domains and tasks.

Certain limitations should be taken into consideration. The relatively small sample size poses difficulties in the interpretation of the data due to low power and may lead to ambiguous conclusions. In particular, considering the lack of significant differences between ASD-only and ADHD-only when analysed in the four group design, replication is warranted. Higher ASD symptom scores were demonstrated in the ASD+ADHD group, which may indicate exacerbation of autistic traits with comorbid ADHD, in line with other findings (e.g. Yerys et al. 2009). Alternatively, inflation of ASD scores by less obvious features in the defining features of the disorders, such as idiosyncratic attention-inattention patterns in ASD or peer rejection in ADHD, may occur (Clark et al., 1999). The
presence of subthreshold symptoms of ADHD in a few of the controls, and of other disorders associated with impaired inhibitory processing, such as conduct disorder in the diagnostic groups, may influence group results (Banaschewski et al., 2004). As findings of EF deficits across ADHD and ASD is somewhat dependent on the task used (Sergeant et al., 2002), it may be the case that inhibitory deficits are displayed in ASD in different tasks or age groups. Similarly, it may be argued that this task taps into response selection processes and interference control rather than response inhibition per se, which should be explicitly tested using alternative tasks. In addition, the exclusion of participants due to poor performance and subsequent insufficient trials may reflect task difficulty, particularly for younger and less attentive participants, and potential floor effects; the pathophysiological correlates of this poor performance would be of interest. Although arguably the stringent criteria applied throughout recruitment and analyses limit generalisability to clinic patients, they have the significant advantage of reducing heterogeneity and helping to define objective markers of the disorders, which is necessary for advancing understanding of these disorders. In addition, these findings broaden previous work to suggest that certain neurophysiological abnormalities are associated with differential symptomatology, on the basis that findings extend from diagnostic group analyses to quantitative symptom measures. While we have proposed shared and distinct markers, these processes do not necessarily have distinct neuroanatomical or biological underpinnings, and as such further work investigating the underlying mechanisms is required.

This is the first study to directly investigate whether ERP correlates of attention are similar or unique in children with ASD, ADHD and ASD+ADHD using the same test paradigm across groups. The findings imply that there may be specific neuronal abnormalities in attention for ASD and ADHD, and suggest an additive model of ASD+ADHD. This complements and extends cognitive findings and suggests previous inconsistent findings in the literature may be due to misspecification in group allocation. Along with accumulating evidence of co-occurring ADHD and ASD, this supports the adoption of a broader view of psychopathology when assessing underlying pathophysiology. Efforts to further define these disorders may help refine classification systems and enhance the assessment of these complex cases for more specific treatment strategies (Banaschewski and Brandeis, 2007). Disentangling behavioural variation in executive function is also likely to aid the identification of shared or disorder-specific susceptibility genes and other causal mechanisms underlying the complex aetiology of ASD and ADHD.
Acknowledgements

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References


[FIGURE LEGENDS]

Figure 1: Flowchart showing assessment of clinical groups for research diagnostic group allocation

TD, typically developing controls; ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity disorder; ASD+ADHD, comorbid ASD and ADHD; ADI-R, Autism Diagnostic Interview-Revised; ADOS-G, Autism Diagnostic Observation Schedule; Conners, Conners 3rd Edition Parent Rating Scale Short Form; PACS, Parental Account of Childhood Symptoms.

a ADI-R cut-off: Impairment of Social Interaction = 10; Impairment of Communication = 8; Stereotyped Behaviour = 3; participants may fall one point below the threshold in one of the behavioural domains according to modified criteria

b ADOS-G cut-off: Social Affect and RRBI = 7

Figure 2: Grand mean ERPs to Cue stimuli for each group and isocontour maps derived for the grand-average in the 400-700ms window for Cue-P3 and 1300-1650ms window for CNV for each group, plus t-maps for the group comparison. Black represents TD, red represents ASD-only; blue represents ADHD-only; green represents comorbid ASD+ADHD.

Figure 3: Grand mean ERPs to NoGo stimuli for each group and isocontour maps derived for the grand-average in the 400-700ms window for NoGo-P3 for each group, plus t-maps for the group comparison. Black represents TD, red represents ASD-only; blue represents ADHD-only; green represents ASD+ADHD.
### Table 1: Clinical and Demographic Characteristics

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>TD (n = 26)</th>
<th>ASD (n = 19)</th>
<th>ADHD (n = 18)</th>
<th>ASD+ADHD (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Age</td>
<td>10.56</td>
<td>1.79</td>
<td>11.69</td>
<td>1.70</td>
</tr>
<tr>
<td>Right-handed (%)</td>
<td>23</td>
<td>88%</td>
<td>18</td>
<td>95%</td>
</tr>
<tr>
<td>Verbal IQ</td>
<td>120.00</td>
<td>14.40</td>
<td>113.79</td>
<td>23.87</td>
</tr>
<tr>
<td>Performance IQ</td>
<td>115.73</td>
<td>13.89</td>
<td>111.05</td>
<td>13.31</td>
</tr>
<tr>
<td>Full-scale IQ</td>
<td>120.04</td>
<td>13.42</td>
<td>115.68</td>
<td>15.73</td>
</tr>
<tr>
<td>SCQ</td>
<td>3.88</td>
<td>3.54</td>
<td>20.11</td>
<td>6.42</td>
</tr>
<tr>
<td>Conners DSM-Inattentive</td>
<td>56.08</td>
<td>11.05</td>
<td>67.11</td>
<td>14.13</td>
</tr>
<tr>
<td>Conners DSM-Hyperactive</td>
<td>58.88</td>
<td>17.02</td>
<td>66.11</td>
<td>12.99</td>
</tr>
</tbody>
</table>

TD, typically developing controls; ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity disorder; ASD+ADHD, comorbid ASD and ADHD; Conners, Conners Third Edition Parent Rating Scale Short Form; DSM, Diagnostic and Statistical Manual of Mental Health Disorders; IQ, intelligence quotient; SCQ, Social Communication Questionnaire.

n.s.d. = non-significant
Table 2: Descriptive Data for Behavioral Measures and ERP Amplitudes

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>TD</th>
<th>ASD</th>
<th>ADHD</th>
<th>ASD+ADHD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 25)</td>
<td>(n = 19)</td>
<td>(n = 16)</td>
<td>(n = 25)</td>
</tr>
<tr>
<td>MRT</td>
<td>485.88 ± 114.15</td>
<td>443.68 ± 69.79</td>
<td>465.56 ± 75.95</td>
<td>494.48 ± 96.05</td>
</tr>
<tr>
<td>SD-RT</td>
<td>137.24 ± 57.31</td>
<td>139.37 ± 34.56</td>
<td>161.56 ± 55.10</td>
<td>160.68 ± 47.87</td>
</tr>
<tr>
<td>CV</td>
<td>0.28 ± 0.07</td>
<td>0.31 ± 0.05</td>
<td>0.34 ± 0.07</td>
<td>0.32 ± 0.06</td>
</tr>
<tr>
<td>Total commission errors</td>
<td>3.96 ± 3.78</td>
<td>4.54 ± 4.30</td>
<td>5.40 ± 8.04</td>
<td>6.88 ± 8.31</td>
</tr>
<tr>
<td>O-not-X commission errors</td>
<td>2.09 ± 2.68</td>
<td>2.23 ± 2.72</td>
<td>1.09 ± 0.85</td>
<td>2.12 ± 4.37</td>
</tr>
<tr>
<td>Omission errors</td>
<td>2.08 ± 2.41</td>
<td>3.16 ± 3.35</td>
<td>4.19 ± 3.04</td>
<td>4.84 ± 3.95</td>
</tr>
<tr>
<td>Cue P3 (area μV at Pz)</td>
<td>9.46 ± 3.56</td>
<td>7.39 ± 4.54</td>
<td>6.72 ± 3.20</td>
<td>5.77 ± 2.76</td>
</tr>
<tr>
<td>CNV (area μV at Cz)</td>
<td>-1.63 ± 3.69</td>
<td>-4.99 ± 6.44</td>
<td>-3.29 ± 3.01</td>
<td>-1.37 ± 4.12</td>
</tr>
<tr>
<td>Go P3 (area μV at Pz)</td>
<td>13.11 ± 6.08</td>
<td>11.21 ± 7.39</td>
<td>10.04 ± 5.28</td>
<td>9.01 ± 5.69</td>
</tr>
<tr>
<td>N2 (peak μV at Fz)</td>
<td>-6.88 ± 4.45</td>
<td>-7.41 ± 5.70</td>
<td>-5.68 ± 4.19</td>
<td>-3.60 ± 3.85</td>
</tr>
<tr>
<td>NoGo P3 (area μV at Cz)</td>
<td>6.82 ± 4.44</td>
<td>6.81 ± 5.64</td>
<td>4.13 ± 2.33</td>
<td>4.95 ± 3.68</td>
</tr>
<tr>
<td>P3 (area μV at Cpz)</td>
<td>7.47 ± 4.63</td>
<td>7.12 ± 4.95</td>
<td>5.17 ± 2.95</td>
<td>3.80 ± 2.16</td>
</tr>
<tr>
<td>P3 (area μV at Pz)</td>
<td>6.96 ± 5.32</td>
<td>5.91 ± 3.00</td>
<td>4.85 ± 3.94</td>
<td>4.22 ± 2.96</td>
</tr>
<tr>
<td>N2 (peak μV at Fz)</td>
<td>-10.28 ± 4.73</td>
<td>-7.32 ± 4.78</td>
<td>-6.44 ± 4.52</td>
<td>-4.69 ± 3.44</td>
</tr>
</tbody>
</table>

TD, typically developing controls; ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity disorder; ASD+ADHD, comorbid ASD and ADHD; ERP, event-related potential; MRT, mean reaction time; SD-RT, within-subject variability in RTs in milliseconds; CV: coefficient of variation (SD-RT/MRT).
Table 3: Summary of Main Behavioural and ERP findings for TD versus each clinical group (Cohen’s $d$, direction of effect shown for significant and/or large effect sizes)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>ASD (n=19)</th>
<th>ADHD (n=16)</th>
<th>ASD+ADHD (n=25)</th>
<th>ASD/ASD+ADHD (n=44)</th>
<th>ADHD/ASD+ADHD (n=41)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SD-RT</td>
<td>0.33</td>
<td>0.58</td>
<td>0.58</td>
<td>0.25</td>
<td>0.46*</td>
</tr>
<tr>
<td>CV</td>
<td>0.54</td>
<td>0.80*</td>
<td>0.66</td>
<td>0.19</td>
<td>0.53*</td>
</tr>
<tr>
<td>Omission errors</td>
<td>0.42</td>
<td>0.65</td>
<td>0.81*</td>
<td>0.38†</td>
<td>0.55**</td>
</tr>
<tr>
<td>Cue-P3</td>
<td>0.51</td>
<td>0.81</td>
<td>1.16**</td>
<td>0.52†</td>
<td>0.69**</td>
</tr>
<tr>
<td>NoGo-P3 a</td>
<td>0.11</td>
<td>0.65</td>
<td>0.76*</td>
<td>0.23</td>
<td>0.69**</td>
</tr>
<tr>
<td>Go-NoGo-N2</td>
<td>0.80*</td>
<td>0.74</td>
<td>0.73†</td>
<td>0.53*</td>
<td>0.31</td>
</tr>
<tr>
<td>CNV</td>
<td>0.83*</td>
<td>0.49</td>
<td>0.13</td>
<td>0.11</td>
<td>0.26</td>
</tr>
</tbody>
</table>

ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity disorder; ASD+ADHD, comorbid ASD and ADHD; CNV, contingent negative variation; CV: coefficient of variation (SD-RT/MRT); ERP, event-related potential; SD-RT, within-subject variability in RTs in milliseconds.

Medium effect sizes in italics (d=0.5), large effect sizes in bold (d=0.8).

a Calculated average for three scalp locations Cz, CPz and Pz.
**Table 4:** Correlations between ERP parameters, symptom scores and performance measures across the whole sample \(^ {a, b}\)

<table>
<thead>
<tr>
<th>ERP parameters</th>
<th>Cue-P3</th>
<th>NoGo-P3</th>
<th>Go-N2 – NoGo-N2</th>
<th>CNV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cue-P3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NoGo-P3</td>
<td></td>
<td>.44**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Go-N2 – NoGo-N2</td>
<td></td>
<td>.07</td>
<td>.05</td>
<td></td>
</tr>
<tr>
<td>CNV</td>
<td></td>
<td>-.08</td>
<td>-.27*</td>
<td>-.07</td>
</tr>
<tr>
<td>Parent-rated symptom scores (^c)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCQ</td>
<td>-.15</td>
<td>-.01</td>
<td>-.24*</td>
<td>.00</td>
</tr>
<tr>
<td>Conners DSM-Inattentive</td>
<td>-.19(^f)</td>
<td>-.23*</td>
<td>-.00</td>
<td>-.09</td>
</tr>
<tr>
<td>Conners DSM-Hyperactive</td>
<td>-.22*</td>
<td>-.25*</td>
<td>.11</td>
<td>.11</td>
</tr>
<tr>
<td>Performance measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Omission errors</td>
<td>-.36**</td>
<td>-.13</td>
<td>-.06</td>
<td>.04</td>
</tr>
<tr>
<td>SD-RT</td>
<td>-.25*</td>
<td>-.29**</td>
<td>-.12</td>
<td>.24*</td>
</tr>
<tr>
<td>CV</td>
<td>-.29**</td>
<td>-.23*</td>
<td>-.23*</td>
<td>.11</td>
</tr>
</tbody>
</table>

\(^{**}\) p<.01 \(^*\) p<.05 \(^\dagger\) p<.10

Conners, Conners Third Edition Parent Rating Scale Short Form; CNV, contingent negative variation; CV: coefficient of variation (SD-RT/MRT); ERP, event-related potential; SCQ, Social Communication Questionnaire; SD-RT, within-subject variability in RTs in milliseconds.

\(^a\) Spearman’s correlations performed only on ERP parameters showing significant group differences.

\(^b\) See Supplementary Material S2 for correlations by group.

\(^c\) Partial correlations between rating scale measures and ERP parameters were conducted to control for the effect of measures that are correlated with both ASD and ADHD, due to correlations between scores on the SCQ and Conners rating scales (SCQ-Conners Inattention: r=.41, p<.001; SCQ-Conners Hyperactivity-Impulsivity: r=.46, p<.001)
Fig. 2: Cue-P3

Amplitude (µV)

Time

0 200 400 600 800 1000 1200 1400 1600

Pz

0

+10

-10

Cz

Amplitude (µV)

0

+10

-10

Time

0 200 400 600 800 1000 1200 1400 1600

0

+10

-10

TD vs ASD

TD vs ADHD

TD vs ASD+ADHD

t-maps

TD vs ASD

TD vs ADHD

TD vs ASD+ADHD

TD

ASD

ADHD

ASD+ADHD

CNV