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Feedback-Related Negativity in Children with Two Subtypes of Attention Deficit Hyperactivity Disorder

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Abstract

Objective: The current model of ADHD suggests abnormal reward and punishment sensitivity, although differences in ADHD subgroups are unclear. This study aimed to investigate the effect of feedback valence (reward or punishment) and punishment magnitude (small or large) on Feedback-Related Negativity (FRN) and Late Positive Potential (LPP) in two subtypes of ADHD (ADHD-C and ADHD-I) compared to typically developing children (TD) during a children's gambling task.

Methods: Children with ADHD-C (n = 16), children with ADHD-I (n = 15) and typically developing children (n = 15) performed a children's gambling task under three feedback conditions: large losses, small losses and gains. FRN and LPP components in brain potentials were recorded and analyzed.

Results: In TD children and children with ADHD-C, large loss feedback evoked more negative FRN amplitudes than small loss feedback, suggesting that brain sensitivity to the punishment and its magnitude is not impaired in children with ADHD-C. In contrast to these two groups, the FRN effect was absent in children with ADHD-I. The LPP amplitudes were larger in children with ADHD-C in comparison with those with ADHD-I, regardless of feedback valence and magnitude.

Conclusion: Children with ADHD-C exhibit intact brain sensitivity to punishment similar to TD children. In contrast, children with ADHD-I are significantly impaired in neural sensitivity to the feedback stimuli and in particular, to punishment, compared to TD and ADHD-C children. Thus, FRN, rather than LPP, is a reliable index of the difference in reward and punishment sensitivity across different ADHD-subcategories.

Introduction

Attention deficit hyperactivity disorder (ADHD), which is the most prevalent childhood neuropsychiatric disorder, is defined in the current Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) as developmentally inappropriate and impairing symptoms of inattention and/or hyperactivity-impulsivity [1]. ADHD affects 5.29% of school-age children worldwide [2], 7.8% in the USA [3] and 7.5% in Taiwan [4]. According to the DSM-IV, ADHD has three subtypes: predominantly inattentive type (ADHD-I), which accounts for 45% of all ADHD patients; predominantly hyperactive-impulsive (ADHD-H), which affects 21% of all patients; and combined-type (ADHD-C), which occurs in 34% of all patients [1,5].

Recent studies imply that ADHD is associated with an aberrant sensitivity to reinforcement [6–11], such as reward and punishment. Since reinforcement is highly associated with motivation, evidence suggests that an unusually low level of effort or intrinsic motivation accounts for the performance deficits in children with ADHD [12–15]. Behavioral studies have demonstrated that

children with ADHD show an abnormal sensitivity to motivational cues. They have problems in maintaining optimal performance when they have to rely solely on their intrinsic motivation, i.e. without external motivators such as feedback or reward [16,17]. Furthermore, children with ADHD show an attention span that is very limited without supervision or when tasks are extremely boring [15], but benefit to a greater extent from reinforcement contingencies implemented in a task [18]. Motivational models of ADHD formulated several different predictions about reinforcement sensitivity (1) a preference for small immediate reward over larger delayed reward [19–21]; (2) reduced neurobiological sensitivity to reward [19,22] and reduced reward anticipation [20,21], and (3) reduced behavioral sensitivity to cues of aversive stimuli in general [23,24]. In addition, from a clinical perspective, reinforcement contingencies are found to normalize behaviors that characterize ADHD [25–27]. However, other studies have predicted that individuals with ADHD have increased sensitivity to punishment [28,29]. Recently, several event-related potential studies investigated how reward and punishment influences the monitoring of performance feedback in children with ADHD. van

Meel et al. [30] reported that the FRN amplitude to losses was more pronounced in the ADHD group, suggesting an enhanced sensitivity to unfavorable outcomes in children with ADHD. However, in another study by van Meel et al. [31], the FRN effect was found to be entirely absent in children with ADHD. The lack of modulation of the FRN by contingencies in ADHD suggests deficient detection of environmental cues as a function of their motivational significance. Interestingly, the finding is consistent with the report by Groen et al. [32] that the Methylphenidate-free (Mph-free) children with ADHD did not show an FRN effect in the loss condition. This may be indicative of either difficulties in computing reward prediction errors or more positive expectancies of their outcomes in the face of losses. These discrepancies arise, at least in part, from the fact that these studies did not classify ADHD children into different subtypes. However, this classification is important, because there are evidences that different subtypes of ADHD are associated with different reward or punishment processing [33,34]. To our knowledge, there are no reports describing differences among ADHD subgroups in the monitoring of performance feedback coupled with reward and punishment.

Emotional-motivational dysfunctions are likely to contribute to ADHD, especially to hyperactive and impulsive symptoms. Regarding subgroup differences, ADHD-C and ADHD-HI in particular should show emotional-motivational dysfunction, while ADHD-I is less likely to show differences. A reduced responsiveness of the reward system was found to be associated with hyperactive-impulsive symptoms but not with inattentiveness [33]. In ADHD-C, symptoms of inattentiveness may be a compensatory factor for blunted response to unpleasant stimuli, as these individuals are associated with internalizing behavior [35] marked by high reactivity to unpleasant stimuli. ADHD-C and ADHD-I differ in a variety of ways that could contribute to different patterns of motivational style. Children with ADHD-C are more likely to show comorbid externalizing and impulsive behavior. Moreover, the nature of the cognitive-attentional deficit appears to differ between subtypes, with the ADHD-C group characterized as distractible, sloppy and disorganized and the ADHD-I group characterized as drowsy, sluggish and less alert [36,37]. Carlson et al. [38] observed some motivational style differences between ADHD subtypes, with the ADHD-C group more motivated by competitiveness and a desire to be perceived as superior to others and the ADHD-I group less uncooperative and possibly more passive in their learning styles. In addition, a recent study [34] showed that healthy subjects exhibited startle response attenuation and potentiation by pleasant and unpleasant pictures, respectively. In ADHD with impulsive and hyperactive symptoms, the startle responses was not attenuated by pleasant and not potentiated by unpleasant stimuli. The startling response in ADHD-I was attenuated to a lesser degree by pleasant stimuli compared to the control group. These findings suggest that blunted emotional reactivity is especially pronounced in ADHD patients with symptoms of hyperactivity and impulsivity (ADHD-C, ADHD-HI). Recently, a fMRI study [39] compared neural activation in the ventral striatum and prefrontal regions during reward processing in ADHD subtypes and healthy adults. The result showed that, compared to ADHD-C and healthy subjects, ADHD-I subjects showed a bilateral ventral striatal deficit during reward anticipation. In contrast, ADHD-C subjects showed orbitofrontal hyporesponsiveness to reward feedback when compared with ADHD-I and healthy subjects.

The late positive potential (LPP) is a central-parietal positive slow ERP that reaches the largest amplitudes at 500–700 ms post-stimulus and lasts for several hundred milliseconds [40]. Specifically, many studies have revealed that the LPP is more pronounced for emotionally salient than for neutral stimuli [41–44]. LPP has been described to reflect increased levels of sustained attention to effective-motivational stimuli [45–47], its amplitude decreased with the reduction of experienced emotion arousal, and increased with enhancement of the arousal [40]. Making use of a time production task with visual performance feedback, van Meel demonstrated that children with ADHD showed a decreased late positivity (after 450 ms) to negative feedback stimuli indicating loss. This result has been interpreted as a deficit in the affective evaluation of feedback signals and altered evaluation of future consequences in children with ADHD. Furthermore, a study of Groen consistently reported aberrant late processing of non-reward and punishment (increased feedback LPP) in children with ADHD. However, another study by Groen [48] demonstrated a trend toward a reduced LPP in response to negative feedback stimuli in children with ADHD.

Numerous studies have reported that the human brain is especially sensitive to emotionally negative events, and that these events are preferentially processed relative to neutral and positive events [49–52]. Behavioral studies [53–55] have demonstrated that, relative to positive events, negative events recruit attentional resources more rapidly, or automatically. Moreover, the magnitude of the negative event is important, as extremely negative events typically represent a greater threat to survival than do moderately negative events [56,57]. Yuan et al. reported that humans are more sensitive to magnitude differences in negative stimuli, and these different magnitudes could be clearly differentiated in each step of information processing stream even when individuals are highly engaged in a non-emotional task [56,58]. In contrast, magnitude differences in positive events are often unattended to in daily life, as positive events typically bring no harm [56]. In our daily life, more negative stimuli are punishments or losses, not violence or traffic accidents. An issue that has yet to be investigated is whether children with ADHD are also sensitive to punishment and its magnitude, and how ADHD children with different symptoms may differ in this sensitivity.

Therefore, the present study investigated the monitoring of performance feedback coupled with score losses and gains in children with two subtypes of ADHD (ADHD-C and ADHD-I). In order to evaluate the effect of punishment on the monitoring of performance feedback, we manipulated the magnitude of punishment (-1, -4). Regarding the typically developing (TD) children, based on the outcomes of the study of van Meel and colleagues [31], we expected that they would show enhanced monitoring of feedback as reflected by an enhanced FRN to large losses compared with that to small losses and gains. Based on the study by Carlson [38], we predict that patients with ADHD-C, a group characterized by competitive motivation and the desire to be perceived as superior to others, would show more sensitivity to large punishment as reflected by an enhanced FRN to large losses compared with that to small losses. Regarding the children with ADHD-I, who have severe attention problems as the core symptom, we expected that they would show aberrant early feedback detection as reflected by a reduced or absent FRN under all conditions. As previous studies have demonstrated, the LPP may reflect the late processing of the affective value of feedback stimuli in the context of feedback processing [31,48,59]. Groen [32] speculated that the children with ADHD attached more value to the feedback stimuli than the TD children, because they are more dependent on external motivators to maintain their performance. Based on this speculation, we predict that children with ADHD-C show an enhanced feedback LPP to larger punishment. As the LPP has been described to reflect increased sustained attention to affective-motivational stimuli and the LPP

amplitude depends on how the emotional stimuli are appraised and attended to, we predicted that children with ADHD-I with severe inattention problems would not show LPP effect during feedback processing.

Methods

Ethics Statement

This study was approved by the Ethics Committee of Xiangya Second Hospital. Written informed consent was obtained from all the children and their parents. All participants were informed of their right to withdraw from the study at any time.

Participants

The participants were 31 medication-free (stimulant-naive) children with ADHD (27 boys and 4 girls), aged 6–14 years, who were outpatients at the Clinic of Child Psychiatry of the Second Xiangya Hospital of Central South University. The inclusion criteria were as follows: meeting the DSM-IV-TR criteria and the Kiddie-Sads-Present and Lifetime Version (K-SADS-PL); no history of serious head injury, epilepsy, drug abuse or psychiatric disorders (e.g., schizophrenia, pervasive development disorder, mental retardation or mood disorder). The children with ADHD were classified into two subtypes: ADHD-I (n = 15), ADHD-C (n = 16). Fifteen TD children served as controls. The TD children were selected from local primary schools, and matched well with the ADHD group with respect to age and gender. The K-SADS-PL served to exclude TD children who displayed symptoms of ADHD. All participants reported normal or corrected-to-normal vision and were right-handed. Their full-scale IQ was above 80, according to the Wechsler Intelligence Scale for Children - Revised in China (C-WISC). Table 1 presents the demographic characteristics of the ADHD group and the TD group. There were no significant differences between the groups with respect to sex and mean age.

The Child Behavior Checklist (CBCL) [60,61] is a well-studied standardized instrument that asks parents to assess their child's competencies and behavioral and emotional problems on 118 specific items, using a 3-point scale (0 = "not true", 1 = "somewhat/sometimes true" and 2 = "very/often true"). The clinical scales of the CBCL contain a Total Problems score, two subscale scores (Internalizing and Externalizing Problems) and eight syndrome scales: Aggressive Behavior, Delinquent Behavior, Withdrawn, Somatic Complaints, Anxious/Depressed, Attention Problems, Social Problems and Thought Problems. The presence of psychopathology of TD children was checked by CBCL. None of the TD children scored within the clinical rage of subscales and the total problem scale of CBCL.

The symptoms at each ADHD cluster (inattention, hyperactivity/impulsivity and combined) were obtained from Swanson, Nolan, and Pelham Scale- version IV (SNAP-IV) [62], a widely used standardized measure of ADHD. The SNAP-IV scale has four subscale (Total Scores: 26 items; Inattention: 9 items, and Oppositional: 8 items). Each item is scored for severity on a 4-point scale (0 = "not at all," 1 = "just a little," 2 = "quite a bit" and 3 = "very much"). The scale was completed by the participants' parents. Individuals with 6 or more symptoms of inattention but fewer than 6 symptoms of hyper-impulsive were identified as inattentive type, participants with 6 or more hyper-impulsive symptoms and fewer than 6 symptoms of inattention were categorized as Hyper-Impulsive type, and individuals with 6 or more symptoms on both dimensions were identified as combined type.

Table 1. Group characteristics (ANOVA test statistics).

Group	TDs (n = 15)	ADHD-C (n = 16)	ADHD-I(n=15)	F value (ANOVA)	p value (ANOVA)	p value (ADHD-I v.s. ADHD-C)	p value (ADHD-I v.s. TD)	p value (ADHD-C v.s. TD)
Gender (M/F)	11/4	13/3	14/1	1.878	ns(Fisher's exact test)			
Age (yrs)	10.47(2.53)	9.50(2.34)	8.87(1.51)		ns			
IQ score	119.07(12.72)	102.53(11.27)	104.50(15.23)	7.053	0.002	0.639	0.005	0.001
SNAP-IV								
Total score	14.64(2.65)	31.38(6.82)	20.07(3.67)	47.52	<0.001	<0.001	0.03	<0.001
Inattentionitem score	7.47(1.68)	16.56(4.27)	14.67(2.72)	46.83	<0.001	0.095	<0.001	<0.001
Hyperactivity/Impulsive item score	7.00(1.46)	14.81(3.39)	5.40(2.47)	59.20	<0.001	<0.001	0.098	<0.001
Child Behavior Checklist								
total problems	34.99(11.00)	63.22(22.57)	48.01(9.20)	12.66	<0.001	0.01	0.028	<0.001
Inattention item score	3.07(2.49)	8.31(3.55)	6.27(2.87)	11.84	<0.001	0.235	0.009	<0.001
internalizing problems	2.60(1.84)	8.31(5.77)	5.13(3.34)	7.78	0.001	0.034	0.093	<0.001
externalizing problems	3.47(2.70)	16.87(10.56)	10.07(8.90)	13.67	<0.001	0.091	0.001	<0.001

Note: TD = Typically developing, SNAP-IV = The Swanson, Nolan and Pelham Rating Scale; CBCL = The Child Behavior Checklist; IQ = Intelligence Quotient.
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Children gambling paradigm

We modified the gambling task according to the children's cognitive characteristics. The experiment was programmed and executed with E-prime (Psychology Software Tools, Pittsburg, PA). The task was administered under three reinforcement-contingency conditions: reward, small punishment and large punishment, which were operationalized as score gains and losses. In each trial, the participants were presented with two "doors" side by side (3000 ms) in the center of a black screen, following a 600–1000 ms central fixation cue. Participants were told that there was a happy face behind one door and a sad face behind the other door. Participants used a response box to make their choices. After an 800 ms interval, the feedback was displayed on the screen (1500 ms) by a number that indicated what the participants gained or lost. The happy face was always "+2" (Reward, RD), while the sad face could be "−1" (Low-deduct, LD) or "-4" (High-deduct, HD). The RD:LD:HD ratio was 6:2:2. All stimuli were randomly presented. If the participants did not respond within the required time (3000 ms), while the doors were on the screen, the computer would choose one door at random.

The task took approximately 30 min and consisted of 10 blocks, with each block including 30 trials. The participants had a rest after each block. The children were told that they would be given the final reward according to the all rewards or punishments of the whole task. However, unknown to the children, happy faces and sad faces were randomly presented independent of their response. The children were simply told to "make as many scores as possible." All subjects were provided with the same amount of compensation, 50 yuan RBM.

EEG acquisition and analysis

The electroencephalography (EEG) measures were recorded continuously (−200 ms–0 ms; 500-Hz sampling rate; FCZ reference; AFZ ground; BrainAmp amplifiers) from 36 scalp sites using Ag/AgC1 electrodes mounted on an elastic cap, according to the 10–20 international system. The array included 7 midline sites (OZ, POZ, PZ, CPZ, CZ, FCZ, and FZ), 12 sites over each hemisphere (O1/O2, PO3/PO4, PO7/PO8, P3/P4, P7/P8, CP3/CP4, C3//C4, FC3/FC4, FT7/FT8, F3/F4, F7/F8 and FP1/FP2), the left and right mastoids (TP9, TP10), and the horizontal electrooculogram (EOG; FP1) and the vertical EOG (FP2) electrodes to monitor the EOG bipolarly. All electrode impedances were kept below 5 kΩ. The EOG was recorded for the purpose of artifact correction; eye movement and blink artifacts were corrected using the Gratton et al. [63] algorithm. Offline analysis was performed using Brain Vision Analyzer software 2.0 (Brain Products, Munich, Germany). All data were re-referenced to the average reference offline and digitally low-pass-filtered at 30 Hz. Epochs of 1200 ms were extracted from the continuous data file for analysis, commencing 200 ms before the feedback stimulus. Grand-average ERPs were obtained by averaging the data of individual participants according to each condition and feedback type. The average number of trials across the three feedback conditions was not significantly different across the TD, ADHD-I and ADHD-C groups [$F = 1.000$, $P = 0.371$]. The averaged number of trials was 84.49 for TD group, 78.98 for ADHD-I group, 70.85 for ADHD-C group. Additionally, there was no significant interaction effect between group and feedback [$F = 1.943$, $P = 0.156$]. The average number of trials in the reward condition was 151.33 for TD group, 133.62 for ADHD-C group, 140.07 for ADHD-I group [$F = 1.670$, $P = 0.20$]. In addition, the averaged number of trials in the small loss condition was 55.80 for TD group, 51.53 for ADHD-I group, 48.81 for ADHD-C group [$F = 2.64$, $P = 0.08$]. Lastly, the averaged number of trials during

the large loss condition was 46.33 for TD group, 45.33 for ADHD-I group, 43.00 for ADHD-C group [$F = 0.64$, $P = 0.53$].

To assess the ERP waves elicited by feedback stimuli, we measured the average amplitude of FRN (250–350 ms) from Fz to Cz sites and the average amplitude of Lpp (400 ms–800 ms) from Pz site. A three-way ANOVA was conducted on the FRN component. ANOVA factors were feedback type (larger loss, smaller loss and gain feedback), electrode site (Fz, Cz) and group (TD, ADHD-C and ADHD-I participants). The same analysis was conducted for the LPP at Pz. The ERP data were analyzed using Brain Products Analyzer software. The degrees of freedom of the F-ratio were corrected according to the Greenhouse-Geisser method.

Results

The grand-average ERPs depicted in Figure 1. The topographical map of FRN in TD, ADHD-C and ADHD-I group was shown in Figure 2. The 3 (feedback type: large loss, small loss and gain feedback)×2 (electrode: Fz, Cz)×3 (group: TD, ADHD-C and ADHD-I participants) ANOVA revealed a significant effect of feedback type by group interaction effect during 250–350 ms [$F_{(4, 86)} = 2.49$, $P = 0.049$]. When controlled for age and IQ score, the feedback type by group interaction effect was still marginally significant [$F_{(4, 86)} = 2.43$, $P = 0.054$]. To further elucidate this interaction, we analyzed the feedback type effect in each group. In the TD group, the main effect of feedback type was significant [$F_{(2, 28)} = 4.16$, $P = 0.032$], and large loss feedback elicited a larger negativity than did gain feedback [$F_{(1, 14)} = 10.11$, $P = 0.007$] or small loss feedback [$F_{(1, 14)} = 4.34$, $P = 0.056$], whereas no significant difference was observed between small loss and gain feedback [$F_{(1, 14)} = 0.59$, $P = 0.46$]. In the ADHD-C group, the main effect of feedback type was significant [$F_{(2, 30)} = 4.88$, $P = 0.023$], large loss feedback elicited a larger negativity than did small loss feedback [$F_{(1, 15)} = 19.29$, $P = 0.001$]. However, no significant differences were observed between large loss and gain feedback [$F_{(1, 15)} = 0.1$, $P = 0.33$], or between small loss and gain feedback [$F_{(1, 15)} = 3.09$, $P = 0.1$]. In the ADHD-I group, no significant main effect of feedback type was observed [$F_{(2, 28)} = 0.91$, $P = 0.41$]. In addition, we also broke down the feedback type by group interaction effect by analyzing the group effect during each feedback condition. No significant group effects observed during big loss feedback [$F_{(2, 43)} = 2.05$, $P = 0.14$], small loss feedback [$F_{(2, 43)} = 0.03$, $P = 0.97$], and gain feedback [$F_{(2, 43)} = 0.47$, $P = 0.63$] conditions.

In order to analyze the large loss and small loss feedback effect, we further subtracted the gain feedback from large loss and small loss feedback. The 2 (feedback type: large loss vs gain, small loss vs gain)×2 (electrode: Fz, Cz)×3 (group: TD, ADHD-C and ADHD-I participants) ANOVA revealed a significant effect of feedback type by group interaction effect during 250–350 ms [$F_{(2, 43)} = 6.17$, $P = 0.004$]. To break down this interaction, we further analyzed the feedback type effect in each group, respectively. In the TD group, the main effect of feedback type was significant, and the large loss feedback effect is larger than small loss feedback effect [$F_{(1, 14)} = 10.11$, $P = 0.007$]. In the ADHD-C group, the main effect of feedback type was significant, and the large loss feedback effect is larger than small loss feedback effect [$F_{(1, 14)} = 19.29$, $P = 0.001$]. In the ADHD-I group, no significant main effect of feedback type was observed [$F_{(1, 14)} = 0.34$, $P = 0.57$].

In addition, the LPP component was also measured at 100 ms intervals during the 400–800 ms intervals at the Pz electrode site. When controlled for age and IQ score, the main effect of feedback
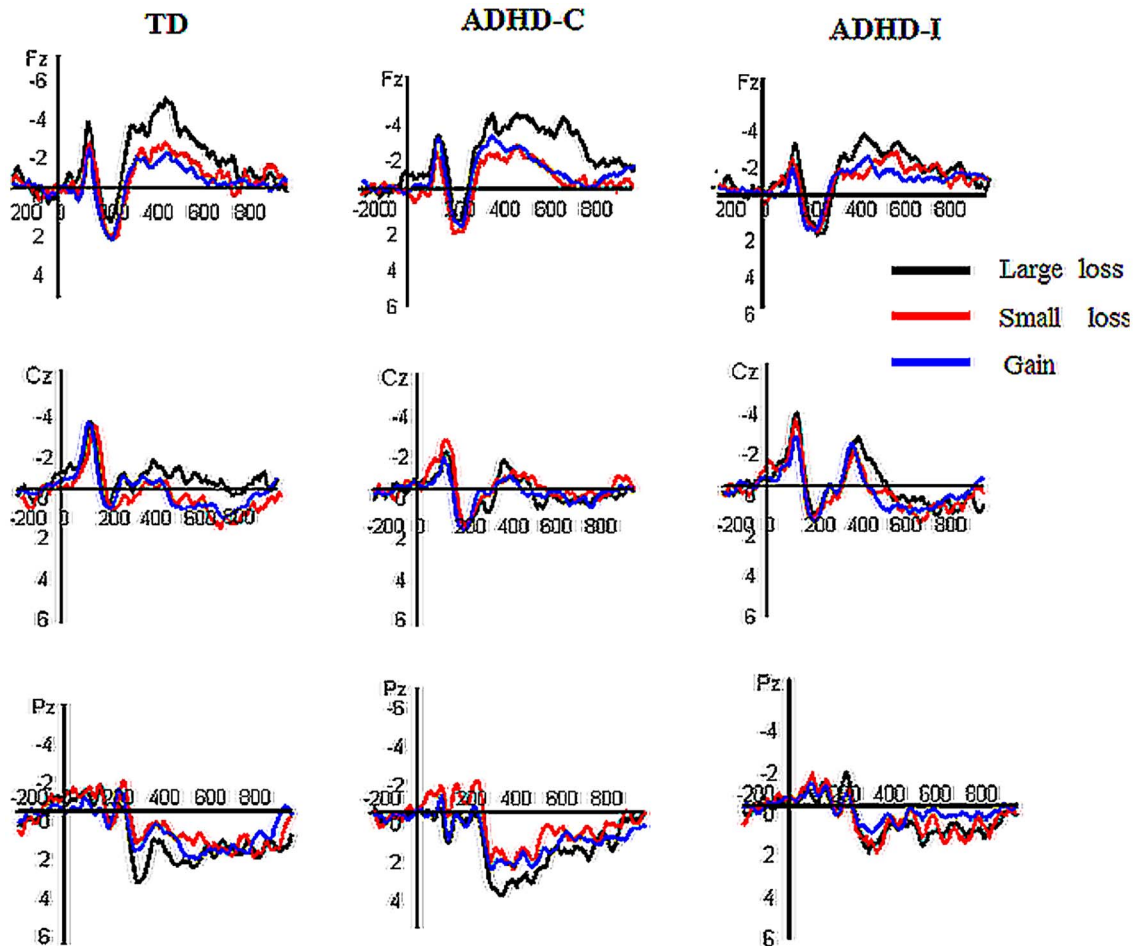
Figure 1. Grand-average of ERPs at Fz, Cz and Pz for the large loss (black lines), small loss (red lines) and gain (blue lines) feedback conditions in the TD, ADHD-C and ADHD-I groups.
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type [$F_{(2, 82)} = 0.21$, $P = 0.8$] and the feedback type by group interaction effect were not significant during 400–500 ms [$F_{(4, 82)} = 1.37$, $P = 0.25$], but there was a significant main effect of group [$F_{(2, 41)} = 4.15$, $P = 0.023$] during 400–500 ms. The LPP differences between the TD and ADHD-C [$F_{(1, 27)} = 2.69$, $P = 0.11$], TD and ADHD-I [$F_{(1, 26)} = 0.39$, $P = 0.54$] groups were not significant, but the LPP was larger in the ADHD-C group than in ADHD-I groups [$F_{(1, 27)} = 9.94$, $P = 0.004$]. However, the main effect of feedback type [500–600 ms: $F_{(2,}$

$_{82)} = 1.27$, $P = 0.29$, 600–700 ms: $F_{(2, 82)} = 0.34$, $P = 0.69$, 700–800 ms: $F_{(2, 82)} = 0.39$, $P = 0.66$], group [500–600 ms: $F_{(2, 41)} = 2.18$, $P = 0.13$, 600–700 ms: $F_{(2, 41)} = 0.72$, $P = 0.49$, 700–800 ms: $F_{(2, 41)} = 0.59$, $P = 0.56$] and the feedback type by group interaction effect [500–600 ms: $F_{(4, 82)} = 1.2$, $P = 0.32$, 600–700 ms: $F_{(4, 82)} = 1.31$, $P = 0.27$, 700–800 ms: $F_{(4, 82)} = 1.35$, $P = 0.26$] were all non-significant during each 100 ms interval of the 500–800 ms intervals.

Discussion

This is the first study to investigate the effect of feedback valence (reward or punishment) and punishment magnitude (small or large) on FRN and LPP in two subtypes of ADHD (ADHD-C and ADHD-I) compared to TD children during a children's gambling task. Analysis of the FRN interval revealed that TD children elicited a more negative FRN potential to large losses than to small losses or gains, which is consistent with previous studies showing larger FRN amplitudes to omitted gains and omitted losses in TD children [31], demonstrating that TD children exhibited enhanced monitoring of feedback when it was made more salient. These observations replicated prior findings that humans (including TD children) are especially sensitive to emotionally negative events, which are preferentially processed relative to neutral and positive events [49–51] and that humans are sensitive to magnitude
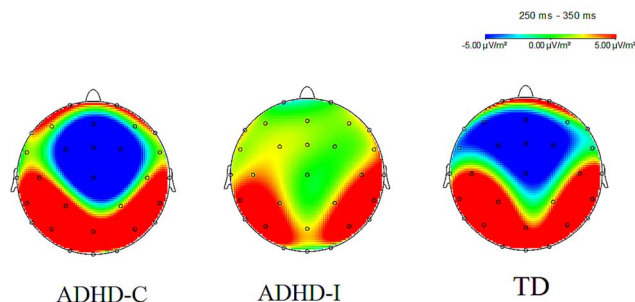

Figure 2. The topographical map of FRN in the TD, ADHD-C and ADHD-I groups in the phase of 250–350 ms.
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differences in negative stimuli [56,58,64]. The children with ADHD-C also showed an enhanced FRN to large losses compared to that to small losses and gains, which is consistent with the finding of an enhanced sensitivity to unfavorable outcomes in children with ADHD [30], probably due to abnormalities in mesolimbic reward circuits. Affective evaluation and the assessment of future consequence of the feedback signal seems to be altered in ADHD. The children with ADHD-C did not differ in their feedback FRN amplitude from TD children, which suggests that children with ADHD are described as benefiting from renforcement contingencies from a clinical perspective. Reinforcement has proved to be highly effective in the treatment of ADHD [65] and that reinforcement contingencies are found to normalize behavior that characterizes ADHD [25]. Therefore, similar to TD children, children with ADHD-C are sensitive to punishment and magnitude differences in punishment. This finding may be explained by the fact that humans are equipped with a special sensitivity to negative stimuli as a result of evolutionary adaptation, as illustrated by the negative bias account [52,56]. Another plausible explanation is that the motivational style of children with ADHD-C is characterized by competitiveness and a desire to be perceived as superior to others, which might result in enhanced sensitivity to negative outcomes [40], therefore, children with ADHD-C paid more attention to the larger losses. However, the FRN effect was absent under all conditions in children with ADHD-I, even under the large punishment condition, which contradicted the bias for emotionally negative events in humans. The absence of the FRN effect in children with ADHD-I may be explained by their nature of the cognitive-attention deficit, which is characterized as drowsy, sluggish and less alert [36,37]. And compared to children with ADHD-C, the children with ADHD-I show different motivational style, possible less uncooperative and more passive in the learning style [38]. The FRN effect was elicited both in children with ADHD-C and in TD children, but not in children with ADHD-I, which may be attributed to the severe inattention problems, as the core symptom in children with ADHD-I, who suffer from a deficit detection of motivationally significant cues. However, one may question that both ADHD-C and ADHD-I showed similar symptoms of inattention, consequently this inattention explanation is probably unconvincing. It is worth note that ADHD-C children are characterized not only by inattention problems but also by competitiveness and perceived self-superiority. As discussed above, the latter characteristics are associated with enhanced sensitivity to negative outcomes which in turn enhances feedback negativity in brain potentials. This may constitute a compensating feature for ADHD-C children and explains why ADHD-C showed a robust FRN effect that was absent in ADHD-I, despite similar inattention problems in both groups. Also, this compensatory mechanism may explain why ADHD-C and TD children showed similar FRN effect, despite the inattention problems in the former group.

The present study observed an LPP component only in the early phase (400–500 ms) in children with ADHD-C, who showed an enhanced LPP amplitude to feedback indicating larger losses than TD children and children with ADHD-I. Furthermore, LPP has been reported to reach the largest amplitudes at 500–700 ms post-stimulus and to last for several hundred milliseconds [40]; In the current study, the LPP was larger in the ADHD-C group than in ADHD-I group [$F(1.27) = 9.94$, $P = 0.004$]. This was consistent with a prior study by Carlson and colleague [38] implying that individuals with ADHD-C were motivated by competitiveness and desired to be suprior to others which might contribute to greater sensitivity to larger losses. However, LPP emerged only in the 400–500 ms interval rather than in a longer time epoch. Thus, this observation should be considered as tentative and awaits future studies to be replicated.

There are some limitations to the interpretation of the current findings. First, of our study was the relatively small sample size, especially for female participants. There was only one girl in the ADHD-I group, three girls in the ADHD-C group and four girls in the TD group, which did not make it possible to examine the potential role of sex. Second, in our study we only recruited children with two subtypes of ADHD (ADHD-I and ADHD-C), and not the hyperactive/impulsive subtype (ADHD-H). Thus, we could assess only differences between the ADHD-I and ADHD-C subtypes. Finally, the children's gambling paradigm used in the present study was designed only for one reward condition (+2), and two different punishment conditions (−4 or −1). We probably should have designed two reward conditions. Future studies are needed to investigate whether the same results can be obtained when reward and punishment have an equal number of conditions.

In conclusion, this is the first study to investigate to the effect of feedback valence and punishment magnitude on feedback negative and LPP in two subtypes of ADHD (ADHD-C and ADHD-I). In TD children and children with ADHD-C, large loss feedbacks evoked more negative FRN amplitudes than small loss feedbacks, suggesting that children with ADHD-C may keep intact brain sensitivity to the punishment and its magnitude. In contrast with the above two groups, the above FRN effect was absent in children with ADHD-I, suggesting that children with ADHD-I are significantly impaired in neural sensitivity to the feedback stimuli and in particular, to punishment. Secondly, the Late positive potential amplitudes were larger in children with ADHD-C in comparison with those with ADHD-I, regardless of feedback valence and magnitude. Therefore, we speculate that FRN, rather than LPP, is a reliable index to detect this difference across different ADHD-subcategories.

Author Contributions

Conceived and designed the experiments: XL JG. Performed the experiments: LS. Analyzed the data: JY SW. Contributed reagents/materials/analysis tools: XC. Wrote the paper: JG JY.

References

1. American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders. 4th ed., revised. Washington, DC: Author.
2. Polanczyk G, de Lima MS, Horta BL, Biederman J, Rohde LA (2007) The worldwide prevalence of ADHD: A systematic review and metaregression analysis. Am J Psychiatry 164: 942–948
3. Centers for Disease Control, National Center for Prevention Services (US), Division of Tuberculosis Elimination, National Center for HIV (2001) Reported tuberculosis in the United States. US Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Center for Prevention Services, Division of Tuberculosis Elimination.
4. Gau SS, Chong MY, Chen TH, Cheng AT (2005) A 3-year panel study of mental disorders among adolescents in Taiwan. Am J Psychiatry 162: 1344–1350.
5. Woo BSC, Rey JM (2005) The validity of the DSM-IV subtypes of attention-deficit/hyperactivity disorder. Aust N Z J Psychiatry 39:344–353.
6. Douglas VI (1989) Can Skinnerian theory explain attention deficit disorder? A reply to Barkley. Attention deficit disorder: Current concepts and emerging trends in attentional and behavioral disorders of childhood 4: 235–254.
7. Haenlein M, Caul WF (1987) Attention deficit disorder with hyperactivity: a specific hypothesis of reward dysfunction,Journal of the American Academy of Child and Adolescent Psychiatry 26: 356–362.

8. Sagvolden T, Aase H, Zeiner P, Berger D (1998) Altered reinforcement mechanisms in attention-deficit/hyperactivity disorder. Behavioural Brain Research 94: 61–71.

9. Quay HC (1988) Attention deficit disorder and the behavioral inhibition system: The relevance of the neuropsychological theory of Jeffrey A. Gray. Attention deficit disorder: Criteria, cognition, intervention 117–125.

10. Quay HC (1988b) The behavioral reward and inhibition system in childhood behaviour disorder. In Bloomingdale LM (Ed.), Attention Deficit Disorder 3: 176–185.

11. Quay HC (1988c) Reward, inhibition, and attention deficit hyperactivity disorder. Journal of the American Academy of Child and Adolescent Psychiatry 27: 262–263.

12. August GJ (1987) Production deficiencies in free recall: A comparison of hyperactive, learning-disabled, and normal children. Journal of Abnormal Child Psychology 15: 429–440.

13. Barber MA, Milich R, Welsh R (1996) Effects of reinforcement schedule and task difficulty on the performance of attention deficit hyperactivity disordered and control boys. Journal of Clinical Child Psychology 25: 66–76.

14. Borcherding B, Thompson K, Kruesi M, Bartko J, Rapoport JL, et al. (1998) Automatic and effortful processing in attention deficit/hyperactivity disorder. Journal of Abnormal Child Psychology 16: 333–345.

15. Van der Meere J, Shalev R, Borger N, Gross-Tsur V (1995) Sustained attention, activation and MPH in ADHD: A research note. Journal of Child Psychology and Psychiatry 36: 697–703.

16. Douglas VI, Parry PA (1994) Effects of reward and nonreward on frustration and attention in attention-deficit disorder. J Abnorm Child Psychol 22: 281–302.

17. Sergeant JA (2000) The cognitive-energetic model: An empirical approach to attention-deficit hyperactivity disorder. Neurosci Biobehav Rev 24: 7–12.

18. Luman M, Oosterlaan J, Sergeant JA (2005) The impact of reinforcement contingencies on AD/HD: A review and theoretical appraisal. Clinical Psychology Review 25: 183–213.

19. Sagvolden T, Johansen EB, Aase H, Russell VA (2005) A dynamic developmental theory of attention-deficit/hyperactivity disorder (ADHD) predominantly hyperactive/impulsive and combined subtypes. Behav Brain Sci 28: 397–468.

20. Sonuga-Barke E (2003) The dual pathway model of AD/HD: An elaboration of neurodevelopmental characteristics. Neurosci Biobehav Rev 27: 593–604.

21. Tripp G, Wickens J (2008) Research review: Dopamine transfer deficit: A neurobiological theory of altered reinforcement mechanisms in ADHD. Journal of child psychology and psychiatry 49: 691–704.

22. Frank M, Santamaria A, O'Reilly R, Willcutt E (2007) Testing computational models of dopamine and noradrenaline dysfunction in attention deficit/hyperactivity disorder. Neuropsychopharmacology 32: 1583–1599.

23. Nigg JT, Casey BJ (2005) An integrative theory of attention-deficit/hyperactivity disorder based on the cognitive and affective neurosciences. Dev Psychopathol 17: 785–806.

24. Patterson C, Newman J (1993) Reflectivity and learning from aversive events - toward a psychological mechanism for the syndromes of disinhibition. Psychol Rev 100: 716–736.

25. Hupp SD, Reitman D, Northup J, O'Callaghan P, LeBlanc M (2002) The effects of delayed rewards, tokens, and stimulant medication on sportsmanlike behavior with ADHD-diagnosed children. Behavior Modification 26: 148–162.

26. Kelly ML, McCain AP (1995) Promoting academic performance in inattentive children: The relative efficacy of school-home notes with and without response cost. Behavior Modification 19: 76–85.

27. Pelham PA, Carlson C, Sams SE, Vallano G, Dixon MJ, et al. (1993) Separate and combined effects of methylphenidate and behavior modification on boys with attention deficit–hyperactivity disorder in the classroom. Journal of Consulting and Clinical Psychology 61: 506–515.

28. Carlson CL, Mann M, Alexander DK (2000) Effects of reward and response cost on the performance and motivation of children with ADHD. Cognitive Therapy and Research 24: 87–98.

29. Carlson CL, Tamm L (2000) Responsiveness of children with attention deficit hyperactivity disorder to reward and response cost: Differential impact on performance and motivation. J Consult Clin Psychol 68: 73–83.

30. van Meel CS, Oosterlaan J, Heslenfeld DJ, Sergeant JA (2005) Telling good from bad news: ADHD differentially affects processing of positive and negative feedback during guessing. Neuropsychologia 43:1946–1954.

31. van Meel CS, Heslenfeld DJ, Oosterlaan J, Luman M, Sergeant JA (2011) ERPs associated with monitoring and evaluation of monetary reward and punishment in children with ADHD. Journal of Child Psychology and Psychiatry 9: 942–953.

32. Groen Y, Tucha O, Wijers AA, Althaus M (2013) Processing of continuously provided punishment and reward in children with ADHD and the modulating effects of stimulant medication: an ERP study. PLOS ONE 8: e59240.

33. Scheres A, Milham MP, Knutson B, Castellanos FX (2007) Ventral striatal hyporesponsiveness during reward anticipation in attention- deficit/hyperactivity disorder. Biol Psychiatry 61: 720–724.

34. Conzelmann A, Mucha RF, Jacob CP, Romanos J, Gerdes AB, et al. (2009) Abnormal affevtive responsiveness in attention-deficit/hyperactivity disorder: subtype differences.Biol Psychiatry 65: 578–585.

35. Power TJ, Costigan TE, Eiraldi RB, Leff SS (2004) Variations in anxiety and depression as a function of ADHD subtypes defined by DSM-IV: Do subtype differences exist or not? J Abnorm Child Psychol 32:27–37.

36. Carlson CL, Tamm L (2000) Responsiveness of children with ADHD to rewardand response cost: Differentialim-pact on performance and motivation. Journal of Consulting and ClinicalPsychol-ogy 68: 73–83.

37. Lahey BB, Carlson CL, Frick PE (1997) Attention deficit disorder without hyperactivity. In I. A.Widiger, A.I. Frances, H.A.Pincus, R.Ross, M.B.First, &W.Davis (Eds.), DSM-IV source book (Vol. 3, pp. 163–188). Washington,DC: American Psychiatric Association.

38. Carlson CL, Booth JE, Shin M, Canu WH (2002) Parent-, teacher-, and self-rated motivational styles in ADHD subtypes. J Learn Disabil 35: 104–113.

39. Edel MA, Enzi B, Witthaus H, Tegenthoff M, Peters S, et al. (2013) Differential reward processing in subtypes of adult attention deficit hyperactivity disorder. J Psychiatr Res 47: 350–356.

40. Yuan JJ, Chen J, Yang JM, Ju E, Norman GJ, et al. (2014) Negative mood state enhanced the susceptibility to unpleasant events: neural correlate from a music-primed emotion classification task. PLOS ONE 9: E89844.

41. Foti D, Hajcak G (2008) Deconstructing reappraisal: Descriptions preceding arousing pictures modulate the subsequent neural response. J Cogn Neurosci 20: 977–988.

42. Krompinger JW, Moser JS, Simons RF (2008) Modulations of the electrophysiological response to pleasant stimuli by cognitive reappraisal. Emotion 8:132–137.

43. Moser JS, Hajcak G, Bukay E, Simons RF (2006) Intentional modulation of emotional responding to unpleasant pictures: an ERP study. Psychophysiology 43: 292–296.

44. Hajcak G, Nieuwenhuis S (2006) Reappraisal modulates the electrocortical response to unpleasant pictures. Cogn Affect Behav Neurosci 6:291–297.

45. Cuthbert BN, Schupp HT, Bradley MM, Birbaumer N, Lang PJ (2000) Brain potentials in affective picture processing: Covariation with autonomic arousal and affective report. Biological Psychology 52: 95–111.

46. Hajcak G, Moser JS, Simons RF (2006) Attending to affect: Appraisal strategies modulate the electrocortical response to arousing pictures. Emotion 6: 517–522.

47. Schupp HT, Cuthbert BN, Bradley MM, Cacioppo JT, Ito T, et al. (2000) Affective picture processing: The late positive potential is modulated by motivational relevance. Psychophysiology 37: 257–261.

48. Groen Y, Wijers A, Mulder L, Waggeveld B, Minderaa R, et al. (2008) Error and feedback processing in children with ADHD and children with autistic spectrum disorder: An EEG event-related potential study. Clinical neurophysiology 119: 2476–2493.

49. Cacioppo JT, Gardner WL (1999) Emotion. Annual Review of Psychology 50:191–214.

50. Delplanque S, Lavoie ME, Hot P, Silvert L, Sequeira H (2004) Modulation of cognitive processing by emotional valence studied through event-related potentials in humans. Neuroscience Letters 356:1–4.

51. Delplanque S, Silvert L, Hot P, Sequeira H (2005) Event-related P3a and P3b in response to unpredictable emotional stimuli. Biological Psychology 68:107–120.

52. Huang YX, Luo YJ (2006) Temporal course of emotional negativity bias: An ERP study. Neuroscience Letters 398: 91–96.

53. Hansen CH, Hansen RD (1988) Finding the face in the crowd: an anger superiority effect. Journal of Personality and Social Psychology 54:917–924.

54. Pratto F, Johu OP (1990) Automatic vigilance: The attention-grabbing power of negative social information. Journal of Personality and Social Psychology 61: 380–391.

55. Wentura D, Rothermund K, Bak P (2000) Automatic vigilance:The attention-grabbing power of approach- and avoidance-related social information. Journal of Personality and Social Psychology 78: 1024–1037.

56. Yuan JJ, Zhang QL, Chen A, Li H, Wang QH, et al. (2007) Are we sensitive to valence differences in emotionally negative stimuli? Electrophysiological evidence from an ERP study. Neuropsychologia 45: 2764–2771.

57. Yuan JJ, Lu H, Yang JM, Li H (2011) Do not neglect small troubles: moderately negative stimuli affect target processing more intensely than highly negative stimuli. Brain research 1415: 84–95.

58. Yuan JJ, Meng XX, Yang JM, Yao GH, Hu L, et al. (2012) The valence strength of unpleasant emotion modulates brain processing of behavioral inhibitory control: neural correlates. Biological Psychology 89: 240–251.

59. Althaus M, Groen Y, Wijers A, Minderaa R, Kema I, et al. (2010) Variants of the SLC6A3 (DAT1) polymorphism affect performance monitoring-related cortical evoked potentials that are associated with ADHD. Biol Psychol 85: 19–32.

60. Achenbach TM (1991). Integrative guide for the 1991 CBCL/4-18, YSR, and TRF profiles[M]. Burlington: Department of Psychiatry, University of Vermont.

61. Achenbach TM, Dumenci L, Rescorla LA (2003) DSM-oriented and empirically based approaches to constructing scales from the same item pools. J Clin Child Adolesc Psychol 32:328–340.

62. Swanson JM, Kraemer HC, Hinshaw SP, Arnold LE, Conners CK (2001) Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. J Am Acad Child Adolesc Psychiatry 40:168–179.

63. Gratton G, Coles MGH, Donchin E (1983) A new method for off-line removal of ocular artifact. Electroencephalogr Clin Neurophysiol 55: 468–484.

64. Yuan JJ, Yang JM, Meng XX, Yu FQ, Li H (2008) The valence strength of negative stimuli modulates visual novelty processing: electrophysiological evidence from an event-related potential study. Nueroscience 157: 524–531.

65. Barkley RA (2002) Psychosocial treatments for attention-deficit/hyperactivity disorder in children. Journal of Clinical Psychiatry 63: 36–43.