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Successful Evidence-Based Parenting Programs Are Associated With Brain Changes and Improved Reward Processing in Boys With Conduct Problems

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ABSTRACT

BACKGROUND: Early parenting interventions are the gold-standard treatment for reducing antisocial behavior (ASB) in children with conduct problems (CPs), but the neurocognitive mechanisms that underpin treatment response are unknown.

METHODS: We assessed functional magnetic resonance imaging (fMRI) and performance data from a reward learning task in boys with CPs (ages 5–10 years) before and after a gold-standard group parenting intervention. Matched control boys were assessed concurrently at 2 equally spaced time points. The CP group was subdivided into boys whose ASB improved or persisted over the course of treatment. Longitudinal group (control, improving CP, persistent CP) × time (pre-, postintervention) analyses were then conducted on task-based fMRI and reinforcement learning data.

RESULTS: Following the intervention, a comparison of the improving CP group with the persistent CP and control groups showed 1) increased neural activity in the direction of typically developing children within the ventromedial prefrontal cortex, insula, posterior cingulate cortex, and hippocampus in the improving CP, but not the persistent CP, group and 2) distinct changes in learning rate, action bias, and reward/punishment sensitivity. Furthermore, changes in insula activity and punishment/reward sensitivity correlated with changes in parenting behavior.

CONCLUSIONS: Improved ASB after early intervention was associated with changes in reward-processing regions and specific reinforcement learning parameters. These changes were not observed in boys with persistent CPs and correlated with changes in parenting behavior. These findings highlight the importance of early interventions for CPs and reveal potential mechanisms that underpin successful treatment.

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Conduct problems (CPs) in children arise from a mixture of genetic predispositions interacting with environmental factors, including suboptimal parenting styles (1). Children with CPs exhibit antisocial behaviors (ASBs), which are core symptoms of conduct disorder and oppositional defiant disorder. ASBs can form part of a lifelong trajectory with significant associated costs to the individual and society (2–6). Current interventions improve behavior and produce lasting protective effects in most of these children but not all (7–9). It is hoped that a better understanding of the biological mechanism(s) and neurocognitive correlates that underlie this disparity will contribute to improvements in future treatments.

ASB in children with CPs is thought to be associated with abnormalities in 1) affective processing (e.g., reduced sensitivity to others' distress and associated amygdala hypoactivity to fear) (10–14) and 2) reward processing (15–19). We recently reported that amygdala hypoactivity to fear was only observed in boys whose ASB persisted following intervention (20). This finding was important as it revealed a neural marker that might predict treatment resistance and provided further evidence of neurocognitive heterogeneity within this population (21). However, this work was unable to establish the putative neurocognitive mechanism(s) that underpin a positive response to treatment.

We hypothesized that mechanisms of improvement during intervention likely involved reward processing. This appears likely, as the methods utilized in parenting interventions such as Incredible Years (IY) program are rooted in operant conditioning principles. Viewed through this lens, positive reinforcement (via warmth, reward, and praise) and consistent discipline are used to increase the frequency of prosocial behavior and reduce the frequency of ASB (22). It follows naturally then that improvement in ASB would be underpinned at the neurobiological level by the child's reward circuitry.

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One of the most widely replicated reward abnormalities in CPs is altered neural processing of reward anticipation/expectation within the ventromedial prefrontal cortex (VMPFC), ventral striatum, and insula. Therefore, we initially sought to examine whether these abnormalities could be improved by group parenting programs in those whose ASB lessens during treatment. We also investigated whether specific neurocomputational mechanisms of decision making were impacted during treatment.

The simplest way of characterizing decision making, and elucidating prospective candidates, involves analysis of the outcome. For example, studies have variously suggested that children with CPs make riskier decisions (23), are less capable of learning in response to punishment (24,25), and show abnormal patterns of reward learning (15,16). However, decision outcomes are subject to various influences, quantifiable as separate reinforcement learning (RL) parameters using computational modeling. For example, the learning rate that someone updates their expectations of reward/punishment differs from person to person. Similarly, the bias to act following a decision, regardless of reward outcome, shows interindividual variability. These RL parameters have dissociable effects on an individual's decision outcome and are considered more closely related to psychopathology (15). Therefore, accurate estimation of these RL parameters is important to characterize how and why treatment of CPs alters reward/punishment processing in some children but not others.

One of the key components of modeling decision making involves the selection of appropriate RL models (26,27). In early studies, it was assumed that a model (or set of parameters of interest) could be accurately estimated from a task without formally testing this. However, this approach may result in poor replicability. Furthermore, there is no consensus on which RL parameters are abnormal in CPs or which might change with reduction in ASBs posttreatment. Bayesian hierarchical model selection can help solve this by directly comparing the fit of different models, thereby assessing whether the parameters included in analyses are robustly estimable (27).

Therefore, we adopted Bayesian hierarchical modeling (26,27) to analyze data from a passive-avoidance reward learning task in 78 boys with CPs (before and after intervention) and 35 typically developing (TD) control boys (assessed at 2 equally spaced time points but did not undergo intervention). This task was performed during functional magnetic resonance imaging (fMRI) scanning to assess whether intervention improved processing within regions that have been observed to be abnormal in CPs (i.e., the VMPFC, striatum, and insula) (15,16).

Boys with CPs were then divided into those whose ASBs improved and those who had persistent CPs after the intervention. fMRI data were analyzed according to a 3-group (control, improving CP, persistent CP) $\times$ 2-time point (pre, post) longitudinal model. Parameter estimates were analyzed in a similar manner. Our methods entailed a data-driven approach to parameter selection. Therefore, we were unable to make directional hypotheses about specific parameters. However, we broadly hypothesized that 1) abnormalities in neural processing (within the striatum, VMPFC, and insula) would normalize (i.e., in the direction of the TD control group) in children with CPs whose ASB improved but not in children whose ASB persisted (i.e., a group $\times$ time effect driven by the improving group); 2) abnormalities in decision making would normalize (i.e., in the direction of the TD control group) in children with CPs whose ASB improved but not in children whose ASB persisted (i.e., a group $\times$ time effect driven by the improving group); and 3) changes in parenting style would be associated with changes in task and fMRI parameters.

METHODS AND MATERIALS

Sample

The sample analyzed is the same cohort as in our previous published work, except for exclusions due to task noncompletion/poor data quality according to the criteria set out in this and previous articles (20,28). Overall, 78 (39 persistent, 39 improving) children with CPs and 35 TD control children, ages 5 to 10 years, participated in the RL task. Boys with CPs and their families were recruited from 10- to 12-week group parenting programs (IY [n = 74] and Triple-P [n = 4]) following referral by Child and Adolescent Mental Health Services, local authorities, and charities/social enterprises. Boys with CPs and their parents/primary caregivers were assessed at the beginning of the program (<3 weeks from enrollment) and 18 $\pm$ 6.4 weeks after the initial assessment. Interventions required attendance by parents/primary caregivers at facilitated weekly group sessions, with homework between meetings. TD boys were recruited from the same schools and geographic areas as boys with CPs and were assessed at 2 equally spaced time points (18 $\pm$ 4.4 weeks) but did not undergo the parenting interventions.

Clinical Assessment

The Parental Account of Childhood Symptoms CP scale was used as the primary clinical outcome measure at both time points. This semistructured clinical interview assesses the frequency and severity of ASB according to specific investigator-based criteria and is highly predictive of later psychosocial outcomes (29).

Following the intervention, a minimally important clinical difference (MICD) approach was used to define clinically meaningful criteria for symptom improvement (30,31). Previous meta-analyses indicate that a 0.6 SD improvement from baseline is associated with high (~92%) satisfaction and enduring symptomatic and functional improvements following parent training (32). To ascertain an MICD, we used a cutoff of two-thirds of this (0.4 SD) to reflect successful treatment. Children with CPs whose CP scores improved by $\geq$0.4 SD of the mean baseline score were classified as improving, and children who did not were classified as having persistent CPs.

At both time points, the Strengths and Difficulties Questionnaire (33), Inventory of Callous-Unemotional Traits (34), Conners 3 short form attention-deficit/hyperactivity disorder (ADHD) assessment (35), and Alabama Parenting Questionnaire (36) were completed by parents. At baseline, boys were administered the Wechsler Abbreviated Scale of Intelligence (37), and parents completed sociodemographic measures, with maternal education used as a measure of socioeconomic status (SES).

MRI Acquisition

Participants underwent a 60-minute MRI scanning session at each time point (King's College London) during which T1-weighted, T2-weighted, diffusion, and fMRI scans were collected. Full acquisition details can be found in Supplemental Methods.

MRI Processing

fMRI data were preprocessed using fMRIPrep version 1.5.1rc1 (38) (RRID:SCR_016216), based on Nipype 1.3.0-rc1 (39) (RRID:SCR_002502). Motion artifacts were removed using ICA-AROMA (Independent Component Analysis–based Automatic Removal of Motion Artifacts) using aggressive denoising (40). Final scanning data after full data cleaning were available for 19 TD children, 21 children with improving CPs, and 26 children with persistent CPs (see Supplemental Methods for further preprocessing details).

RL fMRI Task

The RL task was a passive-avoidance/simplified Go/NoGo task performed during fMRI scanning (Figure 1). During each individual trial (72 overall), one of 2 shapes would appear. One had a fixed probability (85%) of giving a reward (20p or 50p) and a fixed probability (15%) of giving a punishment (subtraction of 20p or 50p). In contrast, the other shape had a

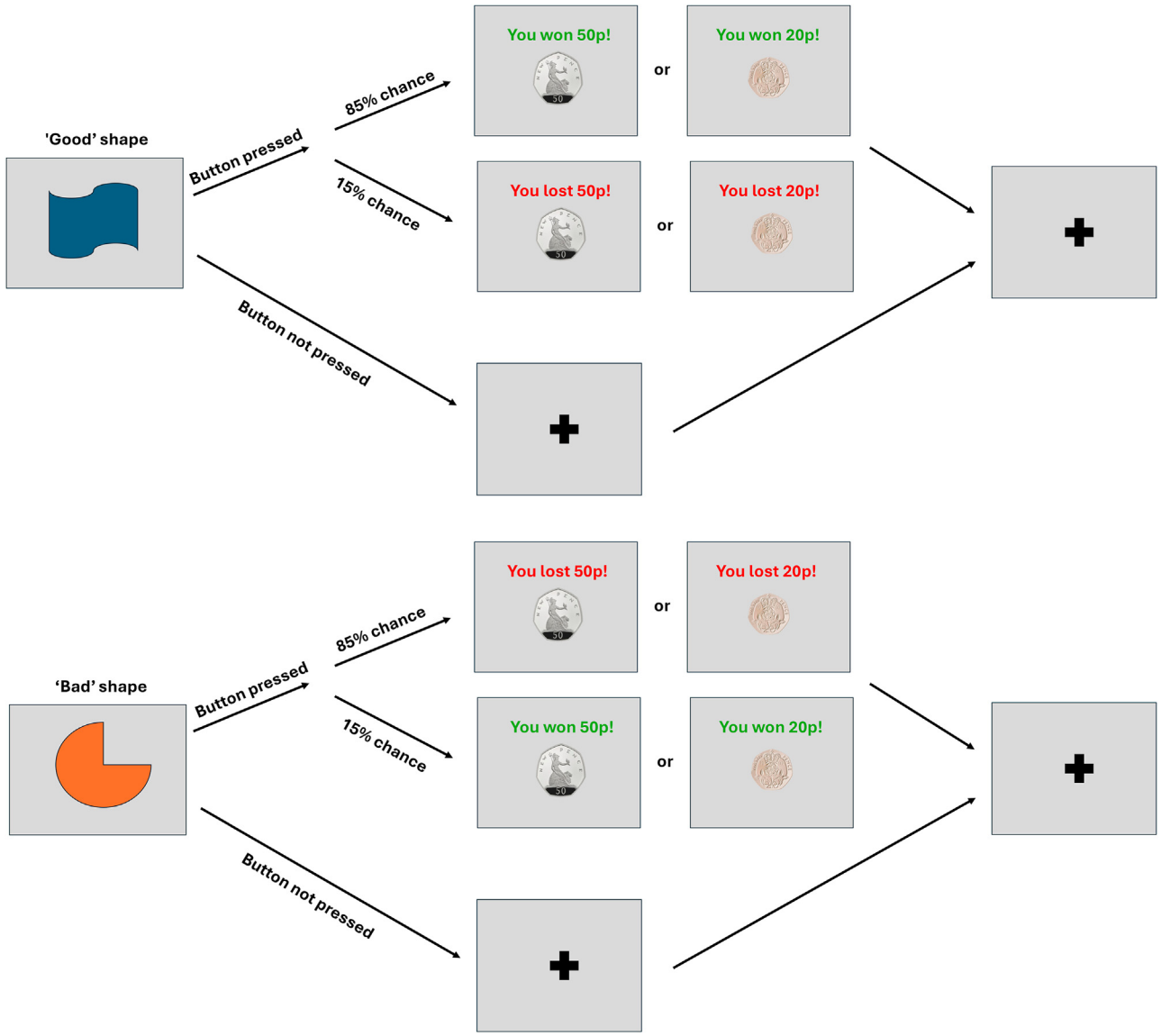

Figure 1. Task structure: During each trial, the participant would be randomly presented with either a "good" or a "bad" shape that had either a high probability of reward or a high probability of punishment. They could then choose to either press the button and receive the associated reward/punishment (if they were anticipating reward from the stimulus) or not press the button and avoid the stimulus to not receive a reward/punishment (if they were anticipating punishment from the stimulus). If this was the case, they would be shown a fixation cross for the outcome phase before proceeding to the intertrial interval.

higher fixed probability of delivering a punishment (85%) and a lower fixed probability (15%) of delivering a reward. On seeing the shape, the participant had the option to press a single button, which would reveal whether the shape on the screen would deliver a reward or punishment on that trial. If the participant did not press the button, they would not receive a reward or punishment. Therefore, to obtain the maximum reward, the participant had to learn which shape had a high probability of reward (and select it when it appeared in a trial) and which one had a high probability of punishment (and not select it). The presentation and outcome phases both lasted 1.5 seconds. Between each trial, there was an interval that varied between 1 and 2 seconds (mean 1.5 seconds) during which a fixation cross was displayed. To ensure that boys understood the task rules, they practiced the RL task with different shapes to the ones used in the main task. Boys were instructed to win as much as they could on the task. However, it was made clear that families would be reimbursed independently of task performance.

fMRI Analysis

Due to the simplified nature of the task (i.e., adapted for 5- to 10-year olds), we utilized a basic fMRI design focused on reward anticipation, a frequently used measure in conduct disorder research (41).

The anticipation phase for trials in which boys expected a reward (i.e., $Q_t > 0$) versus punishment ($Q_t < 0$) were modeled separately (based on the task analysis below). The outcome phase for rewarded and punished trials were also modeled separately. This resulted in 4 variables reflecting the onset times of these conditions (i.e., anticipated reward, anticipated punishment, rewarded outcome, and punished outcome).

These regressors of interest were entered into single-participant linear models (SPM12) together with mean signal for cerebrospinal fluid and white matter as nuisance variables as suggested by Pruim *et al.* (40). Volumes with framewise displacement (FD) >1 mm were also deweighted in the model. These excluded volumes were interpolated from surrounding volumes to mitigate any effects of residual motion artifacts on data processing. Due to the absence of a jittered intertrial interval between the anticipation and outcome phases, we opted to analyze the anticipation conditions alone in group-level analyses.

For group-level analyses, we entered our contrast of interest (anticipated reward > anticipated punishment) into a linear mixed model using 3dLME (AFNI) (42). This comprised a 3 × 2 design modeling group (improving CP, persistent CP, TD) and time (preintervention, postintervention) and a random subjects factor. As above, significant time × group effects were examined to assess for any changes over time that differed according to clinical response profile (i.e., improving CP, persistent CP, or TD group). Age, IQ, SES, and ADHD symptoms were included as covariates. Finally, to ensure that residual effects of motion did not influence the data, mean FD was included as a within-subjects covariate (43).

Group-level statistical maps were initially thresholded at $p < .001$. Simulations (3dClustSim; NN = 2, 2 sided) assuming a mixed autocorrelation function (44) suggested a clustering threshold of 193.4 voxels for whole-brain analyses. Utilizing a small-volume correction approach, simulations were also run for our 3 a priori regions of interest (ROIs), the bilateral VMPFC (k threshold = 2.2), ventral striatum (k threshold = 2.4), and insula (k threshold = 17.4). The ventral striatum ROI was adapted from Martinez *et al.* (45) as was done previously (46). The VMPFC ROI was a 12-mm sphere centered on the coordinates (MNI152 = 5, 64, −15) in which previous work using a similar task reported abnormal reward processing in children with ASB problems (15). Finally, the insula ROI was taken from the Automated Anatomical Labeling Montreal Neurological Institute (MNI) atlas (47). For post hoc investigations of significant interaction effects, mean raw data were exported at the cluster level, and pairwise comparisons were performed following modeling using the same linear mixed effects (LME) structure and covariates as above.

Computational Modeling

Computational modeling was performed in HBayesDM (27), testing 4 models adapted from inbuilt Go/NoGo models that have been described elsewhere (48). This enabled us to assess whether the task could accommodate, for example, separate learning parameters for reward and punishment. This has been proposed to be important in this patient group but has rarely been tested with robust comparison to more parsimonious models (Table 1).

Model 1: Learning Rate, Sensitivity, and Noise. The probability $p(a_t, s_t)$ of an action a being chosen on a given trial t that contains a given stimulus (i.e., shape) s_t was determined according to an action weight ($W(a_t, |s_t)$) passed through a squashed softmax function with a noise parameter ξ:

$$p(a_t, s_t) = \frac{\exp W(a_t, s_t)}{\sum_{a'} \exp W(a'|s_t)}(1-\xi) + \frac{\xi}{2} \quad (1)$$

For model 1, the action weight $W_t(a, s)$ was equivalent to $Q_t(a, s)$ as determined by a Rescorla-Wagner–like update equation:

$$W_t(a, s) = Q_t(a, s)$$

$$Q_t(a_t, s_t) = Q_{t-1}(a_t, s_t) + \epsilon(\rho r_t - Q_{t-1}(a_t, s_t)) \quad (2)$$

where ϵ is learning rate and ρ is a free parameter that determines the effective size of reinforcements or sensitivity for a participant.

Table 1. LOOIC for Each Model by Group and Session

Group	Session	Model 1	Model 2	Model 3	Model 4
Ctrl	A	2402.169	2266.886	2249.624	2249.291
	B	1953.660	1769.209	1660.998	1643.136
Imp CP	A	2329.147	2041.696	2022.414	1990.420
	B	2306.938	2019.518	1953.092	1929.577
Pers CP	A	2320.521	2022.202	1984.180	1987.181
	B	2218.124	2056.217	2009.756	1999.183

CP, conduct problem; Ctrl, control; Imp, improved; LOOIC, leave-one-out cross-validation information criterion; Pers, persistent.

Model 2: Learning Rate, Sensitivity, Noise, and Action Bias. Model 2 was identical, except that a static action bias parameter b was added to the expected value $Q_t(a,s)$ of each Go action:

$$W_t(a,s) = \begin{cases} Q_t(a,s)+b \text{ if } a = go \\ Q_t(a,s) \text{ else} \end{cases} \quad (3)$$

This was to capture the tendency to respond to a trial with a response rather than a nonresponse.

Model 3: Learning Rate, Reward Sensitivity, Punishment Sensitivity, Noise, and Action Bias. Model 3 was identical to model 2 but contained separate sensitivity parameters for reward ρ_rew and punishment ρ_pun.

Model 4: Reward Learning Rate, Punishment Learning Rate, Sensitivity, Noise, and Action Bias. Model 4 was identical to model 2 but contained separate learning rate parameters and allowed different potential learning rates for reward ε_rew and punishment ε_pun.

Computational Analysis

Following model selection, detailed in the Supplement, we adopted model 2 for our analyses. Finally, we analyzed individual-level parameter estimates for the task separately using LME models with a 3 × 2 design, modeling group (improving CP, persistent CP, TD control) and time (preintervention, postintervention) and a random subjects factor. Of particular interest to our hypotheses, significant time × group effects were examined to assess for any changes over time that differed according to the clinical response profile (i.e., improving CP, persistent CP, or TD control groups). Age, IQ, SES, and ADHD symptoms were included as covariates.

RESULTS

Demographics

There were no significant differences between the control group and either CP group in age, follow-up time, ethnicity, or IQ (all $ps > .05$). SES did not differ between the CP groups, but both CP groups differed from the control group (Table 2). ASB scores decreased in the CP groups in response to the intervention (Cohen's d = 0.70, SE = 0.171, $F_{1,71.7}$ = 17.53, $p < .001$). ADHD (Cohen's d = 0.47, SE = 0.175, $F_{1,67.1}$ = 7.4, p = .008) and callous-unemotional (CU) traits (Cohen's d = 0.53, SE = 0.199, $F_{1,66.3}$ = 6.8, p = .011), but not internalizing symptoms (Cohen's d = 0.16, SE = 0.171, $F_{1,68.9}$ = 0.9, p = .348), decreased over time. Importantly, at baseline, the improved and persistent CP groups did not differ in any clinical symptomatology, and excluding change in CPs, these did not differ following treatment (Table 3).

Functional Magnetic Resonance Imaging

Reward Anticipation: Group × Time Effects. We observed a significant group × time interaction within the VMPFC (k = 4, MNI = 0, −62, −6) (Figure 2A), which was driven by differential activation in the improving CP group compared with the control (k = 5, MNI = 0, −62, −6) and persistent CP (k = 15, MNI = 0, −62, −6) groups. Post hoc tests showed that, at baseline, VMPFC activity was lower in the improving CP group compared with the control group (marginal mean difference [MMD] ± SE = −2.6 ± 0.9, t = −2.9, p = .004) and the persistent CP group (MMD = −1.5 ± 0.7, t = −2.2, p = .031). The persistent CP group did not differ from the control group at baseline (MMD = −1.2 ± 0.8, t = −1.4, p = .160).

VMPFC activity increased over time in the improving group (MMD = 3.4 ± 0.6, t = 6.1, $p < .001$) but not the others (control: MMD = 0.06 ± 0.5, t = 0.1, p = .912; persistent: MMD = −0.6 ± 0.5, t = −1.3, p = .212). Consequently, at follow-up, the improving CP group did not differ from the control group on VMPFC activity (MMD = −0.7 ± 0.9, t = 0.8, p = .429) and showed enhanced VMPFC activity compared with the persistent CP group (MMD = −2.5 ± 0.7, t = −3.7, $p < .001$).

We also observed a significant interaction between the control group and the improving CP group over time in the right insula (k = 64, MNI = −44, 4, −6) (Figure 2B). At baseline, insula activity was lower in the improving CP group compared with the control group (MMD = −2.2 ± 0.6, t = −3.7, $p < .001$) and the persistent CP group (MMD = −1.5 ± 0.5, t = −3.2, p = .002). The persistent CP group did not differ from the control group (MMD = −0.7 ± 0.5, t = 1.2, p = .239). Insula activity increased over time in the improving CP group (MMD = 1.4 ± 0.5, t = 2.8, p = .006), whereas there was a reduction in the control group (MMD = −1.4 ± 0.5, t = −2.7, p = .007) and no change in the persistent CP group (MMD = −0.6 ± 0.5, t = −1.4, p = .166). At follow-up, the improving CP group did not differ in insula activity from the control group (MMD = 0.6 ± 0.6, t = 1.0, p = .326) or the persistent CP group (MMD = −0.5 ± 0.5, t = −1.0, p = .296).

Outside of our ROIs, we observed a significant interaction between the improving and persisting CP groups in a cluster spanning the posterior cingulate cortex (PCC), hippocampus, and midbrain (k = 382, MNI = 8, 44, −2) (Figure 2C). A similar pattern was found within the hippocampus in the right hemisphere but only met an extent threshold of $p < .1$ (k = 159,

Table 2. Key Demographic Data (Neurocomputational Data)

Measure	Ctrl, n = 35	Imp CP, n = 39	Pers CP, n = 39	Omnibus Test	Ctrl vs. Imp, p	Ctrl vs. Pers, p	Imp vs. Pers, p
Age, Years	8.7 (1.6)	8.4 (1.5)	8.7 (1.5)	$F_{2,110}$ = 0.4, p = .689	.974	.454	.462
Follow-Up Time, Weeks	18.2 (4.4)	18.9 (7.5)	17.4 (5.0)	$F_{2,96}$ = 0.6, p = .579	.583	.667	.298
ADHD	16.1 (10.4)	52.9 (13.1)	49.5 (18.4)	$F_{2,110}$ = 71.7, p = .000*	<.001	.000	.301
IQ	106.2 (16.0)	104.5 (14.1)	101.9 (15.7)	$F_{2,110}$ = 0.7, p = .478	.232	.643	.450
SES	5.6 (2.1)	3.8 (2.4)	4.2 (2.5)	$F_{2,110}$ = 5.7, p = .004*	.012	.002	.502

Values are presented as mean (SD). ADHD was measured by the Conners 3. SES was indexed by maternal education.
ADHD, attention-deficit/hyperactivity disorder; CP, conduct problem; Ctrl, control; Imp, improved; Pers, persistent; SES, socioeconomic status.

Table 3. Key Behavioral Data at Baseline and Follow-Up

				Omnibus Test[a]		
	Control	Improved CP	Persistent CP	Group	Time	Group × Time
PACS						
CP symptoms T1	0.6 (0.38)	1.7 (0.36)	1.4 (0.46)	$F_{1,75.7} = 0.4$, $p = .542$	$F_{1,69.9} = 46.8$, $p < .001$*	$F_{1,69.9} = 116.7$, $p < .001$*
CP symptoms T2	0.6 (0.36)	1.2 (0.43)	1.6 (0.45)			
SDQ						
CP symptoms T1	1.3 (1.42)	5.9 (1.89)	5.8 (2.16)	$F_{1,75.8} = 2.5$, $p = .118$	$F_{1,70.7} = 15.5$, $p < .001$*	$F_{1,70.7} = 6.3$, $p = .015$*
CP symptoms T2	0.9 (0.84)	4.4 (2.43)	5.4 (2.38)			
CU Traits						
T1	22.1 (10.60)	38.4 (10.92)	36.3 (13.62)	$F_{1,71.8} = 0.1$, $p = .708$	$F_{1,66.3} = 6.8$, $p = .011$*	$F_{1,66.3} = 0.0$, $p = .840$
T2	21.9 (8.56)	34.4 (13.90)	33.5 (11.27)			
ADHD						
T1	17.1 (10.57)	51.4 (18.46)	54.8 (13.82)	$F_{1,74.8} = 0.3$, $p = .589$	$F_{1,67.1} = 7.4$, $p = .008$*	$F_{1,67.1} = 1.3$, $p = .253$
T2	16.1 (10.32)	49.6 (17.23)	47.2 (19.84)			
Internalizing						
T1	3.4 (2.75)	8.4 (4.30)	8.3 (3.94)	$F_{1,74.9} = 0.1$, $p = .732$	$F_{1,68.9} = 0.9$, $p = .348$	$F_{1,68.9} = 0.3$, $p = .564$
T2	3.1 (2.82)	8.1 (3.71)	7.5 (4.67)			
APQ						
Positive parenting T1	13.8 (1.69)	13.7 (1.89)	13.4 (1.95)	$F_{1,71.0} = 0.7$, $p = .407$	$F_{1,66.6} = 5.6$, $p = .021$*	$F_{1,66.6} = 0.3$, $p = .589$
Positive parenting T2	13.7 (1.77)	14.0 (1.36)	13.8 (1.73)			
Inconsistent discipline T1	7.3 (2.39)	8.2 (2.23)	8.1 (2.19)	$F_{1,70.7} = 0.0$, $p = .895$	$F_{1,68.5} = 10.2$, $p = .002$*	$F_{1,68.5} = 0.3$, $p = .568$
Inconsistent discipline T2	7.8 (2.44)	7.2 (2.44)	7.4 (2.18)			
Poor supervision T1	3.6 (1.15)	4.2 (1.77)	4.1 (1.72)	$F_{1,66.6} = 1.8$, $p = .181$	$F_{1,61.9} = 0.0$, $p = .845$	$F_{1,61.9} = 3.7$, $p = .058$
Poor supervision T2	3.5 (1.43)	3.7 (1.25)	4.5 (2.24)			
Involvement T1	12.9 (1.71)	12.6 (1.56)	12.8 (1.65)	$F_{1,72.2} = 0.4$, $p = .539$	$F_{1,65.6} = 0.3$, $p = .592$	$F_{1,65.6} = 0.3$, $p = .573$
Involvement T2	12.6 (1.47)	12.7 (1.67)	12.6 (1.75)			
Corporal punishment T1	3.9 (1.29)	4.1 (1.33)	4.1 (1.18)	$F_{1,67.4} = 0.6$, $p = .428$	$F_{1,63.0} = 10.0$, $p = .002$*	$F_{1,63.0} = 2.8$, $p = .102$
Corporal punishment T2	3.9 (1.32)	3.5 (0.87)	3.7 (1.30)			

Values are presented as mean (SD).

*Statistical significance at $p < .05$.

ADHD, attention-deficit/hyperactivity disorder; APQ, Alabama Parenting Questionnaire; CP, conduct problem; CU, callous-unemotional; PACS, Parental Account of Childhood Symptoms; SDQ, Strength and Difficulties Questionnaire; T, time.

[a]The omnibus tests were run on the improved vs. persisted groups only.

MNI = 26, 20, −18). See the Supplement for task-effect analysis and non-ROI post hoc tests.

RL Parameters

Learning Rate. We observed a significant group × time interaction for learning rate ($F_{2,75.9} = 14.5$, $p < .001$) (Figure 3A). Post hoc tests revealed that boys whose CPs improved showed a decrease in learning rate over time ($p < .001$). This contrasted with the absence of a significant change in learning rate in the control group ($p = .928$) and an increased learning rate in boys with persistent CPs ($p < .001$). However, we observed no baseline differences between boys whose CPs improved over time and the boys in the control group ($p = .709$) or the persistent CP group ($p = .743$). The control and persistent CP groups also did not differ at baseline ($p = .894$).

Action Bias. We observed a significant group × time interaction for action bias ($F_{2,96.1} = 17.6$, $p < .001$) (Figure 3B). Post hoc tests revealed that, before the intervention, boys whose CPs improved had higher action bias than boys in both the control ($p < .001$) and persistent CP ($p = .002$) groups. This significantly reduced following the intervention ($p = .002$) (i.e., in the direction of the control group at baseline). Furthermore, there was no significant difference between the improved CP group postintervention and baseline control group performance ($p = .103$). Interpretation of these changes as being consistent with a normalization effect is complicated by the increase in action bias that we observed in the control group over time. These behavioral differences might be explained by the effect of task repetition in TD individuals ($p < .001$). The persistent CP group showed no change in action bias over time ($p = .813$).

Sensitivity. We observed a significant group × time effect for the sensitivity parameter ρ ($F_{2,87.5} = 1215.6$, $p < .001$) (Figure 3C). Post hoc tests showed high levels of sensitivity in the improving and persistent CP groups compared with the control group (both $ps < .001$). The control and improving CP group both showed patterns of increasing sensitivity over time (both $p < .001$), whereas the persistent CP group showed a decrease ($p < .001$).

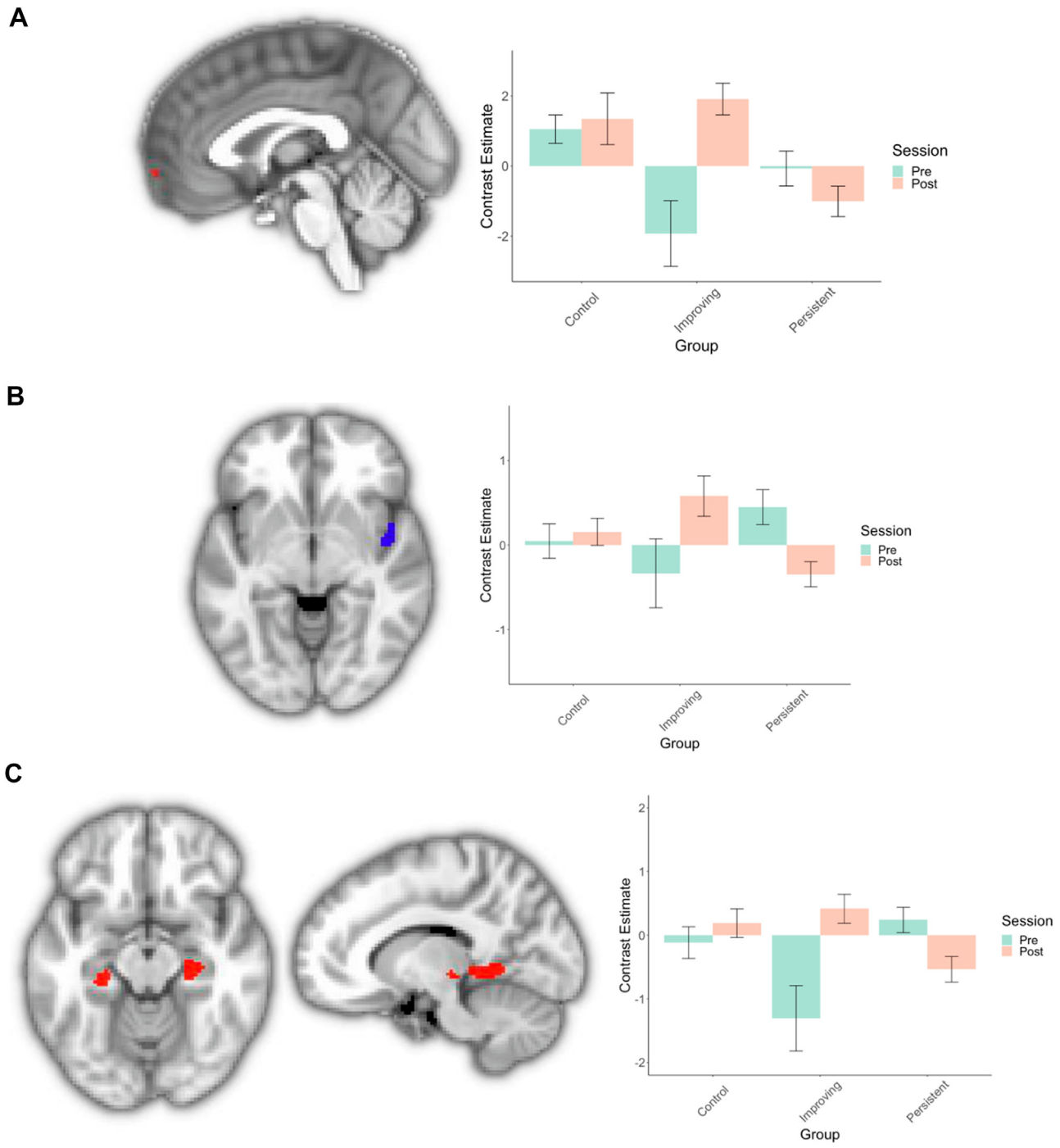

Figure 2. Functional magnetic resonance imaging results. **(A)** Significant group × time (overall) interaction in the ventromedial prefrontal cortex. **(B)** Significant group (control vs. improving conduct problem [CP]) × time interaction within the left insula. **(C)** Significant group (improving CP vs. persistent CP) × time interaction within the left posterior cingulate cortex, hippocampus, and midbrain. Also shown is a trendwise interaction for the same contrast within the right hippocampus ($p < .1$).

Noise. We observed no group × time effect for noise ($F_{2,89.6} = 0.9$, $p = .412$), but we observed a significant effect of session, suggesting an increase in noise over time ($F_{2,89.5} = 7.1$, $p = .009$) (Figure 3D).

Post Hoc Tests: Effects of Parenting

Parenting behaviors changed significantly during the intervention. Specifically, improved positive parenting ($F_{1,66.6} = 5.6$, $p = .021$) was observed together with reduced inconsistent

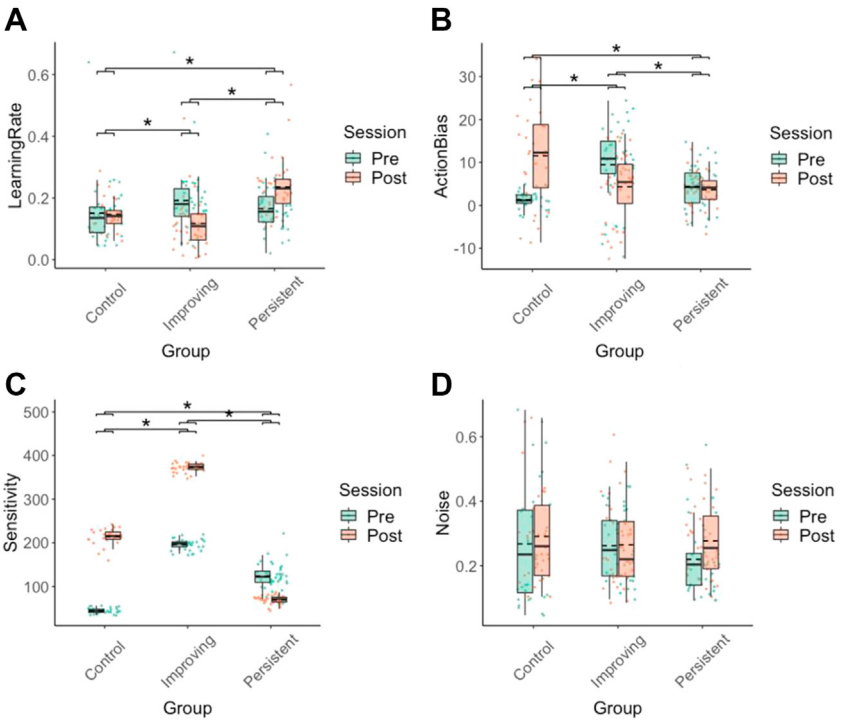

Figure 3. Significant effects in computational parameters. Significant group × time interaction for learning rate **(A)**, action bias **(B)**, and sensitivity **(C)**. Only a significant effect of time was observed for the noise parameter **(D)**. *$p < .001$.

discipline ($F_{1,68.5}$ = 10.2, p = .002) and corporal punishment ($F_{1,63.0}$ = 10.0, p = .002). Importantly, no significant group × time effects were observed (Table 3), with improvements in parenting found equally across both the improving and persistent CP groups.

Next, we explored whether changes in parenting behavior might explain shifts in neural and computational parameters associated with improvement in CP symptoms (using rmcorr) (49). Specifically, we assessed parenting relationships with 1) a priori hypothesized brain regions where we observed significant change (i.e., the insula and VMPFC) and 2) computational parameters that were linked to improving CPs (i.e., action bias [b], sensitivity [ρ], and learning rate).

Across the CP groups, we found that decreased corporal punishment (r_{25} = −0.50, p = .007) and increased positive parenting (r_{26} = 0.40, p = .033) and involvement (r_{26} = 0.49, p = .007) were associated with increased insula activity over time (Figure 4 and Figure S5). In addition, reducing corporal punishment over time was associated with increased reward/punishment sensitivity (r_{64} = 0.29, p = .019). No other relationships were observed between parenting and neural/computational measures.

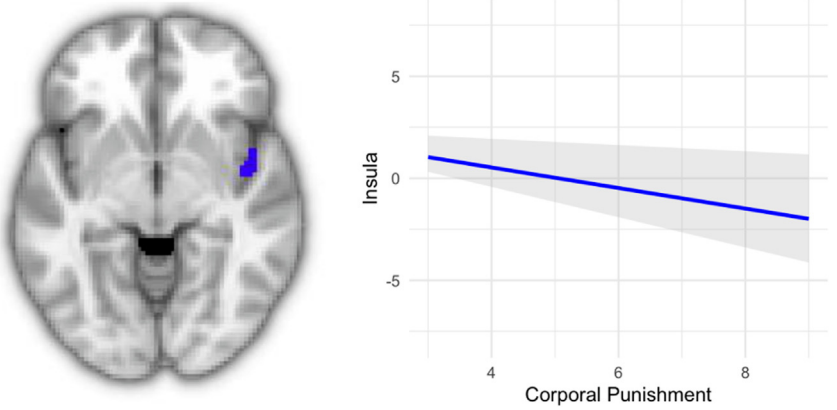

Figure 4. Repeated-measure correlation between insula activity and corporal punishment. The graph represents the overall r of the model, with confidence bands (see the Supplement for full within-subjects correlation graphs for all brain-parenting relationships).

DISCUSSION

In this study, we observed changes in regional brain activation and RL parameters that were associated with treatment outcome in boys with CPs. Reduced ASB after the group parenting intervention was associated with increased activity during reward/punishment anticipation within the insula, VMPFC, PCC, and hippocampus. These changes resulted in neural activity that was more closely aligned with that of TD children. Additionally, we observed decreased learning rate and action bias (i.e., in the direction of control children) and increased sensitivity to reward and punishment. Furthermore, changes in parenting style targeted by the intervention correlated with some of these changes.

Brain activity in several key regions effectively normalized in boys whose ASB improved. For example, we found that reduction in VMPFC activity at baseline was remediated during treatment. This is significant because previous studies of CPs have reported that VMPFC activity was impaired during reward anticipation (15,18,50), likely due to reduced signaling of the expected value of a choice (15). Similarly, we found that impaired insula activity (15), typically associated with avoidance of punishing options (51,52) and valuation of stimulus (53,54), was also ameliorated in boys whose ASB improved. A similar pattern was also observed within the PCC, which plays a role in tracking subjective reward, risk, and shifts in strategy during learning (55,56). Reductions in PCC activity have been observed in children with CPs during reward anticipation (41). These findings are consistent with a broader literature that suggests the importance of the PCC as a node of the dorsal default mode network (57), corresponding anatomically to the dorsal cingulum (58–60).

Our findings also provide novel insight into the neurocognitive correlates of positive behavioral change following parenting interventions. Firstly, improving ASB was associated with a decreased learning rate. This results in more gradual evaluation of whether future choices will be rewarded or punished. Although a slower learning of reward may not intuitively appear to be beneficial, it may be protective against ASB in several ways. For example, it may deter against premature positive valuation of a bad choice after a single and unlikely positive experience. Equally, with a lower learning rate, if a choice is good in the long run, it is more likely that this positive behavior will be maintained in the face of unexpected punishment. Future work is necessary to determine whether this pattern of findings is also observed in adolescents with CPs who appear to have lower punishment learning rates than control adolescents (24) and to what extent these differences reflect true age effects versus different task structures.

Secondly, improved ASB was associated with a reduced bias toward action regardless of outcome. Therefore, this shift away from a more impulsive decision-making style (61) appears to play a role in mitigating ASB through intervention. Finally, our findings suggest that ASB that is resistant to change may be driven by an inability to fully estimate the severity of a reward or punishment. Specifically, while boys with CPs who improved (and control children) were able to estimate higher expected reward/punishments for their choices at the second time point (i.e., higher sensitivity), boys with persistent CPs showed the opposite effect.

Our study provides the first evidence of a direct impact of parenting on these neural and computational learning markers. Specifically, improved involvement, positive parenting, and reduced corporal punishment positively modulated brain function within the insula, and reduced corporal punishment also increased reward/punishment sensitivity. These findings highlight the value of mediator-led parenting change in shifting the underlying neural and computational correlates of ASB.

However, our findings also suggest that there is a subgroup of children who do not respond to mediator-led parenting interventions despite the same positive changes in parenting style. It is also noteworthy that in this persistent CP group, the initial reward deficits found in the improving CP group were not evident. Combined with our previous findings in the same cohort (20), this suggests that distinct neurophenotypes underpin CPs that are fixed versus reversible (20,21). Specifically, it suggests that persistent CPs are associated with amygdala hypoactivity to others' distress, while reversible CPs are associated with reward learning abnormalities. It is of particular interest that these 2 groups of children did not differ on any clinical parameters, including CU traits, at baseline. This is consistent with a recent meta-analysis showing that children with high CU traits do not inherently reflect a group nonresponsive to intervention (62). Furthermore, it appears that the neurophenotypes that we observed in this and our previous work (20) seem to be clearer markers of CP persistence/improvement in CPs than CU traits, at least at the group level.

Conclusions

We observed remediation of specific neurocognitive reward-processing deficits in a subgroup of boys with CPs whose behavior improved following positive changes in parenting. Future studies are needed to examine whether these changes have a causative role in sustained remission (7,8) and/or whether the absence of these deficits in some boys with CPs can be used as biomarkers to predict treatment resistance.

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