Reward and Punishment Sensitivity are Associated with Cross-disorder Traits

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ABSTRACT

Reward and punishment sensitivity are associated with cross-disorder traits, including attention deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), and callous-unemotional traits (CU). Reversal learning deficits following reward and punishment processing are observed across disruptive behaviors. These impairments are linked to altered reinforcement sensitivities and perseverative behavior that are characteristic of these disorders. Understanding how these sensitivities are associated with cross-disorder traits may help in the development of targeted interventions for these complex conditions.
Reversal learning deficits based on altered reward sensitivity are hallmarks of disruptive behavior (DB) and attention-deficit/hyperactivity disorder (ADHD) (Blair, Leibenluft, & Pine, 2014). However, it remains unknown to what extent these altered reinforcement sensitivities are linked to the co-occurrence of oppositional behavior, ADHD symptomatology, and/or the presence of callous-unemotional (CU) traits. Additionally, literature on punishment sensitivity is limited. Reversal learning is a form of conditional associative learning in which individuals are required to adapt their behavior according to changes in stimulus-reward contingencies (Cools, Clark, Owen, & Robbins, 2002). Altered reinforcement sensitivity can lead to insufficient learning, resulting in behavior that cannot be adequately adjusted to changing environmental contingencies (Barkley, 1997). Most studies assessing reversal learning have used the amount of reversal errors as a measure of altered reinforcement sensitivity, associating more reversal errors to decreased reinforcement sensitivity. However, solely measuring the amount of reversal errors does not capture the differential effects of reward and punishment (Xue et al., 2013), nor does it explain which strategies are applied that result in increased reversal errors. Both reward and punishment sensitivity are often altered in individuals with DB (Byrd, Loeber, & Pardini, 2014; O’Brien & Frick, 1996) and/or ADHD (Furukawa et al., 2018; Ibanez et al., 2012; Li, 2018; Plichta & Scheres, 2014). Therefore, the current study aimed to examine reward and punishment sensitivity and perseverative behavior in relation to co-occurring traits within the externalizing cluster of disorders; more specifically, ADHD symptomatology, oppositional behavior, and CU traits.

Disruptive behavior is a hallmark of conduct disorder (CD) and oppositional defiant disorder (ODD). Children diagnosed with CD violate basic rights of others, or otherwise disregard age-appropriate societal norms or rules (American Psychiatric Association, 2013). ODD is characterized by hostile, negative and defiant behavior towards authority, or irritable and disobedient attitudes towards others. Both disorders often occur together with ADHD, a neurodevelopmental disorder characterized by attention-deficits and/or hyperactivity and impulsivity (American Psychiatric Association, 2013). One overlapping dimension that is present in both ADHD and DB is CU traits (lack of remorse/empathy, shallow, constricted affect, and limited prosocial emotions; American Psychiatric Association, 2013); individuals with high levels of CU traits tend to have more severe, persistent, and more heritable antisocial behavior (Viding, Jones, Paul, Moffitt, & Plomin, 2008) and early criminal behavior (Frick & Dickens, 2006). With an overlap in symptoms and high comorbidity rates among this spectrum of disorders, researchers are increasingly moving away from categorical classifications towards dimensional analyses of symptoms and disease-relevant traits (Herpers, Rommelse, Bons, Buitelaar, & Scheepers, 2012).

The few studies that assessed the relations between symptom dimensions and reinforcement sensitivity have shown rather consistent results. Where oppositional behavior has been associated with hyporesponsivity to reward (Matthys, Vanderschuren, Schutter, & Lochman, 2012), impulsivity relates to hypersensitivity to immediate reward and hyporesponsivity to punishment (Plichta & Scheres, 2014). ADHD symptoms in children were additionally related to increased sensitivity to both reward and punishment, depending on their parents’ reported parenting strategies (Li, 2018). Hyporesponsivity to punishment has also been found in children with high levels of CU traits (Viding, Fontaine, & McCrory, 2012), which is proposed to lead to insufficient learning from negative reinforcement and consequentially to disruptive and impulsive behavior (Byrd et al., 2014). With regards to perseverative behavior, it appears that response perseveration is present in both CD (Daughterty & Quay, 1991) and ODD (Matthys, van Goozen, Snoek, & van Engeland, 2004), and is associated with reward sensitivity in CD but punishment sensitivity in ODD. Thus, inconsistencies across studies are reported, possibly reflecting the complexity of reinforcement sensitivity across these symptom dimensions but may as well be due to different experimental paradigms that assessed reinforcement sensitivities separately. Also, previous studies have often focused on either reward processing or perseverance, but punishment processing has been largely overlooked.

With studying developmental disorders, an important factor to consider is age. Age is often corrected for when studying (neuro)developmental disorders, yet it has been argued that ADHD is represented by a delay in cortical maturation (Shaw et al., 2007). Whilst ADHD is presented as a lifelong neurodevelopmental disorder, hyperactivity-impulsivity symptoms tend to decline with age in both clinical (Biederman, Mick, & Faraone, 2000; Mick, Faraone, & Biederman, 2004) and non-clinical samples (Döpfner et al., 2015). Moreover, overall externalizing behavior tends to decrease with increasing age (Bongers, Koot, Van Der Ende, & Verhulst, 2004). Recent multimodal evidence showed age-dependent brain alterations in frontal regions within multiple networks, including those that have been frequently associated with ADHD symptoms (Wu et al., 2019). Additionally, meta-analytic evidence showed age-related effects when assessing inhibition in ADHD (Hart, Radua, Nakao, Mataix-Cols, & Rubia, 2013). This study therefore additionally assessed the role of age in reinforcement sensitivity across clinical populations.

In the current study we aimed to assess the dimensional relationships between probabilistic reversal learning (PRL) response strategies and ADHD symptom severity, oppositional behavior, and CU traits in a sample of children, adolescents, and young adults with and without DB and ADHD, coming from two large (international) cohorts, NeuroIMAGE II and Aggressotype/MATRICS. Based on previous studies, expectations were that ADHD symptom severity and CU traits would be associated with increased reward and decreased punishment sensitivity (Ibanez et al., 2012). Oppositional behavior was expected to be associated with both decreased punishment sensitivity and decreased reward sensitivity (Matthys et al., 2012). Lastly, oppositional behavior and CU traits was expected to additionally relate to elevated perseverative behavior (Daughterty & Quay, 1991; Matthys et al., 2004; Byrd et al., 2014). We expected most of these relations to decline with increasing age, except the relations with ADHD symptom severity, because of the stable trajectory of inattentive symptomatology.

Methods

Participants

The original sample consisted of two clinical groups and healthy controls from two separate studies: children and adolescents aged 7-18 years with DB (n = 183), ADHD-diagnosed participants aged 11-28 years (n = 144), and healthy controls (n = 191) aged 8-26 years. Written consent was obtained from every participant above 18, from both parent and participant for adolescents aged 12-18, and from parents for children under the age of 12; children themselves gave oral assent. Data from participants with DB and from 95 healthy controls were collected...
as part of the multi-center MATRICS/Aggressotype study (www.matrics-project.eu and www.aggressotype.eu), conducted among nine different research centers across Europe. Inclusion criteria for the DB sample were a CD or ODD diagnosis based on DSM-5 criteria (American Psychiatric Association, 2013) and/or presence of aggression in the clinical range (T > 70 on the aggression or delinquency subscale measured by the Youth Self Report [YSR], the Teacher Report Form [TRF], or the parent-reported Child Behavior Checklist [CBCL]; Achenbach, 1999), and being of Caucasian descent. Exclusion criteria for the MATRICS/Aggressotype study were an IQ below 80 as estimated with subtests (block design, vocabulary, picture completion and similarities) from the Wechsler Intelligence Scale (WISC/WAIS; Wechsler, 2002), contra-indications for magnetic resonance imaging (MRI) scanning, and a primary DSM-5 diagnosis of psychosis, bipolar disorder, depression, or anxiety. Participants were included as healthy controls if they had no primary diagnosis of any DSM-5 Axis I disorder or any psychiatric diagnosis in their relatives, nor did they have clinically elevated levels of symptoms on any of the rating scales. Both medicated and unmedicated participants entered the study, and medicated participants were required to be on a stable dose of medication for two weeks. If participants were on medication during testing, interviews and questionnaires were based on (assumed) behavior and interference in daily life without medication.

Exclusion criteria for the NeuroIMAGE2 study were an IQ below 70 (as measured with the block design and vocabulary subtests from the WISC/WAIS), contra-indications for MRI scanning, and a diagnosis of autism, epilepsy, learning difficulties, brain disorders, or known genetic disorders. Unaffected siblings were excluded from this study but affected siblings remained as cases. Participants had an ADHD diagnosis if they had ≥6 inattentive and/or hyperactive-impulsive symptoms below the age of 18 years, or ≥5 symptoms for participants older than 18 years on the Conners rating scales. Additionally, they had to meet the DSM criteria for pervasiveness and impairment and an age of onset before 12 years, as determined by diagnostic interviews held by trained researchers under the supervision of a clinician and trained child and adolescent psychiatrist. Exclusion criteria for the NeuroIMAGE2 study were an IQ below 70 (as measured with the block design and vocabulary subtests from the WISC/WAIS), contra-indications for MRI scanning, and a diagnosis of autism, epilepsy, learning difficulties, brain disorders, or known genetic disorders. Medicated participants were required to be on a stable dose of medication for two weeks and were asked to abstain from stimulant medication 48 hours prior to the testing day. Again, if participants had used medication prior to testing, interviews and questionnaires were based on (assumed) behavior and interference in daily life when no medication was used.

**Phenotypic measures**

The YSR, TRF, and the CBCL (Achenbach, 1999) were used for the assessment of aggression and rule-breaking behavior. To confirm the diagnosis of ADHD and disruptive behavior disorder and for the assessment of comorbid disorders, the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS-PL; Kaufman et al., 1997) was administered by trained researchers. ADHD diagnosis was additionally confirmed by Conners rating scales (Conners, Erhardt, & Sparrow, 1999; CTRS-R.L parent-report for participants under the age of 18 years and the CAARS-S:II self-report for participants 18 years and older). Subscales from these questionnaires in the NeuroIMAGE2 study and subscales from the parent-reported SNAP-IV (Swanson, Nolan, and Pelham IV questionnaire; Swanson, 1981) in the MATRICS/Aggressotype study were used for the assessment of ADHD and oppositional symptom severity. Items were scored on a 4-point scale, and the sum of these scores belonging to these dimensions were added to create a severity score. Overlapping questions between the SNAP-IV and Conners were summed to calculate symptom severity across the studies. Both questionnaires have the same measures of symptom dimensions, with the Conners using multiple questions to measure the same constructs. The self-reported Inventory of Callous-Unemotional traits (Kimonis et al., 2008) (ICU) was used for the measurement of CU traits in both cohorts. IQ was estimated using subtests from the WISC/WAIS (Wechsler, 2002). Handedness was assessed by asking whether the participant was left- or right-handed during screening. Lastly, demographic variables such as age and (biological) sex were gathered through self-report.

**Probabilistic Reversal Learning task**

A PRL task (see Figure 1) was administered to investigate strategies in processing of reward and punishment and perseverative behavior (Cools et al., 2002; Lawrence, Sahakian, Rogers, Hodges, & Robbins, 1999). Win-stay scores indicated the proportion of trials where the subject remained with the previously rewarding stimulus (i.e. reward sensitivity), whereas lose-shift scores indicated the proportion of trials on which the subjects altered their response after punishment (i.e. punishment sensitivity; den Ouden et al., 2013). Perseveration errors were defined as the sequence of two or more errors during the reversal phase and reflect the inability to adapt response choice after reversal. The task also measured a learning criterion of eight consecutive trials, to account for learning effects. Two sites did not administer the PRL in the MATRICS/Aggressotype study and were therefore excluded from the analyses.

**Statistical analyses**

Statistical analyses were performed with the R statistical program (R Core Team, 2013). Reward, punishment, and perseverative summary scores of the PRL task were extracted with MATLAB R2016b (The MathWorks Inc., 2016) using in-house developed scripts. Data were analyzed by applying a multilevel linear model with a maximum likelihood (ML) fit using the *nlme* package (Pinheiro, Bates, DebRoy, Sarkar, & Team, 2007) (see supplementary materials for model statements). The PRL summary scores (win-stay, lose-shift, and perseveration errors) were outcome variables in these models, and ADHD symptom severity, oppositional symptom severity, and ICU scores were added as predictors corrected for the other domains. Interactions between ADHD symptom severity, oppositional symptom severity, and ICU scores were also tested in a separate model. In all analyses, site was added as a first-level random factor. Family relatedness (only applicable for NeuroIMAGE2) was added as a random factor nested in site. Age was separately added to assess its influence on the relations between variables of interest. Variables of non-interest (IQ, sex, medication, and the learning criterion of 8 consecutive trials) were added, when the base model yielded a significant effect of the variable of interest on the PRL summary scores. Results of the effects of covariates of non-interest can be found in the supplementary materials. Model fits were compared with the *anova* function in R, and the log likelihood ratio test was used to assess model significance. For an overview of the average PRL summary scores per site, see Figure S1. To control for multiple testing the effective number of tests method was used (Galwey, 2009; Nyholt, 2004), calculating an adjusted *α* of 0.0193 taking into account the dependency between the variables of interest (original *n* = 3 tests). Effect sizes were estimated by calculating the Pearson correlations, with *r* = 0.1 representing a small effect size, *r* = 0.3 a medium effect size, and *r* ≥ 0.5 a large effect size (Cohen, 2013).

**Results**

**Demographics**

The final analysis, after excluding participants and sites without PRL administration, included 438 participants, including 145 participants...
with DB (either above cut-off aggression scores or a primary diagnosis of ODD/CD), 123 participants with a primary diagnosis of ADHD, and 170 controls. The three groups (DB ADHD, and controls) differed significantly regarding age, IQ, and sex (see Table 1 for details). Among the DB group, 26.9% had comorbid ADHD, and 19.5% of the ADHD sample had comorbid ODD/CD. Figure S2 shows the division of the parameters per group.

### Associations of PRL with ADHD symptoms, oppositional behavior, and CU traits

ADHD symptom severity was negatively associated with win-stay scores ($\beta = -0.004$, $t(113) = -3.085$, $p = 0.004$, $r = 0.278$) and positively associated with lose-shift scores ($\beta = 0.004$, $t(113) = 3.109$, $p = 0.004$, $r = 0.281$). After correction for oppositional symptom severity and CU traits, a trend for the ADHD effect on lose-shift remained ($\beta = 0.003$, $t(113) = 1.781$, $p = 0.083$, $r = 0.165$), and ADHD symptom severity remained significantly related to decreased win-stay scores ($\beta = -0.004$, $t(113) = -2.476$, $p = 0.018$, $r = 0.227$; see Figure 2).

Oppositional symptom severity and ICU scores did not significantly relate to win-stay scores, lose-shift scores, or perseveration errors (all $p$-values > 0.0193). Contrary to expectations, none of the variables of interest were associated with perseveration errors (all $p$-values > 0.0193).

### Interactions between PRL and ADHD symptoms, oppositional traits, and CU traits

There was no three-way interaction-effect of ADHD symptoms, oppositional traits and CU traits on any of the PRL parameters ($p$-value > 0.0193). There was a significant interaction-effect of ADHD severity with oppositional behavior on perseveration errors ($\beta = -0.029$, $t(113) = -2.436$, $p = 0.0192$, $r = 0.223$; see Figure 3). With an increase of ADHD severity, the effect of oppositional behavior on perseveration decreased. Both main effects showed a non-significant negative slope (ADHD severity: $\beta = -0.151$, $t(113) = 1.486$, $p = 0.146$, $r = 0.138$; oppositional: $\beta = -0.646$, $t(113) = 2.007$, $p = 0.052$, $r = 0.186$). There were no interactions between any of the other continuous measures on any of the other PRL parameters (all $p$-values > 0.0193).

### Age and the relations between symptom dimensions and PRL parameters

We additionally assessed whether the linear and interaction effects were driven by age. First, we investigated whether age interacted with any of the predictors in all models. Age did not significantly interact

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### Table 1

Demographic characteristics of the full sample ($N = 438$).

<table>
<thead>
<tr>
<th></th>
<th>DB 145</th>
<th>ADHD 123</th>
<th>control 170</th>
<th>Test statistic</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>119</td>
<td>69 (56.1)</td>
<td>102</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>26</td>
<td>54 (43.9)</td>
<td>60 (40.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handicapped, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>19</td>
<td>13 (10.6)</td>
<td>22 (12.9)</td>
<td>$\chi^2(2) = 0.701$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>116</td>
<td>88.6</td>
<td>85.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ODD severity, M (SD)</td>
<td>14.16</td>
<td>7.08</td>
<td>2.17</td>
<td>$F(2, 364) = 0.001^{**}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(5.46)</td>
<td>(4.26)</td>
<td>(2.99)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADHD severity, M (SD)</td>
<td>31.12</td>
<td>22.62</td>
<td>7.10</td>
<td>$F(2, 362) = 0.001^{**}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(11.83)</td>
<td>(7.99)</td>
<td>(6.35)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CU traits, M (SD)</td>
<td>29.67</td>
<td>23.91</td>
<td>20.97</td>
<td>$F(2, 392) = 0.001^{**}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(9.52)</td>
<td>(7.49)</td>
<td>(6.92)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRL win-stay, M (SD)</td>
<td>0.70</td>
<td>0.79</td>
<td>0.82</td>
<td>$F(2, 351) = 0.001^{**}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(0.172)</td>
<td>(0.149)</td>
<td>(0.149)</td>
<td></td>
<td></td>
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<tr>
<td>PRL lose-shift, M (SD)</td>
<td>0.49</td>
<td>0.47</td>
<td>0.40</td>
<td>$F(2, 351) = 0.001^{**}$</td>
<td></td>
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<tr>
<td></td>
<td>(0.157)</td>
<td>(0.147)</td>
<td>(0.178)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRL perseveration errors, M (SD)</td>
<td>11.6</td>
<td>10.0 (7.2)</td>
<td>8.9 (7.4)</td>
<td>$F(2, 351) = 0.024^*$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(7.6)</td>
<td>(6.3)</td>
<td>(7.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note:

- * $p < 0.05$, two-tailed.
- ** $p < 0.01$, two-tailed.
- DB = disruptive behaviors, ADHD = attention-deficit/hyperactivity disorder, ODD = oppositional defiant disorder, CU = callous-unemotional, PRL = probabilistic reversal learning, M = mean, SD = standard deviation. ADHD total scores were calculated with the use of the SNAP-IV and Conners rating scales.
- $^a$ 39 participants with DB had comorbid ADHD diagnosis.
- $^b$ 24 ADHD participants had comorbid ODD diagnosis.
with ADHD symptoms nor oppositional behavior (lowest p-value = 0.651). However, age itself was positively associated with win-stay scores ($\beta = 0.015, t(113) = 4.231, p = 0.001, r = 0.370$). Adding age to the ADHD severity model only changed the slope but not the significance of ADHD symptom severity on win-stay ($\beta = -0.003, t(113) = -2.769, p = 0.008, r = 0.252$).

Both the linear and interaction analyses were then repeated within the two cohorts (MATRICS/Aggressotype and NeuroIMAGE2) separately, since both cohorts recruited matched controls in their samples. Repeating the analyses within the MATRICS/Aggressotype cohort led to non-significance in the relations between win-stay and ADHD severity ($\beta = -0.001, t(140) = -0.600, p = 0.549, r = 0.051$) and the interaction of ADHD severity and oppositional behavior on perseveration ($\beta = -0.001, t(128) = 0.247, p = 0.805, r = 0.022$). Both effects remained significant in the NeuroIMAGE2 cohort (win-stay: $\beta = -0.004, t(113) = 2.156, p = 0.016, r = 0.199$; perseveration: $\beta = -0.029, t(110) = -2.242, p = 0.0192, r = 0.209$), indicating that these effects were apparently more pronounced in the older age ranges.

The effects of variables of non-interest

Regarding the variables of non-interest, the learning criterion of 8 consecutive trials was significantly associated with all parameters (all p-values < 0.001). IQ and sex were no significant correlates of any of the
variables (all $p$-values $> 0.0193$). Medication was not significantly associated with win-stay scores, lose-shift scores, or perseveration (lowest $p$-value = 0.290 for lose-shift). Since IQ inclusion criteria differed by 10 points between the two cohorts, all analyses were repeated without the participants with an estimated IQ of below 80 ($n = 10$). This did not change the relation between ADHD symptom severity and win-stay adoption ($\beta = -0.004$, $t(103) = -2.498$, $p = 0.017$, $r = 0.227$), and strengthened the interaction between ADHD symptom severity and ODD symptom severity on perseverative behavior ($\beta = -0.032$, $t(103) = -2.636$, $p = 0.0126$).

Post-hoc analyses

To see whether the ADHD symptom relations with win-stay scores, lose-shift scores, or perseveration were driven by hyperactivity-impulsivity or inattention, the scores were divided into these two subcategories. Inattention was significantly associated with both win-stay ($\beta = -0.006$, $t(113) = -2.637$, $p = 0.012$, $r = 0.241$) and lose-shift scores ($\beta = 0.007$, $t(113) = 3.182$, $p = 0.002$, $r = 0.287$). Hyperactivity-impulsivity was also significantly related to win-stay ($\beta = -0.007$, $t(113) = -3.089$, $p = 0.003$, $r = 0.279$) and lose-shift scores ($\beta = 0.006$, $t(113) = 2.534$, $p = 0.015$, $r = 0.232$). Correcting for the other domains led to both effects becoming non-significant (smallest $p$-value = 0.079).

To examine if the win-stay scores were driven by strategies adopted in the acquisition phase or reversal phase, the model was repeated in both phases. Win-stay scores were negatively related with ADHD symptom severity in the acquisition phase ($\beta = -0.005$, $t(113) = -2.675$, $p = 0.011$, $r = 0.244$) but not the reversal phase ($\beta = -0.003$, $t(113) = -1.640$, $p = 0.110$, $r = 0.152$), indicating that, with increasing ADHD severity, the tendency to switch stimulus after reward was no longer apparent in the presence of the reward reversal manipulation.

Discussion

This study examined the associations between reinforcement sensitivities and ADHD symptoms, oppositional behavior, and CU traits across a diagnostic population of children, adolescents and adults with ADHD and DB. ADHD symptom severity was associated with decreased reward sensitivity independent of oppositional symptom severity and CU traits. Severity of oppositional symptoms and CU traits on itself were not related to any of the reversal learning strategies. Adding interaction terms showed that ADHD severity alleviated the effect of oppositional behavior on perseveration, whereas the effect of ADHD on perseveration was opposite depending on the degree of oppositional symptoms.

Figure 3. The effect of oppositional traits on perseverative behavior depends on the severity of ADHD and vice versa. 

Note: For visual purposes, ADHD severity (top panel) and oppositional severity (bottom panel) scores are here divided in three groups: One group with symptom scores around 1 standard deviation or more above the mean, one group with symptom scores around the mean, and one group with symptom scores around 1 standard deviation below the mean. In the analyses and the subsequent results, however, they were entered as continuous measures.
Our finding of an association between ADHD symptom severity and hyposensitivity to reward, independent of oppositional and CU traits aligns with some of the previous studies on reward-sensitivity in ADHD samples (Furukawa et al., 2018; Furukawa, Shimabukuro, Alsop, & Tripp, 2017; Geurts, Van der Oord, & Crone, 2006). Moreover, they suggest that the reduced sensitivity to reward observed in previous ADHD studies may partly be related to ADHD symptom severity in both clinical and non-clinical populations. Adding age only changed the slope but not the significance of this relation, yet repeating analyses showed that this effect was only present in the NeuroMAGE2 cohort. Age in itself was however significantly associated with increased win-stay adoption, and repeating the analyses showed that in the older cohort, which consisted of ADHD-diagnosed participants and healthy controls, the association between ADHD symptom severity and win-stay scores remained. The reason that this effect was only visible in the ADHD sample may be because the relation between ADHD symptom severity and sensitivity to reward is mostly driven by inattentive symptoms rather than impulsivity. Inattentive symptoms are relatively static across the lifespan, whereas impulsive-hyperactive symptoms often decrease with increasing age (Biederman et al., 2000; Despert et al., 2015). It is possible that in the older age groups, ADHD symptom severity was mostly driven by the inattention subtype rather than the combined subtype.

The negative association between ADHD severity and reward sensitivity was present in the acquisition phase but not the reversal phase, suggesting that sensitivity to reward increased during the task. Participants with DB and ADHD reached the learning criterion of 8 consecutive trials less often than controls (see Figure 54), perhaps suggesting that children with DB and ADHD needed a longer time to adjust to the task (Luman, Oosterlaan, Knol, & Sergeant, 2008). The delayed win-stay adoption may in part reflect the well-documented prefrontal and orbitofrontal metabolic dysfunction during cognitive tasks in externalizing and disruptive disorders (Finger et al., 2008; Itami & Uno, 2002; Rubia et al., 2009; Zametkin et al., 1993; Zametkin et al., 1990). Further research is required to assess whether the delayed win-stay adoption is caused by stabilization of metabolic rates in the frontal lobes by measuring PRL-related brain activity in clinical and non-clinical samples with the use of fMRI.

No associations were detected between CU traits and reversal learning. The current results, using CU traits across disorders, are inconsistent with previous research that assessed CU traits categorically with a cut-off at the median (Budhani & Blair, 2005; Finger et al., 2008). Since high CU traits are highly comorbid with oppositional behavior and ADHD (Herpers et al., 2012), a possible explanation for the current finding would be that most of the effects found in previous studies (Byrd et al., 2014; O’Brien & Frick, 1996; Rubia et al., 2009) may have been due to other overlapping traits or a combination of traits that defined these diagnoses.

Where several studies associated CU traits with increased reversal errors in previous literature (Byrd et al., 2014; O’Brien & Frick, 1996; Rubia et al., 2009), we found a small moderating effect of oppositional behavior and ADHD symptomatology explaining perseveration in this study. For high-oppositional people, more ADHD-symptoms reduced perseveration errors, whereas for the low oppositional group, ADHD severity increased perseveration. It has been discussed that ODD was associated with deficits in inhibition, especially when motivational factors are involved, leading children with ODD and CD experiencing greater difficulty to learn to make appropriate decisions (Mathys et al., 2012). Perhaps diagnostic categorization of previous studies has masked the conflicting role of ADHD symptomatology in ODD studies. Published research on oppositional traits is scarce, and could benefit from subsequent studies trying to disentangle the roles of oppositionality and ADHD symptomatology in relation to perseverance in probabilistic learning tasks.

A limitation of the current study was the substantial age difference across the samples. Linearly correcting for age, checking for age interactions and repeating analyses in each cohort ensured that any differences between ADHD and DB were unlikely due to age alone, but on the other hand may have led to false negative findings to the extent that age and group effects of interest explained the same variance. Sensitivity analyses showed that the results only held up for the NeuroMAGE2 cohort with an age range of 11-28 years. Lastly, our findings had small to medium effect sizes, meaning that the results should be interpreted relative to its contributions. Nonetheless, by combining data from two cohorts, it was possible, for the first time, to investigate reward and punishment processing in relation to ADHD and DB symptomatology across different disorders. Previous studies that found reward and punishment processing deficits in both diagnoses failed to investigate the deficits in the context of its potential associations.

Conclusions

This study suggests that reduced reward sensitivity as measured by a probabilistic reversal-learning task is unrelated to oppositional behavior and CU traits but rather depends on ADHD hyposensitivity to reward across disorders and in healthy controls. ADHD severity alleviated the effect of oppositional behavior on perseveration, whereas the effect of ADHD on perseveration is opposite depending on the degree of oppositional symptoms. The dissociation between results from categorical and dimensional analyses provide evidence that different traits may relate to different reward processing deficits that appear transdiagnostic.

Disclosures

T Banaschewski served in an advisory or consultancy role for Actelion, Hexal Pharma, Lilly, Medice, Novartis, Oxford outcomes, PCM scientific, Shire and Viforapharma. He received conference support or speaker’s fee by Medice, Novartis and Shire. He is/has been involved in clinical trials conducted by Shire & Viforapharma. The present work is unrelated to the grants and relationships noted earlier. C Arango has been a consultant to or has received honoraria or grants from Acadia, Ambrosseti, Caja Navarra, CIBERSAM, Fundación Alicia Koplowitz, Forum, Instituto de Salud Carlos III, Gedeon Richter, Janssen Cilag, Lundbeck, Merck, Ministerio de Ciencia e Innovación, Ministerio de Sanidad, Ministerio de Economía y Competitividad, Mutua Madrileña, Otsuka, Roche, Servier, Shire, Schering Plough, Sumitomo Dainippon Pharma, Sunovio and Takeda. S. Walitza has received in the last 5 years royalties from Thieme Hogrefe, Kohlhammer, Springer, Belz. S. Walitza has received lecture honoraria from Opopharma in the last 5 years. Her work was supported in the last 5 years by the Swiss National Science Foundation (SNF), diff. EU FP7s, HSM Hochspezialisierte Medizin of the Kanton Zurich, Switzerland, Bfarm Germany, ZInEP, Hartmann Müller Stiftung, Olga Mayenfisch, Gertrud Thalmann Fonds. D Brandeis serves as an unpaid scientific advisor for an EU-funded Neurofeedback trial unrelated to the present work. JC Glennon has acted as a consultant for Boehringer Ingelheim GmbH. B Franke received an educational speaking fee from Medice. JK Buitelaar has been consultant to/member of advisory board of and/or speaker for Janssen Cilag BV, Eli Lilly, Bristol-Myer Squibb, Shering Plough, UCB, Shire, Novartis, and Servier. He is not an employee of any of these companies, nor a stock shareholder of any of these companies. He has no other financial or material support, including expert testimony, patents, and royalties. The other authors do not report any biomedical financial interests or potential conflicts of interest.

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Supplementary materials


References


