LITERATURE REVIEW: Childhood Abuse, High-Risk Behaviour and Reward Processing: A Systematic Review

EMPIRICAL PAPER: Reward Processing and High-Risk Behaviour in Adolescents with a History of Childhood Abuse

Submitted by **Pia Pechtel**, to the University of Exeter

as a thesis for the degree of **Doctor of Clinical Psychology**, April 29th 2016

I certify that all material in this thesis which is not my own work has been identified and that no material has previously been submitted and approved for the award of a degree by this or any other University.

Signature: 

Author's Declaration

Pia Pechtel completed the literature review independently. For the empirical paper, approximately half of the data collection was partially completed by Loes Koorenhof, an associate research fellow, who was employed and supervised by Pia Pechtel. The analyses and the write-up of the empirical paper were completed independently by Pia Pechtel.

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SCHOOL OF PSYCHOLOGY

DOCTORATE IN CLINICAL PSYCHOLOGY

LITERATURE REVIEW

Childhood Abuse, High-Risk Behaviour and Reward Processing: A Systematic Review

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Abstract

Objective: Childhood abuse (CA) is commonly associated with increased frequency of high-risk behaviours (HRB) in adolescence. Similarly, research has highlighted links between CA and blunted responses to reward. To date, little attention has been devoted to examine if altered reward processes may also be linked to increased engagement in HRB. To explore this hypothesis, this systematic review collated research that investigated the relationship among CA, reward processes and HRB. Specifically, the review addressed the question: Are HRB associated with altered reward processes in children and adults with a history of CA?

Method: Behavioural and neurobiological studies on CA, reward processing and HRB in children and adults were selected from multidisciplinary and subject-specific databases published prior to the 1st of March 2016. The systematic literature search yielded 271 records with 198 non-duplicated results. Screening of 14 full-text publications led to five eligible studies synthesized in this review.

Results: Results confirmed impaired reward learning and increased HRB in those with a history of CA. Associations of blunted anticipatory or consummatory reward processing and HRB in individuals with CA remained inconclusive.

***Conclusions*:** Reward learning appears to be associated with CA. Further research is required to explore the relationship between reward processes and HRB. Understanding CA from a neurodevelopment perspective is a critical step to developing effective intervention strategies to reduce HRB.

Keywords*: child abuse, reward, high-risk behaviour, systematic review*

Introduction

This review explores the potential links between childhood abuse (CA), high-risk behaviour (HRB) and reward processing in adolescents. Although an array of research has demonstrated associations between CA and HRB, and CA and disrupted reward processing, to date there has been no systematic review of research evidence to examine if neural responses to reward could mediate the relationship between childhood stress and high-risk behaviour. To address this gap, the current paper will systematically review behavioural and neurobiological research that investigates the relationships between CA, reward processing and HRB.

Childhood Abuse, HRB and Reward Processing

According to the HM Government safeguarding protocol (2015), CA is defined as physical, emotional or sexual abuse in which an individual or a group of individuals inflict harm to a child under the age of 18. Epidemiological studies have linked CA with chronic levels of stress and mental health difficulties across the life span (Green et al., 2010; Kilpatrick et al., 2003). From a biological perspective, acute stress activates the hypothalamic-pituitary-adrenal (HPA) axis to mobilize resources and ensure survival (Gunnar & Quevedo, 2007; Yehuda & Seckl, 2011). Chronic levels of stress, however, as expected to occur during CA, can lead to aberrant reactivity of the HPA axis and through an excessive release of glucocorticoids (cortisol) can disturb the structural and functional maturation of brain regions developing at the time (Gunnar & Quevedo, 2007; Lupien,

McEwen, Gunnar, & Heim, 2009). One of the neural networks particularly vulnerable to developmental perturbation due to CA is the brain's reward system (Teicher & Samson, 2016).

As a major risk factor for mental illness, childhood adversity has been associated with 30-70% of the population risk for substance abuse, suicide attempts, depression and anxiety disorders (Teicher & Samson, 2013). Individuals exposed to CA may engage in an array of HRB such as substance misuse (Kendler et al., 2000), self-harm (Pechtel, Evans, & Podd, 2011), unsafe sexual behaviour (Messman-Moore, Walsh, & DiLillo, 2010; Reid, 2011) and dysfunctional eating habits (Smolak & Murnen, 2002). Although HRB are thought to initially relieve CA-related distress, these behaviours can have detrimental effects on a person's emotional and physical wellbeing (Messman-Moore, Ward, & Brown, 2009). However, relatively little is known about the behavioural and neurobiological mechanisms that link CA and maladaptive behaviours.

The ability to evaluate reward-predicting cues, process reward stimuli and learn from reward is critical to optimize decision-making, and may be impaired in those who engage in HRB (Ernst & Paulus, 2005; Pechtel & Pizzagalli, 2011). According to the Research Domain Criteria (RDoc) matrix, the positive valence or reward system suggests at least eight partially dissociable constructs (https://www.nimh.nih.gov/research-priorities/rdoc/constructs/rdoc-matrix.shtml). Important for the current review are (1) the anticipatory phase of reward processing or '*wanting'*, (2) the consummatory phase of reward processing or '*liking'* and (3) the process of adjusting behaviour to optimize outcome based on

reward information or '*reward learning'* (Berridge & Kringelbach, 2008; Berridge, Robinson, & Aldridge, 2009). Reward 'wanting' attributes incentive salience to reward-predicting cues, which affects a person's motivation to engage with the stimulus. Reward 'liking' refers to the hedonic value or experienced pleasure when exposed to a reward (Berridge et al., 2009). Reward learning is the reinforcement process by which individuals acquire information to predict positive outcomes and modify their behaviour to optimize outcomes (Frank, Seeberger, & O'Reilly, 2004). Reward processes rely on dopaminergic pathways and key components of the reward circuit, such as the ventral and dorsal striatum and prefrontal cortex regions, which undergo significant changes throughout childhood and adolescence leaving it vulnerable to developmental disruptions due to CA (Forbes & Dahl, 2005; Giedd et al., 2009).

Models and Theories

Although research has shown relationships between (1) CA and HRB, and (2) CA and reward processing, little attention has been devoted to the question of whether neural responses to reward serve as a functional mechanism linking CA to HRB. Interestingly, this hypothesis is tentatively discussed in recent neurobiological and neurodevelopment models. In their neurobiological model of addiction, Koob and Le Moal (2005) argue that stress experienced after excessive drug use dampens neural responses to stimuli that are typically considered rewarding (i.e., natural rewards). Koob and Le Moal (2005) hypothesize that this blunted reward experience elicits negative emotions, which

then motivates individuals to further use substances in an attempt to alleviate distress. Over time, drug use is therefore not maintained by a sensitized reward state but rather is motivated by a process of negative reinforcement to seek relief from an aversive state (Koob & Le Moal, 2005). Although the Koob and Le Moal (2005) model associates blunted reward processing with stress following drug use, the same principle may apply when stress is experienced due to CA. It is important to note that the Koob and Le Moal's (2005) model does not assume an orthogonal structure of positive and negative affect, but rather that reduced positive affect can produce increased negative affect. This theory is at odds with some other prominent models of emotion, such as Gray's Reinforcement Sensitivity Theory of reward and punishment sensitivity (Gray & McNaughton, 2000) or Clark and Watson's (1991) tripartite model of positive affect and negative affect, both of which consider positive and negative affect to be broadly orthogonal. Although some research suggests that positive and negative affect are relatively orthogonal (Laurent, Catanzaro & Joiner, 2004), overall findings are mixed showing significant correlations between negative affect and positive affect in children and young people (Crook, Beaver & Bell, 1998). Indeed, some research suggested that higher associations of positive and negative affect might be found early in life compared to adulthood (Anderson & Hope, 2008).

Support for Koob and Le Moal's hypothesis is found in neurodevelopmental models, which argue that the brain's reward system is particularly vulnerable to the neurotoxic effects of cortisol release elicited by CA (Andersen & Teicher, 2008; Arnsten & Rubia, 2012; Davey, Yucel, & Allen, 2008; Forbes & Dahl, 2005;

Nelson, Leibenluft, McClure, & Pine, 2005; Spear, 2013). The sensitive period framework would add that reward regions are particularly vulnerable to effects of CA if the timing of the abuse coincides with the developmental growth spurts of the brain's reward system (Teicher & Samson, 2016). These changes may dampen an individual's ability to experience pleasure from natural reward and increase negative emotions from which HRB could provide relief.

In sum, research supports relationships between CA and HRB as well as CA and disrupted reward processing. Neurobiological and neurodevelopmental models hypothesize a mediating role of blunted reward processes in use of HRB, which may represent the functional link between CA and HRB. Therefore, the current systematic review aims to answer the question: *"Are high-risk behaviours associated with altered reward processes (anticipatory, consummatory or learning of reward) in individuals with a history of CA?"*

Methods

A systematic review is a critical building block in the search for evidence-based information (National Institute for Health and Care Excellence, 2012). It uses explicit, pre-defined criteria to identify and evaluate the outcomes of multiple studies to increase the reliability and accuracy of the concluded information (CRC Guidance, 2009). To this end, this systematic review followed the Preferred Reporting Items for Systematic Review and Meta-analysis Protocol (PRISMA-P) to guide identification, screening, eligibility and synthesis of studies (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group, 2009; Moher et al., 2015).

Eligibility Criteria

Characteristics of studies included in this review are based on PECO (Population, Exposure, Comparator, Outcome) criteria as outlined in Table 1. Study designs eligible for the review include (1) cross-sectional experimental studies in which measures of reward functioning are studied in relation to measures of HRB and CA, (2) neuroimaging studies investigating structural changes to the reward circuitry in relation to HRB and CA, and (3) prospective or longitudinal studies that measure at least one variable at two different points in time in relation to the remaining variables.

Table 1

Inclusion and Exclusion Criteria for Eligibility for Systematic Literature Review

INCLUSION	EXCLUSION
Population • Human (all ages)	**Participants** • Learning Disabilities • Animal studies
Exposure • Childhood abuse (see operationalization)	**Exposure** • Questionnaire only • Qualitative studies
Comparator • Non-abused controls OR • No high-risk behaviour controls	**Limitations** • Languages other than English or German
Outcome • Behavioural measures of anticipatory reward, consummatory reward or reward learning *AND/OR* • MRI, EEG, PET • High-risk behaviour (see operationalization)	**Outcomes** • Non-reward processes

Note. MRI = Magnetic Resonance Imaging, EEG = Electroencephalography, PET = Positron Emission Tomography

In line with the national safeguarding protocol, we operationalized CA as exposure to physical, sexual or emotional abuse characterized by actions or words of commission expressed by an individual or a group to cause harm to a child under the age of 18 years (HM Goverment, 2015). For this review, this does not include acts of omission such as child neglect, which is characterized by the failure to protect or attend to the essential needs of a child. Typical measures of CA include standardized self-report measures such as the Childhood Trauma Questionnaire (Bernstein et al., 1994) or the Adverse Childhood Experience Questionnaire (Felitti et al., 1998).

Reward processing was operationalized as a behavioural or neurobiological response during the anticipation of reward, delivery of reward or as a result of receiving a reward (learning). Reward processes are commonly measured using behavioural paradigms such as the Card-Guessing Task (Forbes et al., 2009) or the Probabilistic Stimulus Selection Task (Frank et al., 2004). These can be completed while the person is undergoing an electroencephalogram (EEG), magnetic resonance imaging scan (MRI) or positron emission tomography (PET). Studies may also include assessment of structural changes of the brain's reward system implicated in these reward processes (i.e., striatum, orbitofrontal cortex).

Finally, HRBs were operationalized as behaviours associated with high risk of negative consequences for the person's health, safety or wellbeing (Weller, Leve, Kim, Bhimji, & Fisher, 2015). These include alcohol misuse, illicit substance use, risky sexual behaviours, self-harm, disordered eating patterns associated with bulimia and anorexia nervosa, and behaviours associated with

antisocial or conduct difficulties (i.e., gambling, reckless driving, vandalism, theft, aggression). Although this is not a comprehensive list of all HRB, I focused on behaviours included in the standardized assessment measures such as Risky Behaviour Questionnaire (Auerbach & Gardiner, 2012) and the Youth Self Report Questionnaire (Achenbach, 1991).

Information Sources

Relevant literature was identified using a computerized core search of multidisciplinary and subject-specific databases supplied by Ovid[1] and Web of Science[2]. Supplementary searches were conducted using the NSPCC library, Open Thesis and Electronic Thesis Online System (EThOS), UK Clinical Research Network Portfolio Database, and Grey Literature Report. Databases were searched from the beginning point of each database through to 1st March 2016.

Search Strategy

In line with the Cochrane Library guidance (Higgins & Green, 2011), an initial scoping review was used to generate search terms that could be used in combination. Keywords of seminal publications (Dillon et al., 2009; Metha et al.,

[1] Ovid included the following databases: PsycArticles, EMBASE, Ovid Medliner(r) In-Process & Other Non-indexed Citation and Ovid Medline(r), PsycINFO and Social Policy and Practice.
[2] Web of Science included the following databases: Science Citation Index Expanded (1900-present), Social Sciences Citation Index (1956-present), Arts & Humanities Citation Index (1975-present), Conference Proceedings Citation Index – Science (1990-present), Conference Proceedings Citation Index – Social Science & Humanities (1900-present), Emerging Sources Citation Index (2015-present).

2010) and critical reviews (Casey, Jones, & Somerville, 2011; Heim & Binder, 2012) were also checked for additional search terms. Table 2 details the search terms entered for CA, reward and HRB. Database-specific truncation and wildcards were used (e.g., child* abuse to cover child abuse and childhood abuse, behavio?r to include alternative spelling behaviour and behavior). The search terms were further combined using Boolean operator "OR" to combine terms within each section and Boolean operator "AND" to combined search terms across each section (Table 2).

Table 2

Search Terms for Ovid Databases

	Child Abuse ***Section 1*** ***"OR"***	**Reward** ***Section 2*** ***"OR"***	**High-risk Behaviour** ***Section 3*** ***"OR"***
Individual Search Terms (in title or abstract)	Child* abuse, maltreatment, physical abuse, sexual abuse, emotional abuse, psychological abuse, verbal abuse, bullying	Reward, anticipatory reward, consummatory reward, reward learning, decision-making, reinforcement, reward system	Risk-taking, risk* behavio?r, high risk behavio?r, Sexuali* behavio?r, risky sexual* behavio?r, sexual activity, alcoholism, alcohol misuse, alcohol abuse, alcohol disorder, addiction, alcohol consumption, binge drinking, substance abuse, substance misuse, substance disorder, self-harm, self injury, non-suicidal self injury, self mutilation, deliberate self-harm, self-harming behavio?r, eating disorder, anorexia, bulimia, eating behavio?r, purging, binge eating, restricted eating, weight loss, gambling, reckless driving, conduct disorder, antisocial disorder, antisocial behavio?r, aggressive behavio?r, shoplifting, vandalism
Search	**Section 1 AND Section 2 AND Section 3**		

Combined (in title or abstract)

Study Records

The titles and abstracts of the records generated by the search terms were initially screened for eligibility using PECO criteria (Population, Exposure, Comparator, Outcome; Table 1) (Higgins & Green, 2011). An independent reviewer assessed 20 records for reliability of eligibility yielding 100% inter-reliability for inclusion and exclusion of screened studies. As recommended by CRD (2009), eligible records were then reviewed in full to confirm suitability. An independent reviewer again confirmed eligibility of two randomly full-text records (100% inter-rater reliability). Finally, as recommended by the NICE (2012) guidelines for compiling systematic reviews, the reference lists of all included publications were screened for further relevant materials that may have been missed in the search strategy.

Data Extraction

Compiling studies of insufficient quality can lead to a biased estimation of the concluded effects (CRC Guidance, 2009). After relevance was determined using PECO criteria, data were evaluated using the standardized and validated Quality Assessment Tool (QAT) for Quantitative Studies from the Effective Public Health Project (Armijo-Olivo, Stiles, Hagen, Biondo, & Cummings, 2012; Appendix A-B). The QAT allows evaluating studies in relation to selection, study design, confounders, blinding, data collection method and study attrition. The author rated all eligible papers using QAT and an independent researcher rated two

studies of records for reliability of quality criteria. No disagreement on component ratings or global QAT quality ratings emerged (100% inter-rater reliability). Finally, PECO criteria and study results on the three key variables (CA, reward processing and HRB) and their interrelationship were extracted as reported in the result section. After extraction, all data were cross-checked with the original publications to ensure the accuracy of data and comprehensiveness in addressing the research question. This final step was not checked by an independent reviewer.

Results

A total of 271 citations derived from the search terms across the identified databases and online searches (Table 2). After deletion of duplicates, 198 title and abstracts were screened for inclusion. Of these, 184 did not meet the specified PECO criteria. Fourteen full-text records were assessed for eligibility based on specified inclusions and exclusion criteria (Table 1). Five records met eligibility criteria and data was extracted using QAT. Exclusion criteria for the nine non-eligible studies are listed in Appendix C. An independent reviewer confirmed eligibility and data extraction of two records (100% inter-rater reliability). Reference lists of all full-text papers were reviewed for relevant records but no additional publications were identified.

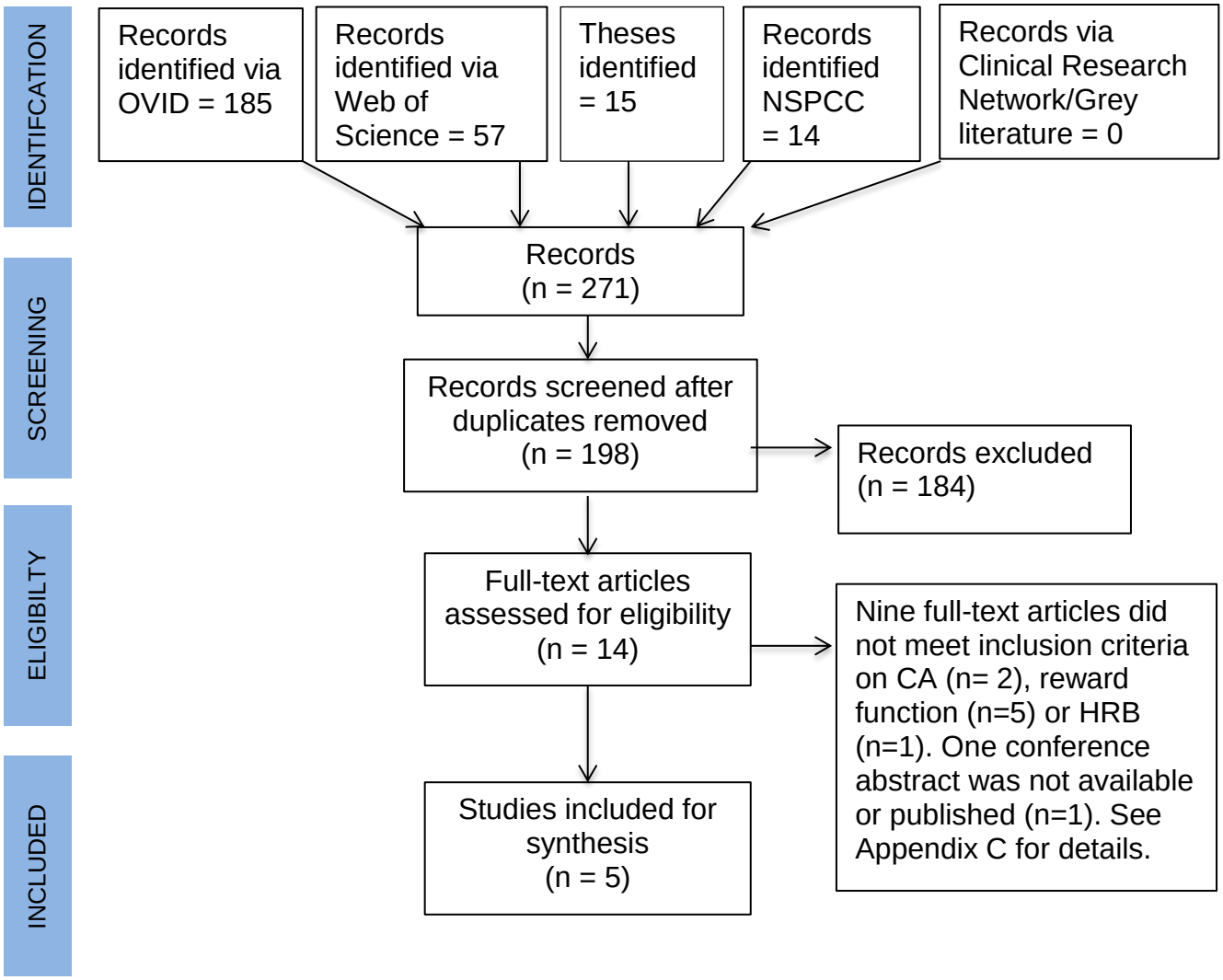

Figure 1. Results of literature search strategy and eligibility screening. Flowchart is based on PRISMA protocol (adapted from Moher et al., 2009)

Table 3

Summary of Eligible Studies in Alphabetic Order by Author

Author	**P**opulation	**E**xposure: **Child Abuse (CA)**	**C**omparator	**Outcome: (1) Reward & (2) HRB**	**Results and Conclusion**	**Evaluation**	**QAT**
1. DeBrito et al. (2013)	Child	18 maltreated children (M_{age}=12.1 years, SD=1.4, no. of males = 11),	20 non-maltreated controls (M_{age} =12.6 years, SD=1.3, no. of males = 10)	(1) Structural MRI: Voxel-based morphometry of reward regions implicated in anticipatory and consummatory reward processing and reward learning (orbito-frontal cortex; OFC) (2) HRB: Conduct problems assessed by SDQ	Compared to non-maltreated controls, maltreated adolescents showed (1) reduced grey matter volume in medial OFC implicated in consummatory reward function, (2) more conduct problems and (3) no correlation between OFC and conduct problems. **KEY FINDINGS:** Maltreated children showed reduced volume in reward brain region (OFC; *d* = 3.25) and higher conduct problems (*d* = 1.24). No correlation between OFC volume and HRB (no *r* provided). **Conclusion:** Support for relationship between CA and structural change in OFC implicated in consummatory reward function and HRB and CA. No support for link between HRB and changes in reward region.	**Strengths:** Matched for psychiatric diagnosis and cognitive ability, well-documented history of CA **Limitation:** No behavioural task, structural changes do not imply functional changes, grey matter volume differences not added as covariate	A – strong B – moderate C – strong D – moderate E – strong F – strong **Global: STRONG**
2. Guillaume et al. (2013)	Adults	218 adults with history of suicide attempts (M_{age}=39.71 years, SD=not provided, no. of females =	19 non-abused controls within sample of suicide attempters	(1) Iowa Gambling Task (IGT) assessed reward-based decision making and risk-taking, genotyping for single-nucleotide polymorphisms within CRHR1 and	(1) Patients with history of child sexual abuse had lower IGT scores compared to those with other types of CA or without CA. (2) Polymorphisms within CRHR1 genes interacted with CSA to impact IGT performance **KEY FINDINGS**: Of adults with history of sexual abuse who attempted suicide, only C allele carriers but not T allele carriers continued to opt for high immediate reward despite negative long-term	**Strengths:** Endophenotypic approach, large sample **Limitation:** Reinforcement learning is ratio of 'safe-to-risky' choices, no inference if due to reduced sensitivity to	A – moderate B – moderate C – moderate D – moderate E – strong

		154) of which 199 experienced CA		CRHR2 genes (2) HRB: Suicide attempts	consequences (high risk/high reward) over safe options (low risk/low reward) (*b* = .42). **Conclusion**: Partial support for link between CA and disrupted reward learning and HRB (based on genes).	reward or punishment or both, small sample of non-abused controls (n=19), confounding variables (medication, psychopathology, multiple CA), no assessment of other HRB	F – weak **Global: MODERATE**
3. Guyer et al. (2006)	Child	38 maltreated children (M_{age}=11.53 years, SD=1.54, no. of males = 21)	21 non-abused demographically matched controls (M_{age}=11.28 years, SD=1.91, no. of males = 12)	(1) Probabilistic behavioural decision-making task with monetary rewards (Wheel of Fortune Task); self-reported positive and negative ratings of reward (2) HRB: High-risk behavioural choices on Wheel of Fortune Task (risky vs. safe)	(1) RT times for maltreated group invariant as chance of winning increased compared to non-maltreated group who increased RT (2) No group difference in risky choices between CA and controls (3) Risk aversion in CA+MDD group (favor safe over risky choice) compared to CA with no MDD (3) No difference in self-reported affective responses (anticipatory or consummatory reward) **KEY FINDINGS**: Reduced reward sensitivity in children with CA (*d* = .51). Children with CA and MDD avoided risky choices more than children with CA and no MDD (*d* = .74). **Conclusion:** Support for link between CA and blunted reward learning but no change to anticipatory or consummatory reward processing. Partial support for link between CA and HRB (based on MDD).	**Strengths:** Standardized behavioural paradigm using response speed and risk/reward ratios **Limitation:** Suboptimal operationalization of anticipatory reward as 'confidence in outcome' and consummatory reward as on self-report ratings (happy-sad); no inferences to actual HRB in sample, risky choices always linked to highest reward value	A – strong B – moderate C – strong D – moderate E – strong F – strong **Global: STRONG**
4. Pechtel & Pizzagalli (2013)	Adults	15 women with sexual abuse and remitted depression (CSA+rMDD;	18 healthy, non-abused female controls (M_{age}=30.44, SD=10.78), 16 women	(1) Probability behavioural task of reward learning (EEG: electrophysiological indices of reward learning	CSA+rMDD showed: (1) more HRB than rMDD-only and controls (2) lower accuracy on trials that relied on previously rewarded information than rMDD-only and controls (3) lower RT on reward trials correlated with more HRB (4) blunted neural differentiation to positive and	**Strengths:** Timing of CSA coincided with sensitive period of brain development for region of interest, merging clinical, behavioural and	A – strong B – moderate C – strong D –

		M_{age}=31.60, SD=10.98)	with remitted depression-only (rMDD; M_{age}=24.81, SD=3.94) matched to CSA+rMDD group for number of MDD episodes and previous treatment	(FRN, ERN/ CRN) Low Resolution Electromagnetic Tomography on reward trials (2) HRB: Youth Risk Behaviour Survey	negative feedback (relative to controls) (5) increased subgenual anterior cingulate cortex activation (compared to rMDD-only) (6) No group differences in learning reward contingencies or consummatory reward when receiving explicit feedback **KEY FINDINGS:** Sexual abuse did not affect learning reward contingencies or consummatory reward if explicit feedback was provided. CA did affect ability to use rewarded information to make novel decision (*d* = 0.85) which was associated with higher use of self-harm and suicidal behaviour (*d* = 0.87). **Conclusion**: Support for all associations between sexual abuse, impaired reward learning and increased HRB.	electrophysiological data, use of clinically relevant HRBs **Limitation:** Link between blunted reward learning and HRB did not survive Bonferroni correction, blunted electro-physiological differentiation between correct and incorrect trials is non-specific to CA	moderate E – strong F – strong **Global: STRONG** (100% inter-rater agreement)
5. Roos, Pears, Bruce, Kim, & Fisher, (2015)	Child	67 maltreated children in foster care (M_{age}=5.19 years, SD=.30, no. of males = 30)	Control group with low impulsivity (median split)	(1) Behavioural task with performance feedback (Flanker task: inhibitory control) EEG: Feedback-related negativity to positive (FRNp) and negative feedback (FRNn) (2) HRB: Care-giver reported impulse behaviour on CBQ	(1) No group differences in neural responses to positive feedback (2) Children with CA and high impulsivity showed (a) exaggerated neural differentiation in response to positive and negative feedback (FRN), (b) greater post-error slowing and (c) correlation between exaggerated FRN and accuracy. **KEY FINDING:** No significant difference in neural response to reward feedback (FRNp: consummatory reward) between maltreated children with high and low impulsivity (*d* = .02). **Conclusion**: No support for difference in consummatory reward processing and CA or HRB.	**Strengths:** Validated task, linking behavioural and neural measures **Limitation:** Indirect measure of reward (FRN)**,** no assessment of types or severity of CA or psychiatric symptoms, high error rate suggests non-compliance of task	A – weak B – moderate C – moderate D – moderate E – strong F – strong **Global: MODERATE**

Note: CA=childhood abuse. M=mean, SD=standard deviation, no.= number, HRB=high-risk behaviour, MRI= magnetic resonance imaging, SDQ=Strength and Difficulties Questionnaire, QAT=quality assessment tool: A=selection bias, B=study design, C=confounders, D=blinding, E=data collection method, F=withdrawals and dropouts, HPA=hypothalamic-pituitary-adrenal, RT=reaction time, CA+MDD=child abuse and major depressive disorder, FRN=feedback related negativity, ERN=error-related negativity, CRN=correct-related negativity, MDD = major depressive disorder, CSA = child sexual abuse, FRNp= FRN to positive feedback, FRNn=FRN to negative feedback, CBQ=children's behaviour questionnaire

Critical Summary

The Role of Reward Learning in HRB following CA

Out of three studies investigating reward learning, two studies supported the systematic review question that HRB is associated with altered reward learning in individuals who had experienced CA (Table 4). Pechtel and Pizzagalli (2013) found that women with a history of sexual abuse showed deficits in reward learning, which was related to more frequent self-harming and suicidal behaviours. At this stage, results will need to be considered preliminary, as associations did not survive the required Bonferroni correction. Similarly, Guillaume et al. (2013) found that only adults with a history of sexual abuse but not other types of CA showed blunted reward learning. Of these women, only those who carried the T-allele of the CRHR1 gene but not carriers of the C-allele selected risky behavioural options more frequently. Moreover, all of the women in Guillaume et al.'s (2013) study had previously engaged in HRB as they were recruited after suicide attempts.

Although Guyer et al. (2006) also found that CA was associated with blunted reward learning, their findings only partially support a role for reward learning in the use of HRB. They found that children with CA demonstrated lower reward sensitivity by failing to adjust their responses as chances of winning changed. Unlike Pechtel et al. (2013) and Guillaume et al. (2013), Guyer and colleagues (2006) did not find that this deficit was associated with risker choices. Instead, they found that when considering psychological disorders, children who experienced CA and current MDD were more likely to avoid risky options than children with CA but no MDD who performed similar to controls. It could be argued that like individuals with current depression, a history of CA and MDD may be characterised by an increased sensitivity to

punishment, which may lead to suboptimal decision-making and greater risk avoidance (Santesso et al., 2008).

In sum, there is support that individuals who experienced CA show deficits in reward learning, which is linked to more frequent HRB. However, these associations are likely to be influenced by the type of abuse (i.e., sexual abuse), current depression and genetic factors.

Table 4

Overview of Findings on CA, HRB, and Reward Processing

Authors	CA and HRB	CA and Reward	Reward and HRB
DeBrito et al. (2013)	YES	YES for CR	No
Guyer et al. (2006)	NO	YES for RL NO for AR NO for CR	UNCLEAR
Guillaume et al. (2013)	PARTIAL	YES for RL	UNCLEAR
Pechtel & Pizzagalli (2013)	YES	YES for RL NO for CR	YES
Roos et al. (2015)	PARTIAL	NO for CR	NO

Note. CA=child abuse, HRB=high-risk behaviour, RL=reward learning, AR=anticipatory reward processing, CR=consummatory reward processing

The Role of Anticipatory Reward Processing in HRB following CA

Only one study assessed the role of anticipatory reward processing in HRB in individuals who experienced CA (Guyer et al., 2006). The authors did not find changes in anticipatory reward processing or links to HRB. However, it should be noted that Guyer and colleagues (2006) operationalized anticipatory reward

processing as children's confidence ratings in their decision before receiving the outcome. This is not in line with the generally accepted definition of anticipatory reward processing as an attribution of incentive salience to reward-predicting cues (Berridge et al., 2009). As a result, Guyer et al.'s (2006) findings need to be considered with caution. This is particularly important as research has demonstrated that individuals who experienced CA show blunted anticipatory reward processing, although these studies did not investigate links to HRB (Dillon et al., 2009; Teicher & Samson, 2016). More research is needed to delineate if blunted experiences of reward-predicting cues are common after CA and possibly increase the motivation to seek HRB.

Overall, the systematic review highlighted a significant lack of research investigating the role of anticipatory reward processing in HRB following CA.

The Role of Consummatory Reward Processing in HRB following CA

The majority of studies did not find support for blunted consummatory reward function in individuals with HRB with the exception of DeBrito et al. (2013). Guyer et al. (2006) and Pechtel et al. (2013) found no differences between abused and non-abused individuals with respect to reward 'liking'. Although Roos et al. (2005) did not recruit a non-abused control group, their study showed no difference in consummatory reward function amongst children with CA with either high or low impulsivity. This was the case irrespective of whether rewards were delivered as monetary incentives (Guyer et al., 2006) or social praise (Pechtel & Pizzagalli, 2013; Roos et al., 2015). Moreover, none of the studies confirmed a relationship of consummatory reward processing and HRB.

Interestingly, Pechtel et al. (2013) and Roos et al. (2015) both used EEG to assess consummatory reward processing as indexed by feedback-related negativity (FRN) responses to positive feedback. Several methodological concerns need to be considered. First, the FRN is not a direct measure of consummatory reward function as it is typically generated in the anterior cingulate cortex implicated in response monitoring and punishment sensitivity (Holroyd & Coles, 2002; van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005). Secondly, the FRN is most commonly calculated as a difference waveform of neural responses to negative and positive feedback. Evaluating FRN responses to positive feedback only may therefore represent a reduced need to attend to feedback, as no error was committed, rather than assessing consummatory responses to reward. Behavioural reward tasks paired with functional neuroimaging methods are recommended to sufficiently explore consummatory reward processing.

One study provided indirect support by finding structural changes in brain regions expected to play a key role in consummatory reward function but functional changes were not directly assessed and structural changes were not associated with HRB. DeBrito and colleagues (2013) found reduced gray matter volume in the medial OFC, a region critically implicated in consummatory reward processing (Diekhof, Kaps, Falkai & Gruber, 2012; National Institute of Mental Health, n. d.). As part of the prefrontal cortex, the OFC has a late maturational period extending into the mid-twenties (Gogtay et al., 2004; Mills, Lalonde, Clasen, Giedd, & Blakemore, 2014; Tamnes et al., 2010). According to the sensitive period model, this prolonged phase of development may leave the OFC vulnerable to structural and functional changes following the stressful experience of CA (Heim & Binder, 2012; Teicher & Samson, 2016). Critically, it

needs to be acknowledged that morphometric changes in the OFC do not necessarily imply differences in actual hedonic experiences when attaining a reward.

In sum, studies did not confirm the role of blunted consummatory reward process in HRB in individuals who experienced CA. Future research is advised to utilize behavioural tasks in combination with functional neuroimaging methods to explore this hypothesis further.

Discussion

The review demonstrated that CA is related to blunted reward learning, which is linked to more frequent HRB. No conclusive support was found for a link between CA and anticipatory or consummatory reward processing and HRB. As a result, the review question of whether HRBs are associated with altered reward processes in individuals with a history of CA can only be confirmed for reward learning. These findings will be discussed in light of important learning outcomes that emerged from this review.

First, the search of multiple scientific databases and subsequent eligibility screens only generated a small number of studies to be synthesized in this review. However, with the exception of Roos et al. (2015), it should be noted that all key findings summarized in this review indicated medium to large effect sizes (>.4). It could further be argued that only a small number of studies were found as the review question addressed a relatively novel area of understanding HRB in the neurodevelopmental context of CA and reward processing. This is supported by the fact that all but one study were published within the past three years. Complementing this argument, I noticed a recent influx of animal studies investigating the link between early-life stress, reward

and risk-taking (Hensleigh & Pritchard, 2014; Lomanowska et al., 2011). The systematic review therefore appears to summarize a rapidly growing field of research, which may warrant an update in the near future.

Secondly, it emerged that the reviewed studies examined reward processing across a range of developmental stages. In fact, one study focused on children (Roos et al., 2015), two studies recruited pre-adolescents (DeBrito et al., 2013, Guyer et al., 2006) and two studies examined young adults (Guillaume et al., 2013; Pechtel et al., 2013). Given the neural changes of the reward network in adolescence, differences in reward processing may be expressed differently in children or pre-adolescents compared to adolescents or adults (Casey et al., 2011). Hence it could be speculated that direct associations of blunted reward processing and HRB may not be observed until the key changes of reward-related regions have developed in adolescence. Future studies may benefit from focus on adolescence as a primary developmental stage to observe the hypothesized associations.

Finally, the review highlighted the critical roles of the type of abuse and current depression. The association of blunted reward learning and frequency of HRB behaviour was only found in individuals who experienced sexual abuse compared to other forms of abuse (Guillaume et al., 2013; Pechtel & Pizzagalli, 2013). Moreover, current depression in individuals with history of CA was associated with avoidance of risk behaviour (Guyer et al., 2006), whereas remitted depressed individuals who experienced CA reported higher frequency of HRB (Pechtel & Pizzagalli, 2013). Critically, some studies did not specify the type of abuse or assessed for MDD, thus making it difficult to determine if blunted reward processing was indeed related to HRB (Roos et al., 2015).

Limitations

Several limitations need to be acknowledged. First, the search yielded only a small number of studies. Although this limits the generalizability of the findings, it may also indicate a novel and growing area of research. Secondly, each study used a different behavioural task to measure reward processing. Despite showing sufficient validity and reliability, the tasks assessed slightly different aspects of reward processing such as reinforcement learning (Pechtel & Pizzagalli, 2013) compared to decision-making based on reward-risk ratios (Guillaume et al., 2013; Guyer et al., 2006). Ideally, the review would have focused on one reward process assessed by the same task across studies. Given the small number of published studies this would have not warranted a systematic review. Finally, although abuse occurred in childhood, no conclusions can be drawn on the causal relationships among the variables. Indeed, it could be argued that different preceding variables could act on all three factors and therefore increase the risk of CA and HRB as well as alter reward functioning. For example, maternal prenatal substance abuse has been associated with higher risk of CA (Kelley, 1992), blunted reward processing (Mueller et al., 2013) and increased HRB as mother's offspring are more likely to use substances themselves (O'Brien & Hill, 2014). In addition, prospective longitudinal studies are necessary to disentangle if CA in fact alters reward functioning or whether blunted reward processing is a predisposition placing children at greater risk for CA through involvement in HRB. Moreover, prospective longitudinal studies are necessary to disentangle if CA in fact alters reward functioning or whether blunted reward processing is a predisposition placing children at greater risk for CA through involvement in HRB.

Future Research

Future research may further investigate the link between reward processing and specific HRB seen in clinical settings (e.g., self-harm, substance misuse). Indeed, studies inquiring about frequencies of observed clinical HRB showed stronger links to CA than research assessing risky choices as part of a behavioural paradigm. Secondly, it is recommended to examine the link between reward processing and HRB in adolescence when both processes undergo peak neurodevelopmental changes (Casey et al., 2011). Thirdly, research needs to carefully consider the type of abuse and depressive symptoms given their role in blunted reward processing and approach or avoidance of risk. Finally, most studies focused on reward learning. Anticipatory and consummatory reward needs to be assessed using functional neuroimaging methods as these processes are difficult to disentangle when solely relying on behavioural paradigms.

Conclusions

The systematic review highlighted the importance of viewing CA in the context of a person's neurodevelopment of reward processing and HRB. Specifically, studies to date supported that impaired reward learning is associated with more frequent HRB in individuals who experienced CA. Further research is needed to investigate if other forms of reward processing may play a similar role in HRB following CA. Despite being limited in generalizability, the review was an important first step to summarize evidence, identify voids in knowledge and explicitly guide future research to achieve the ultimate goal of preventing HRB and promoting resilience following child abuse.

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Appendix A

Quality Assessment Tool for Quantitative Studies

QUALITY ASSESSMENT TOOL FOR QUANTITATIVE STUDIES

EPHPP
Effective Public Health Practice Project

COMPONENT RATINGS

A) SELECTION BIAS

(Q1) Are the individuals selected to participate in the study likely to be representative of the target population?

1 Very likely
2 Somewhat likely
3 Not likely
4 Can't tell

(Q2) What percentage of selected individuals agreed to participate?

1 80 - 100% agreement
2 60 – 79% agreement
3 less than 60% agreement
4 Not applicable
5 Can't tell

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

B) STUDY DESIGN

Indicate the study design

1 Randomized controlled trial
2 Controlled clinical trial
3 Cohort analytic (two group pre + post)
4 Case-control
5 Cohort (one group pre + post (before and after))
6 Interrupted time series
7 Other specify _____
8 Can't tell

Was the study described as randomized? If NO, go to Component C.

No Yes

If Yes, was the method of randomization described? (See dictionary)

No Yes

If Yes, was the method appropriate? (See dictionary)

No Yes

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

C) CONFOUNDERS

(Q1) Were there important differences between groups prior to the intervention?

1 Yes
2 No
3 Can't tell

The following are examples of confounders:

1 Race
2 Sex
3 Marital status/family
4 Age
5 SES (income or class)
6 Education
7 Health status
8 Pre-intervention score on outcome measure

(Q2) If yes, indicate the percentage of relevant confounders that were controlled (either in the design (e.g. stratification, matching) or analysis)?

1 80 – 100% (most)
2 60 – 79% (some)
3 Less than 60% (few or none)
4 Can't Tell

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

D) BLINDING

(Q1) Was (were) the outcome assessor(s) aware of the intervention or exposure status of participants?

1 Yes
2 No
3 Can't tell

(Q2) Were the study participants aware of the research question?

1 Yes
2 No
3 Can't tell

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

E) DATA COLLECTION METHODS

(Q1) Were data collection tools shown to be valid?

1 Yes
2 No
3 Can't tell

(Q2) Were data collection tools shown to be reliable?

1 Yes
2 No
3 Can't tell

RATE THIS SECTION	STRONG	MODERATE	WEAK
See dictionary	1	2	3

F) WITHDRAWALS AND DROP-OUTS

(Q1) Were withdrawals and drop-outs reported in terms of numbers and/or reasons per group?

1 Yes
2 No
3 Can't tell
4 Not Applicable (i.e. one time surveys or interviews)

(Q2) Indicate the percentage of participants completing the study. (If the percentage differs by groups, record the lowest).

1 80 -100%
2 60 - 79%
3 less than 60%
4 Can't tell
5 Not Applicable (i.e. Retrospective case-control)

RATE THIS SECTION	STRONG	MODERATE	WEAK	
See dictionary	1	2	3	Not Applicable

G) INTERVENTION INTEGRITY

(Q1) What percentage of participants received the allocated intervention or exposure of interest?

1 80 -100%
2 60 - 79%
3 less than 60%
4 Can't tell

(Q2) Was the consistency of the intervention measured?

1 Yes
2 No
3 Can't tell

(Q3) Is it likely that subjects received an unintended intervention (contamination or co-intervention) that may influence the results?

4 Yes
5 No
6 Can't tell

H) ANALYSES

(Q1) Indicate the unit of allocation (circle one)

community organization/institution practice/office individual

(Q2) Indicate the unit of analysis (circle one)

community organization/institution practice/office individual

(Q3) Are the statistical methods appropriate for the study design?

1 Yes
2 No
3 Can't tell

(Q4) Is the analysis performed by intervention allocation status (i.e. intention to treat) rather than the actual intervention received?

1 Yes
2 No
3 Can't tell

GLOBAL RATING

COMPONENT RATINGS
Please transcribe the information from the gray boxes on pages 1-4 onto this page. See dictionary on how to rate this section.

A	**SELECTION BIAS**	**STRONG**	**MODERATE**	**WEAK**	
		1	2	3	
B	**STUDY DESIGN**	**STRONG**	**MODERATE**	**WEAK**	
		1	2	3	
C	**CONFOUNDERS**	**STRONG**	**MODERATE**	**WEAK**	
		1	2	3	
D	**BLINDING**	**STRONG**	**MODERATE**	**WEAK**	
		1	2	3	
E	**DATA COLLECTION METHOD**	**STRONG**	**MODERATE**	**WEAK**	
		1	2	3	
F	**WITHDRAWALS AND DROPOUTS**	**STRONG**	**MODERATE**	**WEAK**	
		1	2	3	Not Applicable

GLOBAL RATING FOR THIS PAPER (circle one):

1	STRONG	(no WEAK ratings)
2	MODERATE	(one WEAK rating)
3	WEAK	(two or more WEAK ratings)

With both reviewers discussing the ratings:

Is there a discrepancy between the two reviewers with respect to the component (A-F) ratings?

No Yes

If yes, indicate the reason for the discrepancy

1	Oversight
2	Differences in interpretation of criteria
3	Differences in interpretation of study

Final decision of both reviewers (circle one):

1	**STRONG**
2	**MODERATE**
3	**WEAK**

Appendix B

Quality Assessment Tool for Quantitative Studies Dictionary

The purpose of this dictionary is to describe items in the tool thereby assisting raters to score study quality. Due to under-reporting or lack of clarity in the primary study, raters will need to make judgments about the extent that bias may be present. When making judgments about each component, raters should form their opinion based upon information contained in the study rather than making inferences about what the authors intended.

A) SELECTION BIAS

(Q1) Participants are more likely to be representative of the target population if they are randomly selected from a comprehensive list of individuals in the target population (score very likely). They may not be representative if they are referred from a source (e.g. clinic) in a systematic manner (score somewhat likely) or self-referred (score not likely).

(Q2) Refers to the % of subjects in the control and intervention groups that agreed to participate in the study before they were assigned to intervention or control groups.

B) STUDY DESIGN

In this section, raters assess the likelihood of bias due to the allocation process in an experimental study. For observational studies, raters assess the extent that assessments of exposure and outcome are likely to be independent. Generally, the type of design is a good indicator of the extent of bias. In stronger designs, an equivalent control group is present and the allocation process is such that the investigators are unable to predict the sequence.

Randomized Controlled Trial (RCT)

An experimental design where investigators randomly allocate eligible people to an intervention or control group. A rater should describe a study as an RCT if the randomization sequence allows each study participant to have the same chance of receiving each intervention and the investigators could not predict which intervention was next. If the investigators do not describe the allocation process and only use the words ‘random’ or ‘randomly’, the study is described as a controlled clinical trial.

Was the study described as randomized?

 _Score YES, if the authors used words such as random allocation, randomly assigned, and random assignment.

 _Score NO, if no mention of randomization is made.

Was the method of randomization described?

 _Score YES, if the authors describe any method used to generate a random allocation sequence.

 _Score NO, if the authors do not describe the allocation method or describe methods of allocation such as alternation, case record numbers, dates of birth, day of the week, and any allocation procedure that is entirely transparent before assignment, such as an open list of random numbers of assignments.

 _If NO is scored, then the study is a controlled clinical trial.
Was the method appropriate?
 _Score YES, if the randomization sequence allowed each study participant to have the same chance of receiving each intervention and the investigators could not predict which intervention was next. Examples of appropriate approaches include assignment of subjects by a central office unaware of subject characteristics, or sequentially numbered, sealed, opaque envelopes.
 _Score NO, if the randomization sequence is open to the individuals responsible for recruiting and allocating participants or providing the intervention, since those individuals can influence the allocation process, either knowingly or unknowingly.
 _If NO is scored, then the study is a controlled clinical trial.

Controlled Clinical Trial (CCT)
An experimental study design where the method of allocating study subjects to intervention or control groups is open to individuals responsible for recruiting subjects or providing the intervention. The method of allocation is transparent before assignment, e.g. an open list of random numbers or allocation by date of birth, etc.

Cohort analytic (two group pre and post)
An observational study design where groups are assembled according to whether or not exposure to the intervention has occurred. Exposure to the intervention is not under the control of the investigators. Study groups might be non-equivalent or not comparable on some feature that affects outcome.

Case control study
A retrospective study design where the investigators gather ‘cases’ of people who already have the outcome of interest and ‘controls’ who do not. Both groups are then questioned or their records examined about whether they received the intervention exposure of interest.

Cohort (one group pre + post (before and after)
The same group is pretested, given an intervention, and tested immediately after the intervention. The intervention group, by means of the pretest, act as their own control group.

Interrupted time series
A time series consists of multiple observations over time. Observations can be on the same units (e.g. individuals over time) or on different but similar units (e.g. student achievement scores for particular grade and school). Interrupted time series analysis requires knowing the specific point in the series when an intervention occurred.

C) CONFOUNDERS
By definition, a confounder is a variable that is associated with the intervention or exposure and causally related to the outcome of interest. Even in a robust study design, groups may not be balanced with respect to important variables prior to the intervention. The authors should indicate if confounders were controlled in the design (by stratification or matching) or in the analysis. If the allocation to intervention and control groups is randomized, the authors must

report that the groups were balanced at baseline with respect to confounders (either in the text or a table).

D) BLINDING

(Q1) Assessors should be described as blinded to which participants were in the control and intervention groups. The purpose of blinding the outcome assessors (who might also be the care providers) is to protect against detection bias.

(Q2) Study participants should not be aware of (i.e. blinded to) the research question. The purpose of blinding the participants is to protect against reporting bias.

E) DATA COLLECTION METHODS

Tools for primary outcome measures must be described as reliable and valid. If 'face' validity or 'content' validity has been demonstrated, this is acceptable.

Some sources from which data may be collected are described below:

Self reported data includes data that is collected from participants in the study (e.g. completing a questionnaire, survey, answering questions during an interview, etc.).

Assessment/Screening includes objective data that is retrieved by the researchers. (e.g. observations by investigators).

Medical Records/Vital Statistics refers to the types of formal records used for the extraction of the data.

Reliability and validity can be reported in the study or in a separate study. For example, some standard assessment tools have known reliability and validity.

F) WITHDRAWALS AND DROP-OUTS

 _Score YES if the authors describe BOTH the numbers and reasons for withdrawals and drop-outs.

 _Score NO if either the numbers or reasons for withdrawals and drop-outs are not reported.

The percentage of participants completing the study refers to the % of subjects remaining in the study at the final data collection period in all groups (i.e. control and intervention groups).

G) INTERVENTION INTEGRITY

The number of participants receiving the intended intervention should be noted (consider both frequency and intensity). For example, the authors may have reported that at least 80 percent of the participants received the complete intervention. The authors should describe a method of measuring if the intervention was provided to all participants the same way. As well, the authors should indicate if subjects received an unintended intervention that may have influenced the outcomes. For example, co-intervention occurs when the study group receives an additional intervention (other than that intended). In this case, it is possible that the effect of the intervention may be over-estimated. Contamination refers to situations where the control group accidentally receives the study intervention. This could result in an under-estimation of the impact of the intervention.

H) ANALYSIS APPROPRIATE TO QUESTION

Was the quantitative analysis appropriate to the research question being asked?
An intention-to-treat analysis is one in which all the participants in a trial are analyzed according to the intervention to which they were allocated, whether they received it or not. Intention-to-treat analyses are favoured in assessments of effectiveness as they mirror the noncompliance and treatment changes that are likely to occur when the intervention is used in practice, and because of the risk of attrition bias when participants are excluded from the analysis.

Component Ratings of Study:

For each of the six components A – F, use the following descriptions as a roadmap.

A) SELECTION BIAS

Strong: The selected individuals are very likely to be representative of the target population (Q1 is 1) and there is greater than 80% participation (Q2 is 1).
Moderate: The selected individuals are at least somewhat likely to be representative of the target population (Q1 is 1 or 2); and there is 60 - 79% participation (Q2 is 2). 'Moderate' may also be assigned if Q1 is 1 or 2 and Q2 is 5 (can't tell).
Weak: The selected individuals are not likely to be representative of the target population (Q1 is 3); or there is less than 60% participation (Q2 is 3) or selection is not described (Q1 is 4); and the level of participation is not described (Q2 is 5).

B) DESIGN

Strong: will be assigned to those articles that described RCTs and CCTs.
Moderate: will be assigned to those that described a cohort analytic study, a case control study, a cohort design, or an interrupted time series.
Weak: will be assigned to those that used any other method or did not state the method used.

C) CONFOUNDERS

Strong: will be assigned to those articles that controlled for at least 80% of relevant confounders (Q1 is 2); or (Q2 is 1).
Moderate: will be given to those studies that controlled for 60 – 79% of relevant confounders (Q1 is 1) and (Q2 is 2).
Weak: will be assigned when less than 60% of relevant confounders were controlled (Q1 is 1) and (Q2 is 3) or control of confounders was not described (Q1 is 3) and (Q2 is 4).

D) BLINDING

Strong: The outcome assessor is not aware of the intervention status of participants (Q1 is 2); and the study participants are not aware of the research question (Q2 is 2).
Moderate: The outcome assessor is not aware of the intervention status of participants (Q1 is 2); or the study participants are not aware of the research question (Q2 is 2); or blinding is not described (Q1 is 3 and Q2 is 3).
Weak: The outcome assessor is aware of the intervention status of participants (Q1 is 1); and the study participants are aware of the research question (Q2 is 1).

E) DATA COLLECTION METHODS
Strong: The data collection tools have been shown to be valid (Q1 is 1); and the data collection tools have been shown to be reliable (Q2 is 1).

Moderate: The data collection tools have been shown to be valid (Q1 is 1); and the data collection tools have not been shown to be reliable (Q2 is 2) or reliability is not described (Q2 is 3).

Weak: The data collection tools have not been shown to be valid (Q1 is 2) or both reliability and validity are not described (Q1 is 3 and Q2 is 3).

F) WITHDRAWALS AND DROP-OUTS
Strong: will be assigned when the follow-up rate is 80% or greater (Q2 is 1).
Moderate: will be assigned when the follow-up rate is 60 – 79% (Q2 is 2) OR Q2 is 5 (N/A).
Weak: will be assigned when a follow-up rate is less than 60% (Q2 is 3) or if the withdrawals and drop-outs were not described (Q2 is 4).

Appendix C

Exclusion Criteria for Selected Full-Text Papers

Table C1

Summary and Exclusion Criteria for Studies not Eligible for Review in Alphabetic Order by Author

Author	**P**opulation	**Exposure**: **Child Abuse (CA)**	**C**omparator	**O**utcome (1) Reward & **(2) HRB**	**Reason for Exclusion**
1. Blalock et al., 2011	Adults	201 pregnant female smokers (M_{age}=25.13; *SD*=4.77) (59% reported CA at high level as assessed with CTQ)	41% of sample reported no CA at high level.	1) Negative reinforcement questionnaire subscale on Wisconsin Inventory of Smoking Dependence Motives (2) Nicotine Dependence variables during pregnancy)	**Reward questionnaire only**
2. DeCarva-lho et al., 2015	Adults	8,114 participants (M_{age}=34.8; *SD*=11.30) (assessed with CTQ)	Non-abused participants	(1) Reward dependence subscale on Temperament and Character Inventory-Revised (2) Novelty-seeking and harm-avoidance subscales on Temperament and Character Inventory-Revised	**Reward questionnaire only**
3. Hasking et al. 2007	Adolescents	259 adolescents (M_{age}=14.19; *SD*=1.15). No direct assessment of CA but use of non-productive coping with stressor	Unclear CA history	(1) BIS/BAS scales (2) Self-reported Delinquency Scale	**Unclear CA history**
4. Luiselli et al., 1996	Adolescent	Case study: 14-year of male with CA	No comparison group	(1) Multicomponent program of positive reinforcement/no assessment of reward (2) Frequency measure of aggressive behaviour, property destruction, throwing and sweeping objects (all non-standardized)	**No reward assessment or comparison group**
5. Mueller et al., 2012	Children	17 adopted children (M_{age}=11.32; SD=1.89), Note: Only some adoptees experienced CA hence group was described as having 'early-life stress'.	29 healthy, non-abused controls (M_{age}=11.93; SD=2.36)	(1) Monetary incentive saccade task (reward learning) (2) not explicitly assessed (authors comments on possible link to reward but no data)	**No HRB Unclear CA history**

6. Stangl et al., unpublished	Adults	Of 212 healthy, non-dependent drinkers. 39% reported at least one type of trauma on CTQ (no further information provided in abstract)	61% of sample reported no history of CA	(1) self-report measure of 'wanting' and 'liking' assessed with Drug Effects Questionnaire and Alcohol Urge Questionnaire (2) drinking was assessed using Timeline Follow Back, Alcohol Disorders Identification Test and Computer-Assisted Self-Infusion of Ethanol	**Full-text not submitted to journal or available for review. (*Contacted author via email on 18/3/16*)**
7. Thaler et al., 2014	Women	64 women with bulimia nervosa (*M_{age}*=26.05; SD=6.59) (assessed with Childhood Trauma Interview)	32 non-abused, normal eater control women (*M_{age}*=23.67; SD=5.70)	(1) mention links to reward dependence but no assessment (2) Eating Disorders Examination	**No reward assessment**
8. Weller et al. 2015	Adolescents	92 foster girls (*$Median_{age}$*=16.47; SD=not known), Note: Children primarily experienced neglect which was primary moderator assessed	80 non-abused, control females (*$Median_{age}$*= 16.24; SD=1.18). Non-abused controls matched for low socio-economic status	(1) not clearly assessed but combined assessment of expected value sensitivity to risky vs. safe outcomes (2) Decision-making in risky vs. safe choices on Cup Task Paradigm	**Primarily neglect rather than CA**
9. Zouk et al., 2006	Adults	Of 164 suicide cases, 32 cases indicated CA as assessed by Childhood Experience of Care and Abuse	132 non-abused suicide cases	(1) Novelty seeking and reward dependence subscale from Temperament and Character Inventory (2) Barratt Impulsivity Scale (prior to suicide); Brown Goodwin History of Aggression and Buss-Durkey Hostility Inventory (informant)	**Reward questionnaire only**

Appendix D

Preparation and Submission Requirements for the *Journal of the American Academy of Child and Adolescent Psychiatry*

Scope of the Journal

The Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP) goals is to advance the science and practice of child and adolescent psychiatry by publishing original research and papers of theoretical, scientific and clinical relevance to the field.

Manuscript Preparation

- Each manuscript submitted to JAACAP must contain the following components: cover letter, title page, blinded manuscript, and Manuscript Submission Form.
- Manuscripts must conform to standard English usage and are subject to editing in conformance with the policies of the Journal.
- All text files must be prepared using Microsoft Word, double- spaced with Times New Roman 12-point font.
- After the title page, number pages consecutively throughout.
- Other than on the title page and Manuscript Submission Form(s), blinding is the responsibility of the author.
- When using direct quotations, cite the page number for the quotation along with the source in the reference list.
- Text should begin on the second numbered page, and should be divided into the following sections: Abstract, Introduction, Method, Results, Discussion, References, and Tables (if required). This formatting is not required for Clinical Review articles, but the suggested components should be included where applicable.

Title

The manuscript title should be concise and informative, as titles are often used in information-retrieval systems. Avoid abbreviations and formulae where possible. Titles should be less than 100 characters and a maximum of 15 words. A running title of less than 40 characters should also be included.

Abstract

The structured abstract for Review articles should be a maximum of 250 words and must be formatted with sections entitled as follows: Objective, Method, Results, Conclusion.

Reporting guidelines

Guidelines have been developed for different study designs; examples include (…) PRISMA for systematic reviews and meta- analyses (http://prisma-statement.org/) (…). Authors are strongly encouraged to follow these guidelines because they help authors describe the study in enough detail for it to be evaluated by editors, reviewers, readers, and other researchers evaluating the medical literature. Authors of Review manuscripts are encouraged to describe

the methods used for locating, selecting, extracting, and synthesizing data.

Tables and Figures

Tables should be cited in the text, numbered consecutively (i.e., Table 1, Table 2) in the order of their mention, and include brief descriptions. Tables that constitute a single column are actually lists and should be included in the text. Table footnotes should use superscript lowercase letters rather than symbols.

Figures should be cited in the text, numbered consecutively (i.e., Figure 1, Figure 2) in the order of their mention, and include brief descriptions. Figure titles and legends should be included on a separate page in the manuscript file following the reference list and any tables, rather than in the figure file itself.

SCHOOL OF PSYCHOLOGY

DOCTORATE IN CLINICAL PSYCHOLOGY

EMPIRICAL PAPER

Reward Processing and High-Risk Behaviour in Adolescents with a History of Childhood Abuse

Trainee Name: **Pia Pechtel**

Primary Research Supervisor: **Professor Ed Watkins**

Professor of Experimental and Applied Clinical Psychology, Director of Research for Professional Doctorates, Mood Disorder Centre

Secondary Research Supervisor: **Dr Anna Adlam**

Senior Lecturer, Deputy Director of Research for Professional Doctorates

Target Journal: Biological Psychiatry

Word Count: 7976 words (excluding abstract, table of contents, list of figures, references, footnotes, appendices)

Submitted in partial fulfilment of requirements for the Doctorate Degree in Clinical Psychology, University of Exeter

Abstract

Objective: Following childhood abuse (CA), adolescence often sees the onset of depression and high-risk behaviour (HRB). Despite the prevalence, little is known about underlying neurobiological factors linking CA and HRB. To address this gap, I examined if anticipatory and consummatory reward processing in adolescents with CA predict frequency of HRB, irrespective of depressive symptoms.

Methods*:* Thirty-seven adolescents (*M*=17.08 years; *SD* = 1.86) participated in the study: 13 females with CA and current major depressive disorder (MDD), eight females with MDD and no CA, and 16 individuals with no CA and no MDD for comparison (control group). Adolescents completed the Card-Guessing paradigm to assess reward processing, while undergoing a magnetic resonance imaging scan. Neural region-of-interest responses in the striatum and pallidum were assessed during anticipatory and consummatory reward phases. Hierarchical regression models investigated if neural responses to reward were altered based on exposure to CA and if altered neural responses predicted higher use of HRB.

Results*:* Data showed that (1) depressed adolescents engaged more frequently in HRB irrespective of history of CA, (2) anticipatory and consummatory reward processes were not altered based on a history of CA, and (3) blunted activation in right pallidum in anticipation of rewards predicted HRB irrespective of depressive symptoms.

Conclusion: Although the current study did not confirm changes in reward processing following CA, blunted reward ‘wanting’ was linked to more frequent HRB. Findings are relevant to theories highlighting the critical role of the

pallidum in perceiving cues as rewarding and in initiating goal-directed actions to obtain rewards.

Keywords: childhood abuse, reward, risk-behaviour, magnetic resonance imaging, adolescence

Introduction

According to the HM Government safeguarding protocol (2015), childhood abuse (CA) occurs when an individual or a group of individuals inflict harm in form of physical, sexual, or emotional abuse to a child under the age of 18 years (HM Goverment, 2015). In the UK, about one in four young adults (25.3%) experience severe abuse during childhood. Since 2002, the number of children in the child protection system in the UK has increased by 80% (Radford et al., 2011). Moreover, the National Society for the Prevention of Cruelty Against Children (NSPCC) estimates that for each recorded child protection plan, a further eight children are expected to have experienced CA without being recorded by child social care authorities (Jutte et al., 2015). Given this high prevalence, improving our understanding of the clinical, behavioural and neurobiological sequelae of CA is of critical public health significance and provides a vital step to tailoring and delivering effective interventions early in development.

Sequelae of Childhood Abuse

Depression. Research from the UK show that all types of abuse are associated with poorer mental health outcomes (Radford et al., 2011). Based on recent epidemiological data, severe childhood adversity explains about 44% of variance of all psychiatric disorders with an onset in childhood (Green et al., 2010). Major depressive disorder (MDD) is among the most consistent outcomes following CA (Comijs et al., 2007; Cutajar et al., 2010). For those who develop MDD following CA, 56% of individuals experienced their first depressive episodes in adolescence between the ages of 12 to 15 (Teicher, Samson, Polcari, & Andersen, 2009).

High-risk behaviour. Adolescents with a history of CA also commonly engage in an array of maladaptive or high-risk behaviours (HRB) (Accident Compensation Coporation, 2008; Radford et al., 2011). HRB are often operationalized as actions or events that put the individuals' health, well-being or safety at risk of harm (Swahn & Bossarte, 2009). Although HRB may initially alleviate distress, they are primary predictors for continuous abuse including sexual revictimisation (Jonas et al., 2011; Messman-Moore, Ward, & Brown, 2009; Reid, 2011). Among the most common HRB associated with CA are substance misuse, self-harm, risky sexual behaviour and harmful eating habits (Danielson et al., 2010; Kendler et al., 2000; Messman-Moore, Walsh, & DiLillo, 2010; Pechtel, Evans, & Podd, 2011; Radford et al., 2011; Reid, 2011; Smolak & Murnen, 2002). Despite the common co-occurrence of CA and HRB, little is known about the underlying mechanisms that link early experiences of CA to HRB in adolescence. Recent models of addiction argue that excessive drug use decreases neural responses to natural reward, leaving the person less likely to experience pleasure from stimuli typically considered rewarding (Koob & Le Moal, 2005). This blunted experience of reward is expected to increase negative affect, from which a person may seek relief by using drugs or alcohol. HRBs are therefore not necessarily motivated by a sensitized reward state (positive reinforcement), but rather function as a means to relieve aversive emotional states (negative reinforcement; Koob & Le Moal, 2005). The model may be extended to other HRB, such as self-harm and risky sexual behaviour, which have been shown to temporarily alleviate negative affect (ACC, 2008; Messman-Moore et al., 20009). It is important to note that Koob and Le Moal's (2005) conceptualization that a lack of positive rewards is likely to elicit negative affect is at odds with to other prominent models of affect, for example, Clark and

Watson's tripartite model (1991) and Gray's Reinforcement Sensitivity Theory (Gray & McNaughton, 2000). Both of these models propose a broadly orthogonal relationship of positive and negative affect. Although there is support for an independent relationship of positive and negative affect (Laurent, Catanzaro & Joiner, 2004), some studies also highlighted a significant correlation between these constructs particularly in samples of children and young people (Anderson & Hope, 2008; Crook, Beaver & Bell, 1998).

Impact of brain development. From a biological perspective, stress activates the hypothalamic-pituitary-adrenal (HPA) axis (Heim & Binder, 2012). Through a cascade of events, the release of corticotropin-releasing hormones leads to an increased production of glucocorticoids (GCs; cortisol), which bind to glucocorticoid receptors in the brain where they can inhibit glucose utilization and endanger cell survival (Gunnar & Quevedo, 2007). Excessive GCs release can interfere with vital processes of neurogenesis, synaptic overproduction, myelination and pruning that normally occur in childhood (see Teicher & Samson, 2016 for a review). Brain regions are particularly vulnerable to neurotoxic effects of stress if (1) they show a prolonged postnatal development, (2) contain high density of GCs receptors and (3) timing of CA coincides with a critical period of development (Andersen & Teicher, 2008; Pechtel & Pizzagalli, 2011). As a significant stressor, CA is therefore likely to lead to changes in neurodevelopment. The brain's reward system is particularly vulnerable due to its prolonged postnatal development and high GC receptor density (Ahima, Krozowski, & Harlan, 1991; Forbes & Dahl, 2005; Giedd et al., 2009; Lupien, McEwen, Gunnar, & Heim, 2009; Teicher & Samson, 2016).

Reward Processing

Adolescence is a period of increased reward-seeking behaviour (van Duijvenvoorde et al., 2015). Reward processing includes dissociable neural systems often described as (1) *anticipatory* reward processing or the motivation of 'wanting' a reward and (2) *consummatory* reward processing or the 'liking' response when receiving a reward (Berridge & Kringelbach, 2008; Berridge, Robinson, & Aldridge, 2009). Although reward 'wanting' refers to the process of attributing incentive salience to reward-predicting cues, reward 'liking' refers to the hedonic value or experienced pleasure when exposed to a reward (Berridge et al., 2009). Anticipatory and consummatory phases of reward processing rely on dopaminergic pathways extending from the ventral tegmental area through to the ventral striatum (e.g., nucleus accumbens; NAcc, ventral pallidum) and frontal cortex and dopaminergic projections from the substantia nigra to the dorsal striatum (e.g., caudate, putamen) (Der-Avakian & Markou, 2012; Dillon et al., 2014).

Compared to individuals without CA, Edminston et al. (2011) found reductions in gray matter volume in corticostriatal regions following CA. Moreover, adults who experienced CA showed decreased activation in the left pallidus and the left putamen during the anticipatory reward phase compared to non-abused individuals (Dillon et al., 2009). Similarly, decreased ventral striatal activation during reward anticipation was found among Romanian adoptees who experienced global maltreatment in early life (Metha et al., 2010). Complementing human research, isolated housing in adolescent rats was associated with reduced responding to reward-predicting cues compared to adolescent rats without isolation (Spear, 2011).

Although past studies primarily focused on anticipatory reward ‘wanting’, recent research suggests that the impact of CA may also extend to consummatory reward ‘liking’ (Teicher & Samson, 2016). Boecker and colleagues (2014) found altered striatal responses to monetary incentives following early life adversity, whereas Hanson and colleagues (2016) confirmed blunted ventral striatal activation for adults with higher cumulative life adversity. These blunted responses to the ‘liking’ and ‘wanting’ of natural rewards may increase negative affect over time, from which a person may seek relief by engaging in HRB (Koob & Le Moal, 2005). To date, no study has explored this hypothesis explicitly using a neuroimaging method. Although Pechtel and Pizzagalli (2013) and Guillaume (2013) found that reduced reward learning was associated with greater risk for self-harm, suicidal behaviours and riskier choices following CA, these studies did not assess links of other reward processes to HRB. Furthermore, research to date primarily focuses on adult populations who retrospectively report high-risk behaviour. Research designs also often fail to consider the possible confounding role of MDD, which is one of the most consistent sequels of CA and similarly is characterized by dopaminergic dysfunction associated with blunted reward processing (Dillon et al., 2014).

Together, these findings provide preliminary support that neural systems of reward are vulnerable to CA. However, it remains unclear if blunted neural responses of reward ‘liking’ and ‘wanting’ increase the use of HRB in an attempt to alleviate negative affect that derive from such a lack of pleasure. Identifying functional mechanisms underlying the maladaptive developmental pathway following CA in adolescents, above and beyond the impact of MDD, is pivotal to the development of targeted prevention and intervention strategies.

Aims and Hypotheses

To address these gaps, the current study investigated anticipatory and consummatory reward processes in adolescents with MDD and CA (*CA+MDD*), MDD and no CA (*MDD*), and healthy controls, and examined the role of these reward processes in the frequency of HRB. The research focused on the incentive and hedonic "hotspots" in the brain, namely the ventral striatum (NAcc), ventral pallidum and dorsal striatum (caudate, putamen) (Berridge & Kringelbach, 2008, p. 7). To this end, I specifically examined three primary aims and associated hypotheses:

1. **Investigate HRB in adolescents**
    a. Hypothesis 1: Relative to MDD and controls, the CA+MDD group will show an increased engagement in high-risk behaviours.
2. **Investigate neural substrates of reward processing in adolescents with a history of CA**
    a. Hypothesis 2a: Irrespective of depressive symptoms, a history of CA will predict decreased anticipatory reward processing as marked by decreased neural responses in the striatum (NAcc, caudate, putamen) and pallidum during the anticipation of reward ('wanting').
    b. Hypothesis 2b: Irrespective of depressive symptoms, a history of CA will predict decreased consummatory reward processing marked by decreased neural responses in the striatum (NAcc, caudate, putamen) and pallidum during the delivery of reward ('liking').
3. **Investigate the relationship between reward processing and HRB**

a. Hypothesis 3: Blunted neural responses in the striatum (NAcc, caudate, putamen) and pallidum to the anticipation and delivery of rewards will predict HRB in adolescents.

Methods and Materials

Design

The cross-sectional experimental study used a between-subjects design to assess the associations of CA, reward processing and HRB, while controlling for depressive symptoms. To this end, I compared adolescents with CA+MDD, MDDs and healthy, non-abused controls.

Participants

Forty subjects were initially recruited into the study using printed and online advertisements. The final sample consisted of 37 female adolescents between the ages of 13-19 years: 13 females with a history of sexual, physical or emotional abuse and current MDD (CA+MDD), eight females with current MDD but no history of CA (MDD), and 16 healthy controls with no history of CA or psychological disorders. The clinical groups were recruited in liaison with the Joint Agency of Child Abuse Team (JACAT), the local Child and Adolescent Mental Health Service (CAMHS), the University's Wellbeing Service and local GP practices. Control participants were recruited in collaboration with secondary schools located in the Exeter area using a university-based study pool.

Due to sex-specific differences in brain development, only females were invited to participate (Pechtel & Pizzagalli, 2011). All participants were fluent in

the English language and were compliant with the MRI safety protocol. They reported no neurological conditions including head injury, loss of consciousness (>two minutes), learning disability or epilepsy. Participants were excluded if they reported mania/hypomania, substance dependence, attention-deficit hyperactivity disorder, psychosis, or currently used dopaminergic medication.

Inclusion criteria for the CA+MDD group included a history of sexual, physical or emotional abuse as indicated by clinical cut-off scores on the Child Trauma Questionnaire (CTQ: sexual abuse ≥ 6; physical abuse ≥ 8; emotional abuse ≥ 9; Bernstein et al., 1994). The CA+MDD and MDD group met diagnostic criteria for current MDD as determined by the Kiddie-Schedule for Affective Disorders and Schizophrenia (KSADS; Kaufman et al., 1997) and a score above clinical threshold on the Beck Depression Inventory (≥ 14; Beck, Steer, & Brown, 1996). Participants in the control condition were selected if they did not report previous or current diagnosis of mental health difficulties as assessed by the KSADS. Participants in the control and MDD group scored below the clinical cut-off value on all types of abuse measured by the CTQ. Three recruited subjects were excluded because they did not meet study criteria (CA but no MDD; n=2) and one adolescent did not comply with the task (n=1). All participants agreed to participate in the study.

The National Health Service (NHS) Ethics Committee, the Virgin HealthCare Ethics Board and the Exeter University Ethics Review Board approved the study (Appendix A-C). All participants received a reimbursement of £46 for their time and travel, which included £9 as a monetary incentive for the behavioural paradigm.

Power Analysis

The sample size was estimated after considering effect sizes obtained in previous studies. Women with a history of CA showed reduced reward learning compared to healthy controls without a history of CA (*d* = .85), which was associated with more HRB behaviour (*d* = .87; Pechtel & Pizzagalli, 2013). Moreover, individuals with CA compared to controls showed blunted reward processing indicated by weaker activation in the striatum (*d* = .78; Dillon et al., 2009). Based on these studies, our sample size was estimated assuming a medium to large effect size for multiple regression ($f^2 = .30$) with two tested predictors (Cohen, 1992). Effect sizes were calculated using $\alpha = .05$ for predicting relationships between CA, HRB, and reward processing. Using the G*Power program and the above specified parameters ($\alpha = .05$, $f^2 = .30$), our initial target sample size (*n* = 40) led to a power of >.85 to identify a relationship (Faul, Erdfelder, Lang, & Buchner, 2007). Accounting for the 8% of data loss that occurred in our study (*n* = 37), relationships between CA, HRB and reward processes were still predicted with an acceptable level of power >.82 using the same parameters ($\alpha = .05$, $f^2 = .30$) (Cohen, 1992).

Measures

Clinical measures. Participants completed a standardized diagnostic interview and five self-report questionnaires (see Appendix D for further details).

At the beginning and the end of the MRI session, participants completed the *Positive and Negative Affect Schedule* (PANAS; Watson, Clark, & Tellegen, 1988). The 20-item questionnaire asked participants to rate their momentary positive affect (10 items; PANAS-PA) and momentary negative affect (10 items; PANAS-NA) from 1 (‘very slightly/not at all’) to 5 (‘extremely’). Positive affect

includes experiences of pleasure, enthusiasm and alertness, and negative affect includes descriptors of subjective distress. The PANAS has high internal consistency reliabilities ranging from .86 to .90 for positive affect and .84 to .87 for negative affect. The correlation between the PA and NA scales are low and negative (-.12 to -.23) suggesting quasi-independence (Watson et al., 1988). The PANAS was administered twice to monitor the participants' mood over the course of the session.

To obtain information on psychological disorders, the *Kiddie-Schedule for Affective Disorders and Schizophrenia – Present and Lifetime (KSADS)* was administered (Kaufman et al., 1997). The KSADS is a widely used semi-structured interview to assess past and present psychological disorders according to criteria outlined in the Diagnostic Statistical Manual of Mental Disorders, 4th Edition (DSM-IV; American Psychiatric Association, 1994). The KSADS has shown excellent inter-rater reliability for present and lifetime diagnosis, with percentage agreement ranging from 93% to 100%. Test-retest reliability assessed over mean period of 17.9 days ranged from good (k = .63-.67) to excellent (k = .77-1.00) for both lifetime and present diagnosis (Kaufman et al., 1997).

To measure symptoms of depression, participants completed the *Beck Depression Inventory-II* (BDI; Beck et al., 1996**).** The BDI is 21-item questionnaire with excellent internal consistency (α = .91) and excellent test-retest reliability over seven days (r = .93). Total scores range from 0-63 with higher scores indicating greater levels of depressive symptoms. Scores ranging from 0-13 show minimal depression, scores of 14-19 suggest mild depression, scores of 20-28 show moderate depression, and scores of 29-63 represent severe levels of depression.

To obtain information on reward sensitivity and anhedonia, the *Snaith-Hamilton Pleasure Scale* (SHAPS; Snaith et al., 1995) was administered. The SHAPS is a 14-item questionnaire asking individuals to rate their ability to experience pleasure from 1 ('strongly disagree') to 4 ('strongly agree') with higher scores indicating higher levels of anhedonia (Range 14 – 56). The SHAPS has excellent internal consistency (α = .91) and convergent and discriminant validity (Nakonezny, Carmody, Morris, Kurian, & Trivedi, 2010).

The *Childhood Trauma Questionnaire (CTQ)* is a revised 15-item self-report measure that aims to assess the prevalence of emotional, physical and sexual abuse during childhood and as a teenager (Bernstein et al., 1994). The CTQ's internal consistency ranges from good (α =.79) to excellent (α = .94) and the measure shows good test-retest reliability over 2-6 months (r = .88; Bernstein et al., 1994). Each of the three subscales consists of 5 items to assess emotional, physical and sexual abuse, respectively (subscale range: 5-25). Participants rate the frequency of CA experience from 1 (never) to 5 (very often true) with a total severity score from 15-75. DiLillo et al. (2006) suggest raw scores of at least 9 indicate emotional abuse, while accounting for likelihood of common stressors in adolescence (9-12 = low to moderate; 12-15 = moderate to severe; 16+ severe to extreme). For physical abuse, raw scores of at least 8 indicate physical abuse (8-9 = low to moderate, 10-12 = moderate to severe; 13+ = severe to extreme). Raw scores of at least 6 indicate sexual abuse (6-7 = low to moderate; 8-12 = moderate to severe, 13+ = severe to extreme; DiLillo et al., 2006).

Finally, participants completed the 20-item *Risky Behaviour Questionnaire* (RBQ; Auerbach & Gardiner, 2012) to assess frequency of HRB in the past month (0=Never, 1=Almost Never [1 Time Per Month], 2=Sometimes [2-4 Times

Per Month], 3=Almost Always [2-3 Times Per Week] and 4= Always [4 or More Times Per Week]). The total sum of items ranges from 0-80, with a higher RBQ score indicating more engagement in risky behaviour including unsafe sexual practices, rule-breaking, aggressive or violent behaviour, destructive, dangerous or illegal behaviours, self-injury and substance misuse. The RBQ has shown high internal consistency (α = .84; Auerbach & Gardiner, 2012).

Cronbach alpha values were calculated for BDI-II, SHAPS, CTQ and RBQ. All values exceeded the recommended threshold of .70 and values were comparable to the internal consistency measures from the normative samples cited in the publications of the respective instruments.

Reward paradigm. To examine neural response of anticipatory and consummatory reward processing, participants completed the *Card-Guessing Task* while a magnetic resonance imaging (MRI) scan was recorded (Caseras, Lawrence, Murphy, Wise, & Phillips, 2013; Delgado, Nystrom, Fissell, Noll, & Fiez, 2000; Forbes et al., 2009; Figure 1).

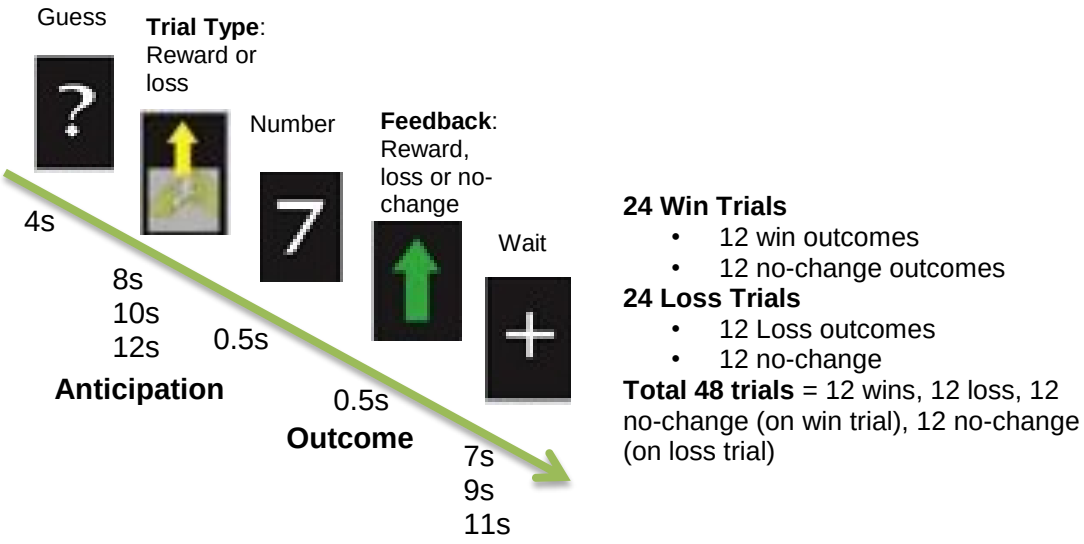

Figure 1. Example of a reward trial sequence of the Card Guessing Task (adapted from Forbes et al., 2009).

The card-guessing task has been effectively used with children with MDD aged eight to 17 years to study reward-related brain function (Forbes et al., 2009). The task was programmed using E-Prime software (Psychology Software Tools; www.psnet.com/eprime) and presented in the MRI suite using an Epson EMP-74 digital projector system. Participants viewed the task using an angled mirror attached to their head coil while lying in the bore of the scanner. Participants selected their responses by pressing buttons with their index and middle finger using a fibre-optic button box.

As part of the card-guessing task, participants received win, loss, or no-change feedback. Neural activation in the striatum and pallidum were measured during the anticipation and delivery of reward. As 'losses' are primarily coded in brain regions other than the reward-specific regions-of-interests (e.g., anterior cingulate cortex; amygdala) these trials were not included to test the study's hypotheses (Holroyd & Coles, 2002; Sokol-Hessner, Camerer, & Phelps, 2013). This is in line with previous studies assessing reward processing using the card-guessing task (Casement, Shaw, Sitnick, Musselman, & Forbes, 2015).

Participants were informed that their performance would determine a monetary reward that was for them to keep after the study. Trials were presented in pseudorandomized order with predetermined outcomes resulting in all participants being rewarded an equal amount of money.

During the task, participants guessed if a card with a possible value of one to nine was higher or lower than five by pressing the respective buttons on a response box. After a choice was made, participants saw a “trial type” slide announcing a reward trial (upward arrow) or loss trial (downward arrow). *Anticipatory reward processing* was operationalized as the neural activity when a reward trial was announced. After seeing the ‘trial type’ slides, participants were shown the actual numerical value of the card. Finally, participants viewed the trial outcome (“feedback’) indicating a win (green arrow), loss (red arrow) or no-change (yellow circle) for no-change. *Consummatory reward processing* was operationalized as neural activity when participants ‘won’ (green arrow). Trials were separated by a fixation cross which served as a baseline for the analysis. Groups were compared on reaction times on reward trials as well as number of missed trials to ensure task compliance. The task lasted approximately 20 minutes.

Magnetic resonance imaging acquisition*.* Structural and functional neuroimaging data was collected on a Philips 1.5T whole-body imager (Gyroscan Intera with Explorer gradients) fitted with a 12-channel quadrature brain array coil. During the card-guessing task, 38 brain slices were acquired using an interleaved and tilted slice acquisition. T2* weighted echoplanar images were acquired using the following parameters: TR/TE = 3000/45ms; 388 volumes; FOV= 240 mm; Matrix=80x80; voxel size = 3x3x3mm; flip angle = 90°). Functional imaging data for each participant was aligned with their own

high-resolution T1-weighted anatomical image for registration into standard space and functional localisation (3D Gradient Echo, TR/TE = 25/4.2ms; 100 volumes, 163 slices, FOV = 230mm; Matrix = 256x204; voxel size = 0.9x.09x1.6mm; flip angle = 30°**)**.

Procedure

After contacting the researcher, participants took part in a brief phone screen to assess their eligibility for the study, check the required MRI safety standards and ask about their mood over past two weeks.

Consent. For participants who were minors (< 16 years), a legal guardian gave verbal consent for the researcher to speak to the young person and to complete the phone screen. For minors, guardians also completed the MRI safety screen as part of the phone screen. Participants who were 16 years or older consented to complete the phone screen. Information materials about the study were sent out to each participant at least 24 hours before the first study visit (Appendix E).

On the day of the study, participants (≥16 years) provided written consent to participate (Appendix F). When participants were minors, their guardian gave written consent to participant and the young person signed an assent form (consisting of the same information; Appendix G-H). Participants were informed about their rights to stop or withdraw from the study and the limitation of confidentiality in case of risk of harm to self or others.

Session one: Clinical interview and questionnaire data. The KSADS was administered and participants completed four self-report questionnaires (BDI, SHAPS, RBQ, CTQ) using Lime Survey, a computer-based survey programme. Participants then completed a reward task while electroencephalography (EEG)

was recorded, which is not part of the current research and will not be discussed. The first session took place at the Mood Disorder Centre at the University of Exeter and lasted approximately two hours. Following the session, participants were debriefed, an information sheet for the MRI was discussed and they received £20 in gift vouchers for their time and travel.

Session two: Reward paradigm and MRI scan. Participants completed the PANAS at the beginning and the end of the second session to monitor their mood. The second session involved a one-hour MRI scan for which participants or their respective guardian completed an updated MRI safety screen prior to entering the scanner suite. The reward task was explained using printed images and a mock response-box. Participant were provided with ear protection, screened for metal objects and positioned on a foam-padded table that was moved into the bore of the MRI scanner. Individuals were visually monitored during the scan and were able to communicate with the researcher via an intercom in the head coil. Participants were given a panic button to set off an alarm in case they wanted to stop the scan. Participants were reminded to remain still and refrain from any head, face, or jaw movements.

For the first part of the scan, participants were invited to relax (10 min) while anatomical and resting state images were recorded. Participants also completed a practice block of the Card-Guessing task (4 minutes) before starting with the actual reward task (20 minutes) (Delgado et al., 2000). Additional scans were collected following the reward task (i.e., diffusion tensor imaging), which are not part of the current study.

The second visit took place at the MR Research Centre at the University of Exeter and lasted about 1.5 hours. Following the MRI scan, participants were fully debriefed and were given an opportunity to look at their brain scan. They received

£26 in gift vouchers (£17 for their time and travel and £9 'wins' from the task). Participants were sent a picture of their brain scan as a thank-you. Approximately one week after the scan, participants were contacted by phone for a follow-up to monitor levels of distress and to signpost to relevant services if needed.

Analyses

Outliers and influential statistics. No missing data were found in the sample. All data were checked for outliers using z-scores and boxplots. Univariate outliers (z-score < 3.29) were found for the RBQ scores, number of missed trials, and on fMRI reward signals in bilateral putamen, right nAcc, left caudate. Outliers were replaced with the value of the next not-outlying score. CTQ and PANAS-NA variables were log-transformed due to outliers and to reduce impact of skewness. As part of the regression, I used Cook's distances to check the influence of a single case on the model (< 1; Cook & Weisberg, 1982), Mahalanobis distances to measure leverage using recommended cut-off <15.6 (Barnett & Lewis, 1978) and DFBeta to measure influence of a single case on regression parameter (< +/-0.33; Field, 2005). No influential cases were identified following the outlier analyses.

Parametric assumptions*.* Residuals of the regression model were approximately normally distributed. Linearity and homogeneity of variances were examined by plotting standardized residuals against range of predicted values of outcomes in the regression (*ZRes x *ZPred). I did not observe a non-linear/curvilinear pattern (linearity assumption met) and no change in dispersion of the residuals at different predicted values of the outcome (no heteroscedasticity). Partial plots were linear and homoscedastic (plotting predictors against outcome after partialling out for other predictors).

Correlations between predictor variables did not exceed >.7 suggesting low levels of collinearity, which allowed me to determine individual importance of predictors (Field, 2005).

Descriptive data. Chi-Square tests and Analysis of Variance (ANOVA) examined group differences in demographics (i.e., age, ethnicity) and questionnaire data (i.e., BDI, SHAPS, CTQ, PANAS). To test the first hypothesis, an ANOVA examined group differences in RBQ scores between controls, CA+MDD and MDD (*Hypothesis 1*). Greenhouse-Geisser correction was used when appropriate; significant findings were followed-up with the Fisher Least Significant Difference (LSD) test.

FMRI pre-processing. Data pre-processing and statistical analyses were conducted using fMRI Expert Analysis Tool (FEAT, Version 5.0) from the FMRIB's Software Library (FSL). Standard pre-processing steps were performed for each individual and included MCFLIRT motion correction, non-brain removal, spatial smoothing (full-width at half-maximum 5mm Gaussian kernel), normalisation on grand-mean intensity, and high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, sigma=50.0s) (Jenkinson, Bannister, Brady, & Smith, 2002). Registration was based on FLIRT (Jenkinson et al., 2002).

FMRI analysis. The primary contrasts of interests were selected in line with previous publications examining the relationships between neural responses to reward and mood using the card-guessing task (Caseras et al., 2013; Forbes et al., 2009). Based on these publications, the anticipatory reward period was divided into two independent events consisting of an 'initial' two-second period and a remaining 'rest' period of the anticipation time (varying from 6-10 seconds). Only the initial period (2s) was extracted and analysed as neural

responses are expected to habituate to reward cues over time and would therefore skew signal when averaged over the entire anticipatory reward period (i.e., total time “trial type” slide is displayed; Figure 1). Similarly, the consummatory reward phases included the first one-second interval during the delivery of reward (‘feedback’; Figure 1).

In summary, the two main contrasts of interest included neural responses to (1) *anticipatory reward*: initial anticipation of reward (2s) vs. baseline (fixation cross) and (2) *consummatory reward*: the win trials of initial reward delivery (1s) vs. baseline (fixation cross).

Region-of-interest analyses. Blood-oxygen-level-dependent (BOLD) signals to the anticipation and delivery of reward were extracted for four bilateral region-of-interests (ROI): NAcc, pallidum, caudate and putamen. For each lateral ROI, masks were created using the Harvard-Oxford Subcortical Structural Atlas in MNI space (Montreal Neurological Institute). Using fslmaths tools, masks were binarized and thresholded to include voxels with at least 10% probability of being part of the ROI. Featquery was used to extract data during reward anticipation (vs. baseline) and reward outcome (vs. baseline) for each participant for each lateral ROI. Data was converted to % signal change and exported into SPSS.

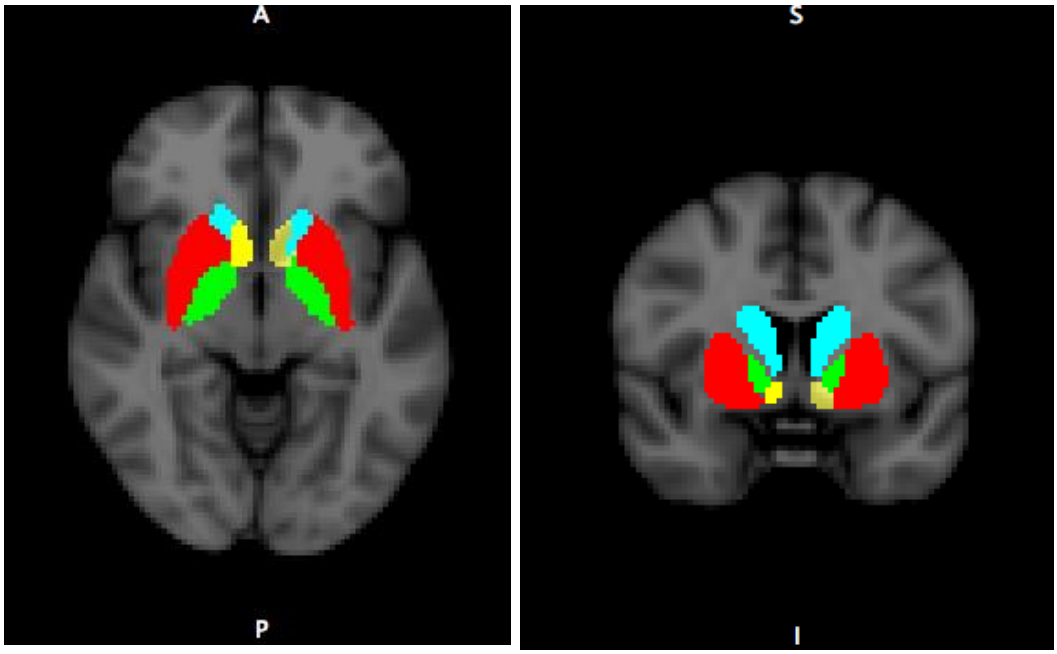

Figure 2. Bilateral masks of brain regions of the reward system (caudate = blue; pallidum = green; putamen = red; nucleus accumbens = yellow).

Regression. Following data cleaning, separate hierarchical regression analyses were run to test the second hypotheses: (a) CA predicts decreased neural responses during anticipation of reward in each lateral ROI (hypothesis 2a: Model 1: Age, BDI score; Model 2: CTQ score) and (b) CA predicts decreased neural responses during delivery of reward in each ROI (hypothesis 2b: Model 1: Age, BDI score; Model 2: CTQ score). Given the high correlation between BDI and SHAPS in the sample ($r(35)$ = .81, p < .01), only BDI was added as a predictor variable. Age was included to account for differences of maturation in brain regions.

To test the third hypothesis, separate hierarchical regression analyses examined if neural responses from each lateral ROI during anticipatory reward (Model 1: % signal change ROI, Model 2: BDI) and consummatory reward processing (Model 1: % signal change ROI, Model 2: BDI) predicted HRB indexed by respective RBQ scores. Due to a significant correlation between

HRB and depressive symptoms ($r(35) = .58$, $p < .001$), BDI was entered in a second step to view unique variance explained by neural activation. Age was not significantly related to HRB ($p = .21$) and thus was not added as a predictor to ensure the most parsimonious model[3].

Results

Demographic and Clinical Data

Participants were on average 17.08 years old ($SD = 1.86$) and the majority described themselves as Caucasian. The clinical groups (CA+MDD, MDD) did not differ in their frequencies of past ($p = .63$) or current ($p = .39$) psychological treatment. There was no difference in the number of group members with at least one anxiety diagnosis (Panic Disorder: CA+MDD=1, MDD=1; Specific Phobia: CA+MDD= 2, MDD=0; Generalized Anxiety Disorder: CA+MDD= 2, MDD=1; Table 1).

Mood. Compared to controls, CA+MDD and MDD reported significantly higher levels of depression ($F(2, 34) = 43.11$, $p < .001$) and anhedonia ($F(2, 34) = 13.16$, $p < .001$). Across MDD and CA+MDD groups, post-hoc tests indicated comparable levels of moderate depression ($p = .68$) and anhedonia ($p = .86$) (Table 1). However, the CA+MDD group reported higher numbers of past depressive episodes ($t(19) = 2.09$, $p = .05$). No group differences emerged in positive and negative state affect (***p's*** > .07). Pre- and post-measures were highly correlated for positive ($r(35) = .83$, $p < .001$) and negative affect ($r(35) = .39$, $p = .02$) suggesting consistent ranking of participants before and after the study.

[3] Regression analyses with age as an additional predictor variable did not yield different results. Data is available upon request.

Childhood abuse. As expected, the CA+MDD group reported significantly higher levels of trauma ($F(2, 34) = 22.36$, $p < .001$) compared to MDD ($p < .001$) and controls ($p < .001$) Within the CA+MDD group, adolescents reported moderate to severe levels of all types of CA (emotional abuse: $M = 13.08$, $SD = 6.59$; physical abuse: $M = 9.69$, $SD = 6.09$; sexual abuse: $M = 9.46$, $SD = 6.72$).

High-risk behaviour. We predicted more frequent HRB behaviour in CA+MDD group compared to MDD and controls (*Hypothesis 1*). ANOVA revealed significant group differences in HRB ($F(2, 34) = 5.93$, $p = .01$), with post-hoc tests indicating significantly higher frequency of HRB in CA+MDD compared to controls ($p = .03$) and MDD compared to controls ($p = .01$), but no differences in HRB between MDD and CA+MDD ($p = .49$). Results thus partially supported our first hypothesis.

Table 1

Data From Participants with a History of Child Abuse and Depression (CA+MDD), Depression but no Child Abuse (MDD) and Healthy Controls

Note. M=mean; SD=standard deviation, Dx=diagnosis; BDI-II=Beck Depression Inventory-II; CA=childhood abuse; CTQ=Childhood Trauma Questionnaire; MDD=major depressive disorder; NA=negative affect; No=Number; PA=positive affect; RBQ=Risk Behaviour Questionnaire; SHAPS=Snaith-Hamilton Pleasure Scale
[a] Fisher's Exact Test (two-tailed). [b] CA+MDD as different from control group (p≤.001, Fisher Least Significant Difference (LSD); Scheffe test (ST)). [c] CA+MDD as different from MDD (p≤.001, LSD, ST). [d] Data was log-transformed but untransformed data is reported for ease of interpretation. [e] MDD as different from the control group (p≤.001, LSD, ST). [f] CA+MDD as different from the control group (p<.05, LSD). [g] MDD as different from the control group (p<.05, LSD, ST).

	CA+MDD (n=13)	MDD (n=8)	Controls (n=16)	χ^2 /t-/F-Value	*P*-Value
Demographics					
Age, M (SD)	17.85 (1.52)	17.13 (1.89)	16.44 (1.97)	2.19	*.13*
Ethnicity: Caucasian, No (%)	12 (92.30)	8 (100.0)	13 (81.30)	15.73	.75
Treatment: Past, No (%)	10 (76.90)	5 (62.50)	N/A	N/A	.63[a]
Treatment: Current, No (%)	8 (61.50)	3 (37.5)	N/A	N/A	.39[a]
No. MDD episodes, M (SD)	2.46 (0.78)	1.63 (1.06)	N/A	2.09	***.05***
Anxiety Dx, No (%)	4 (30.80)	2 (25.00)	N/A	N/A	1.0[a]
Clinical Measures					
CTQ, M (SD)	32.23 (16.39)[b, c]	15.88 (0.83)	16.00 (1.03)	22.36[d]	***<.001***
BDI-II, M (SD)	27.62 (8.93) [b]	26.25 (9.75)[e]	4.63 (3.54)	43.11	***<.001***
SHAPS, M (SD)	29.46 (6.79) [b]	29.88 (5.69) [e]	20.63 (3.36)	13.16	***<.001***
RBQ, M (SD)	9.35 (5.82)[f]	12.25 (6.30)[g]	4.62 (4.65)	5.93	***.006***
State Affect					
PA-pre, M (SD)	24.54 (5.91)	26.25 (8.40)	29.88 (6.09)	2.48	.10
PA-post, M (SD)	24.00 (5.75)	28.13 (10.23)	28.44 (5.20)	1.76	.19
NA-pre, M (SD)	12.85 (2.15)	13.75 (2.12)	11.75 (1.88)	2.96[d]	.07
NA-post, M (SD)	11.23 (2.20)	11.38 (1.69)	10.38 (1.03)	1.41[d]	.26

Reward: Card-Guessing Task

Behavioural data. Groups did not vary in their reaction time on reward trials ($F(2, 34) = 1.98$, $p = .15$) or in the number of missed trials ($F(2, 34) = .36$,

p = .70). On average, participants completed 97% of all trials (*SD* = 4.27) indicating sufficient task compliance.

Anticipatory reward processing. Hierarchical regression tested if a history of CA predicted neural activation during reward anticipation in bilateral NAcc, caudate, putamen and pallidum, irrespective of age and depressive symptoms. Only age significantly predicted left NAcc activation during reward anticipation, with older participants showing increased activation when waiting for a reward (see Table 2).

Table 2

Hierarchical Regression Analyses for Activation in Nucleus Accumbens (NAcc) During Reward Anticipation

	B	**SE B**	β	**Variance Explained**
Left NAcc				
Model 1				
Constant	-.56	.17		
Age	.03	.01	.43*	
BDI	-.003	.001	-.28	R^2 = .18*, $R^2_{adjusted}$ = .14
Model 2				
Constant	-.55	.21		
Age	.03	.01	.44*	
BDI	-.002	.002	-.28	
CTQ_{log}	-.007	.12	-.01	$^{\Delta}R^2$ = .00, $^{\Delta}R^2_{adjusted}$= -.03
Right NAcc				
Model 1				
Constant	-.41	16		
Age	.02	.01	.34	
BDI	-.002	.001	-.21	R^2 = .11, $R^2_{adjusted}$ = .06
Model 2				
Constant	-.26	.20		
Age	.02	.01	.38*	
BDI	-.001	.001	-.13	
CTQ_{log}	-.15	.11	-.23	$^{\Delta}R^2$ = .04, $^{\Delta}R^2_{adjusted}$= .02

Note. * p<.05, ** p<.01; BDI = Beck Depression Inventory; CTQ_{log} = Log transformed Childhood Trauma Questionnaire

As regression models did not yield any significant findings for the predicting role of CA, the first part of the second hypothesis was not supported. Table I1 in Appendix I lists non-significant results for activation in putamen (R^2_{left} = .18, *p* =

.09; R^2_{right} = .14, p = .16), caudate (R^2_{left} = .11, p = .29; R^2_{right} = .09; p = .39) and pallidum (R^2_{left} = .05, p = .62; R^2_{right} = .14, p = .17).

Consummatory reward processing. Hierarchical regression tested if CA significantly predicted neural activation during the consummatory reward period in bilateral NAcc, caudate, putamen and pallidum, irrespective of age and depressive symptoms. The regression model was significant in predicting neural activation in the left NAcc and right NAcc during reward outcome (see Table 3).

Table 3

Hierarchical Regression Analyses for Activation in Nucleus Accumbens (NAcc) During Consummatory Reward Period

	B	SE B	β	Variance Explained
Left NAcc				
Model 1				
Constant	.78	.23		
Age	-.04	.02	-.46**	
BDI	.001	.002	.06	R^2 = .20*, $R^2_{adjusted}$ = .15
Model 2				
Constant	.58	.28		
Age	-.04	.01	-.49**	
BDI	.000	.002	-.02	
CTQ_{log}	.21	.16	.22	ΔR^2 = .04*, $\Delta R^2_{adjusted}$= .01
Right NAcc				
Model 1				
Constant	.74	.23		
Age	-.04	.01	-.46**	
BDI	.004	.002	.31	R^2 = .21*, $R^2_{adjusted}$ = .16
Model 2				
Constant	.56	.28		
Age	-.04	.01	-.49**	
BDI	.003	.002	.24	
CTQ_{log}	.18	.16	.18	ΔR^2 = .03*, $\Delta R^2_{adjusted}$= .01

Note. * p<.05, ** p<.01. BDI = Beck Depression Inventory; CTQ_{log} = Log transformed Childhood Trauma Questionnaire

However, variance in bilateral NAcc activation was primarily explained by participant's age and not by exposure to CA; thus the second part of our second hypothesis was not confirmed. Results showed more blunted bilateral NAcc

response when 'winning' a monetary reward in older participants. Table I2 in Appendix I lists non-significant results for activation in putamen (R^2_{left} = .06, p = .58; R^2_{right} = .09, p = .38), caudate (R^2_{left} = .02, p = .88; R^2_{right} = .09, p = .38) and pallidum (R^2_{left} = .08, p = .40; R^2_{right}.02; p = .88).

High-risk behaviour. Hierarchical regression models were used to test if neural activation in reward-related ROIs during the anticipation and delivery of reward predicted HRB irrespective of depressive symptoms (Table 4).

For reward anticipation, reduced activation in the right pallidum explained unique variance in frequency of HRB in adolescents irrespective of depressive symptoms (see Table 4). This partially confirmed the third hypothesis. Although the remaining regression models also predicted HRB, variance was best explained by depressive symptoms with no significant contribution from activation in left pallidum (β = -.12; p = .39), putamen (β left = -.13; p = .39; right: β right = -.22; p = .13), caudate (β lef= .07; p = .62; β right = .25; p = .08) or NAcc (β lef= -.09; p = .53; β right = -.11; p = .44) during reward anticipation (see Table 3I in Appendix I).

For consummatory reward processing, regression analyses showed that depressive symptoms, but not ROI activation during reward outcome predicted HRB (putamen: β left = -.04; p = .80; β right = .03; p = .82; caudate: β left = -.07, p = .63, β right = .07, p = .65; NAcc: β left = .10, p = .49, β right = -.10; p = .50; see Table 3I in Appendix I).

Table 4

Results of Hierarchical Regression Analyses of Pallidum Activation during Reward Anticipation and Reward Outcome Predicting High-Risk Behaviour

	B	SE B	β	**Variance Explained**
Anticipatory Reward				
Model 1				
Constant	7.06	1.21		
Left pallidum	-14.23	10.85	-.22	R^2 = .05, $R^2_{adjusted}$ = .02
Model 2				
Constant	2.94	1.44		
Left pallidum	-8.09	9.19	-.12	ΔR^2 = .31**, $\Delta R^2_{adjusted}$= .30
BDI	.26	.06	.56**	
Model 1				
Constant	6.66	1.01		
Right pallidum	-30.07	10.04	-.45**	R^2 = .20**, $R^2_{adjusted}$ = .18
Model 2				
Constant	2.98	1.29		
Right pallidum	-21.89	8.80	-.33*	ΔR^2 =.24**, $\Delta R^2_{adjusted}$= .23
BDI	.23	.06	.50**	
Consummatory Reward				
Model 1				
Constant	7.73	.95		
Left pallidum	-21.18	8.51	.39*	R^2 = .15*, $R^2_{adjusted}$ = .13
Model 2				
Constant	3.68	1.36		
Left pallidum	-13.58	7.55	.25	ΔR^2 = .25**, $\Delta R^2_{adjusted}$= .23
BDI	.24	.06	.52**	
Model 1				
Constant	7.77	1.05		
Right pallidum	6.71	9.33	.12	R^2 = .02, $R^2_{adjusted}$ = -.01
Model 2				
Constant	3.18	1.40		
Right pallidum	5.11	7.71	.09	ΔR^2 = .33**, $\Delta R^2_{adjusted}$= .32
BDI	.27	.06	.58**	

Note. * p<.05, ** p<.01; BDI = Becks Depression Inventory

In sum, blunted neural activation in the right pallidum during reward anticipation predicted higher frequency of HRB, irrespective of depressive symptoms. Overall, increased depressive symptoms rather than ROI responses to the anticipation or delivery of reward predicted higher frequency of HRB.

Discussion

This study investigated if, irrespective of current depressive symptoms, a history of CA was associated with blunted neural responses when anticipating

or receiving a monetary reward. Moreover, it was tested if lower reward 'wanting' and reward 'liking' would predict the frequency of HRB in adolescents. Findings will be summarized before discussing the study's strengths and limitations and giving recommendations for future research.

First, findings did not confirm the first hypothesis that HRB are more prevalent in adolescents who experienced CA. Although adolescents in both clinical groups (MDD and MDD+CA) used more HRB than healthy controls, no significant differences emerged between the two clinical groups. Results suggest that a current diagnosis of depression - rather than exposure to CA per se - predicted greater risk-taking among adolescents. This is an unexpected finding given the extensive research showing an increase in HRB following CA (Accident Compensation Coporation, 2008; Radford et al., 2011). Moreover, depression is often associated with higher punishment sensitivity than HRB. Guyer et al. (2006) found that children with depression and CA were more likely to avoid risky choices compared to non-depressed children with CA. However, the current study does not delineate whether results were due to a lower than expected frequency of HRB in the CA group or higher than expected use of HRB in MDD group. One explanation may be that only individuals with CA but no current MDD are likely to seek HRB due to their decreased sensitivity to possible negative consequences, whereas individuals with CA and MDD use fewer HRB due to fear of punishment. This interpretation is supported by Strekalova et al. (2006) who found that rats with anhedonia and chronic stress were avoidant of risk and novelty, whereas rats with chronic stress but no anhedonia showed hyperactive behaviour. The current research is one of the few studies examining individuals who have a MDD diagnosis and CA. More research is needed to investigate possible differences in HRB in abused

individuals with and without MDD. The rationale for not recruiting a group of individuals with CA but no MDD in the current study was twofold – a logistical one that this sample can be difficult to identify as rarely presenting for help to clinical services and a theoretical one in that these individuals were assumed to be elevated in resilience. In retrospect, it would have been beneficial to include abused individuals with and without MDD in order to identify subgroups of adolescents who are a more likely to engage in HRB following CA.

Secondly, contrary to our second hypothesis, a history of CA was not associated with altered neural responses to the anticipation or delivery of rewards in the reward-related regions of interest. However, older participants showed increased activation when waiting for rewards and decreased activation when receiving a reward in the NAcc, a region critically implicated in the hedonic experiences of rewards (Der-Avakian & Markou, 2012). Results suggest that irrespective of depressive symptoms or CA history, older adolescents in our study (upper age range: 19 years) displayed greater reward 'wanting' but blunted reward 'liking' than younger adolescents (lower age range: 13 years). These findings are in line with neurodevelopment research showing that reward-sensitive subcortical regions develop in an inverted U-shape pattern characterized by increased reactivity to rewarding stimuli in early adolescence and reduced reactivity in later life (Casey & Jones, 2010; Galvan et al., 2006; Hare et al., 2008; Spear, 2011; Van Leijenhorst et al., 2010).

Finally, partial support was found for the third hypothesis as blunted neural activation in the right pallidum during reward anticipation predicted greater frequency of HRB irrespective of depressive symptoms. The pallidum plays a critical role in integrating reward information and transmitting it to the motor cortex via the thalamus to elicit goal-directed actions (Der-Avakian & Markou,

2012; Frank & Claus, 2006). Weakened pallidum activity during reward anticipation may therefore indicate difficulties in perceiving the cue as rewarding and failing to initiate goal-directed actions to obtain natural rewards (monetary). According to Koob et al.'s (2005) model, individuals who do not experience the reinforcing features of natural rewards are likely to experience negative affect, which motivates them to seek HRB to alleviate that distress. Understanding neural reward responses and their behavioural implications would allow a targeted treatment approach early on in development (Gogtay et al., 2004).

Contrary to the hypotheses, the current study did not find support for impairments in reward processing following CA. Although altered experiences of pleasure in the face of stress is a more recent and preliminary finding (Boecker et al., 2014; Hanson et al., 2016), blunted anticipatory reward processing has been a consistent finding in neuroimaging studies with individuals who experienced CA (Boecker et al., 2014; Dillon et al., 2009; Metha et al., 2010; see Teicher & Samson, 2016 for a review). Several methodological differences may account for this null finding. First, most research showing altered reward function either focussed on one type of abuse (e.g., Metha et al., 2010) or collected chronological details about the timing of abuse in their longitudinal design (e.g., Dillon et al., 2009; Hanson, 2016). The sensitive period framework suggests that brain regions are most vulnerable to changes in neuroplasticity when stressors coincide with growth spurts of the ROI. Hence, the accumulation of different types of abuse that occurred at various time points may have cancelled out unique implications for the reward system. Future research may benefit from focusing on a single type of abuse occurring during the sensitive period of development of the reward system to explore explicit links between reward and CA (Teicher & Samson, 2016).

Finally, the study was likely to be underpowered for detecting small to medium effects, which may have been necessary to identify incremental differences in CA beyond the large impact of depressive symptoms. A larger sample size in the current study may have helped to differentiate the unique contribution of CA and depression for reward processing. Although, a simple regression analysis (*k*=1) showed that depressive symptoms explained significant variance in left and right putamen during reward anticipation (Appendix J), BDI scores did not predict activation in other striatal regions as previously found in adolescent studies (e.g., caudate; Forbes et al., 2009). Future studies are recommended to recruit larger samples to further delineate this lack of findings. Nevertheless, our sample size was initially estimated after considering effect sizes obtained from previous studies, which yielded medium to large effects for relationships among CA, reward functioning and HRB (Dillon et al., 2009; Pechtel & Pizzagalli, 2013).

Several limitations need to be acknowledged. First, the external and internal validity of the findings is somewhat limited given the small sample size. Although sample size is a common challenge when studying adolescents with CA, the study was only powered to detect moderate to large effects (Mueller et al., 2012). Secondly, I conducted a large number of analyses. However, when I calculated Sidak and Bonferroni corrections to adjust the *p* value to account for multiple comparisons ($p < .002$), all findings remained significant. Thirdly, our sample showed heterogeneity of abuse experiences across childhood, making if difficult to determine if CA occurred during sensitive periods of neurodevelopment for the reward system. Longitudinal samples are needed to study the impact of abuse types and timing across development (e.g., Hanson et al., 2016; Pechtel, Lyons-Ruth, Anderson, & Teicher, 2014). Another

limitation of the study was a lack of group of individuals with CA but no MDD as this could have provided important information on the differential effects of CA and MDD. Finally, our design did not allow us to study the mechanisms linking blunted activity in pallidum to HRB as proposed by Koob and Le Moal's (2005) negative reinforcement model. Studies investigating cross-reactivity of affect and reward processes may be needed to understand if HRB behaviour are indeed used to seek relief from negative affect caused by blunted reward experiences.

Despite these limitations, the study's strengths may help to advance the field. Recognizing cues for natural rewards and experiencing pleasure are important in daily life. Blunted experiences of reward are implicated in psychological disorders affecting young people including depression and substance misuse. As a result, understanding the origins of blunted reward experience is pivotal to identify young people at risk of HRB. To our best knowledge, the current study was the first to study complex brain-behaviour processes during reward processing using functional neuroimaging in relation to HRB in adolescents who experienced CA and MDD. Although the current study did not confirm changes in reward processing following CA, it did provide support for the role of blunted reward processing in HRB beyond the impact of depression. The present study used a translational approach of understanding CA in the context of neurodevelopment before linking it to clinical risk behaviours and psychological symptoms often seen in child and adolescent mental health services. Researchers have argued that translational research is critical to capitalize on the 'windows of opportunities' that emerge in adolescent neurodevelopment to prevent, reduce or reverse the sequelae of CA (Heim & Binder, 2012; Weller, Leve, Kim, Bhimji, & Fisher, 2015). A meta-analysis

established that various strength-based interventions can improve neurodevelopment and behavioural outcomes for those who experienced CA. Leve et al. (2012) identified several child and adolescent interventions that effectively used positive, rewarding parenting strategies to counteract the impact of blunted reward processing, HRB, and HPA axis hyperactivity (Chamberlain, 2003; Dozier et al., 2008; Fisher, Gunnar, Chamberlain & Reid, 2000). However, future research is needed to explore (1) if reward-based interventions help to reduce the 'need' for HRB following CA, (2) when these interventions are best delivered to capitalize on the sensitive periods or 'windows of opportunities' in neurodevelopment and (3) whether interventions are effective on a behavioural (i.e., reduce HRB) and on a neurobiological level (i.e., increase pallidum activation) (Koob & Le Moal, 2005).

In sum, despite several limitations, the current study used an innovative translational approach to examine the relationship among CA, reward processing and HRB. Results highlighted a role of blunted anticipatory reward in increased HRB in adolescents but did not support a link to adverse childhood experiences. Understanding such processes will be pivotal for the development and timing of interventions to prevent HRB and foster resilience after child abuse.

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Appendix A

NHS Ethical Approval

Health Research Authority
NRES Committee South West - Exeter
Whitefriars
Level 3
Block B
Lewins Mead
Bristol
BS1 2NT

Telephone: 0117 342 1332

15 April 2015

Dr Pia Pechtel
Trainee Clinical Psychologist
NHS
Mood Disorder Centre
Sir Wellcome Building for Mood Disorder Research
School of Psychology
University of Exeter
EX4 4QG

Dear Dr. Pechtel

Study title:	**Reward Processing in Adolescents with a History of Childhood Abuse**
REC reference:	**15/SW/0022**
Protocol number:	**ResearchProtocol**
IRAS project ID:	**150989**

Thank you for your letter of 10 April 2015 , responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this favourable opinion letter. The expectation is that this information will be published for all studies that receive an ethical opinion but should you wish to provide a substitute contact point, wish to make a request to defer, or require further information, please contact the REC Manager, Mrs Kirsten Peck, . Under very limited circumstances (e.g. for student research which has received an unfavourable opinion), it may be possible to grant an exemption to the publication of the study.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database. This should be before the first participant is recruited but no later than 6 weeks after recruitment of the first participant.

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to request a deferral for study registration within the required timeframe, they should contact hra.studyregistration@nhs.net. The expectation is that all clinical trials will be registered, however, in exceptional circumstances non registration may be permissible with prior agreement from NRES. Guidance on where to register is provided on the HRA website.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Advert Mood]	V3	07 December 2014
GP/consultant information sheets or letters [Letter Practitioners]	V3	07 December 2014
Interview schedules or topic guides for participants [KSADS]	V1	07 December 2014
IRAS Checklist XML [Checklist_16012015]		16 January 2015
IRAS Checklist XML [Checklist_10042015]		10 April 2015
Other [Phone Screen]	V3	07 December 2014
Other [Debrief]	V3	07 December 2014
Other [Risk Protocol]	V3	07 December 2014
Other [Review Study]	V1	16 January 2015
Other [CV Dr. Anna Adlam]	V1	16 January 2015
Other [CV Prof Ed Watkins]	V1	16 January 2015
Other [Consent Form Parent CLEAN]	V4	02 March 2015
Other [Consent Form Young Adult CLEAN]	V4	02 March 2015
Other [MRI Information Sheet CLEAN]	V4	02 March 2015
Other [Response Letter To Committee]	V1	02 March 2015
Other [Assent Form Minor CLEAN]	V5	31 March 2015
Other [Information sheet participants CLEAN]	V5	31 March 2015
Other [Information sheet parents CLEAN]	V5	31 March 2015
Other [Response Letter To Committee]	V2	31 March 2015
Participant consent form [Consent Form Young Adult]	V4	02 March 2015
Participant consent form [Consent Form Parent]	V4	02 March 2015
Participant consent form [Assent Form Minor]	V4	02 March 2015
Participant consent form [Assent Form Minor]	V5	31 March 2015
Participant information sheet (PIS) [MRI Information Sheet]	V4	02 March 2015
Participant information sheet (PIS) [Information sheet participants]	V5	31 March 2015
Participant information sheet (PIS) [Information sheet parents]	V5	31 March 2015
REC Application Form [REC_Form_12012015]		12 January 2015

Research protocol or project proposal [Research protocol]	V4	31 March 2015
Summary CV for Chief Investigator (CI) [CV]	V1	07 December 2014
Validated questionnaire [BDI]	V1	07 December 2014
Validated questionnaire [PANAS]	V1	07 December 2014
Validated questionnaire [SHAPS]	V1	07 December 2014
Validated questionnaire [Brooding]	V1	07 December 2014
Validated questionnaire [CTQ]	V1	07 December 2014
Validated questionnaire [RBQ]	V1	07 December 2014

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website:
http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at
http://www.hra.nhs.uk/hra-training/

15/SW/0022	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

Kirsten Peck

p.p. Joan Ramsay
Vice Chair

e-mail: nrescommittee.southwest-exeter@nhs.net

Enclosures: "After ethical review – guidance for researchers" *[SL-AR2]*

Copy to: *Ms Gail Seymour*
Mrs Lynda Garcia, RD&E NHS FT

Appendix B

Virgin Care Ethical Approval

Integrated Children's Services
One Capital Court
Bittern Road
Exeter
Devon
EX2 7FW

t:01392 385340
e:jaynecarroll@nhs.net

Pia Pechtel, Ph.D., CPsychol.
Trainee Clinical Psychologist
University of Exeter
Sir Henry Wellcome Building for Mood Disorders Research
University of Exeter
Perry Road
EX4 4QG

13th October 2015

Dear Pia

Re: Devon ICS research study - Letter of Ethical Approval

Please accept this letter as confirmation that Devon Integrated Children's Services are in agreement to work in collaboration with yourselves on the research project "Reward Processing in Adolescents with a History of Childhood Abuse".

We very much look forward to working with yourselves and thank you for your interest in our services.

Yours sincerely,

Jayne Carroll
Regional Director of Operations
Devon Integrated Children's Services

Appendix C

University Ethical Approval

4th of November, 2014

Dear Ms Pechtel,

Following recent review by the Ethics Committee for Psychology at the University of Exeter, I can confirm that your application entitled "Reward processing in adolescents with a history of childhood abuse" (2016/644) has been approved for the duration of your project (4th Nov 2014-4th Nov 2016).

You may now proceed with data collection at your soonest convenience.

Sincerely,

Dr Tim Kurz
Ethics Committee Chair for Psychology

Appendix D

Study Questionnaires

Beck's Depression Inventory – II: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the ONE STATEMENT in each group that bests describes the way you have been feeling during the PAST TWO WEEKS, INCLUDING TODAY. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in sleeping pattern) or Item 18 (Changes in Appetite).

1. Sadness
0 I do not feel sad.
1 I feel sad much of the time.
2 I am sad all the time
3 I am so sad or unhappy that I can't stand it.

2. Pessimism
0 I am not discouraged about my future.
1 I feel more discouraged about my future than I used to be.
2 I do not expect things to work out for me.
3 I feel that my future is hopeless and will only get worse.

3. Past Failure
0 I do not feel like a failure.
1 I have failed more than I should have.
2 As I look back, I see a lot of failures.
3 I feel I am a total failure as a person.

4. Loss of Pleasure
0 I get as much pleasure as I ever did from the things I enjoy.
1 I don't enjoy things as much as I used to.
2 I get very little pleasure from the things I used to enjoy.
3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings
0 I don't feel particularly guilty.
1 I feel guilty over many things I have done or should have done.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6. Punishment Feelings
0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7. Self-Dislike
0 I feel the same about myself as ever.
1 I have lost confidence in myself.
2 I am disappointed in myself.
3 I dislike myself.

8. Self-Criticalness

0 I don't criticize or blame myself more than usual.
1 I am more critical of myself than I used to be.
2 I criticize myself for all of my faults.
3 I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes

0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10. Crying

0 I don't cry any more than I used to.
1 I cry more than I used to
2 I cry over every little thing.
3 I feel like crying, but I can't.

11. Agitation

0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it's hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0 I have not lost interest in other people or activities
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things
3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.
1 I find it more difficult to make decisions than usual.
2 I have much greater difficulty in making decisions than I used to.
3 I have trouble making any decisions.

14. Worthlessness

0 I don't feel I am worthless.
1 I do not consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.
1 I have less energy than I used to have.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern.
1a I sleep somewhat more than usual.
1b I sleep somewhat less than usual.
2a I sleep a lot more than usual.
2b I sleep a lot less than usual.
3a I sleep most of the day.
3b I wake up 1-2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite
1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.
2a My appetite is much less than before.
2b My appetite is much greater than usual.
3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.
1 I can't concentrate as well as usual.
2 It's hard to keep my mind on anything for very long.
3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.
1 I get more tired or fatigued more easily than usual.
2 I am too tired or fatigued to do a lot of the things I used to do.
3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of interest in Sex

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

Childhood Trauma Questionnaire (CTQ)

Instructions: These questions ask about some of your experiences growing up as a child and a teenager. For each question, circle the number that best describes how you feel. Although some of these questions are of a personal nature, please try to answer as honestly as you can. Your answers will be kept confidential.

	When I was growing up,…	Never True	Rarely True	Sometimes True	Often True	Very Often True
1.	People in my family called me things like “stupid,” “lazy,” or “ugly.”	1	2	3	4	5
2.	I thought that my parents wished I had never been born.	1	2	3	4	5
3.	People in my family said hurtful or insulting things to me.	1	2	3	4	5
4.	Someone in my family hated me.	1	2	3	4	5
5.	I believe that I was emotionally abused.	1	2	3	4	5
6.	I got hit so hard by someone that I had to see a doctor or go to the hospital.	1	2	3	4	5
7.	Someone hit me so hard that it left me with bruises or marks.	1	2	3	4	5
8.	I was hit with a belt, a board, a cord, or some other hard object.	1	2	3	4	5
9.	I believe that I was physically abused.	1	2	3	4	5
10.	I got hit or beaten so badly that I was noticed by someone like a teacher, neighbor, or doctor.	1	2	3	4	5
11.	Someone tried to touch me in a sexual way or tried to make me touch them.	1	2	3	4	5
12.	Someone threatened to hurt me or tell lies unless I did something sexual with them.	1	2	3	4	5
13.	Someone tried to make me do sexual things or watch sexual things.	1	2	3	4	5
14.	Someone molested me.	1	2	3	4	5
15.	I believe that I was sexually abused.	1	2	3	4	5

PANAS – Positive and Negative Affects Scale

This scale consists of a number of words that describe different feelings and emotions. Read each item and then mark the appropriate answer in the space next to that word. Indicate to what extent you feel this way right now, that is, at the present moment. Use the following scale to record your answers.

1	2	3	4	5
very slightly or not at all	**a little**	**moderately**	**quite a bit**	**extremely**

_____ interested	_____ irritable
_____ distressed	_____ alert
_____ excited	_____ ashamed
_____ upset	_____ inspired
_____ strong	_____ nervous
_____ guilty	_____ determined
_____ scared	_____ attentive
_____ hostile	_____ jittery
_____ enthusiastic	_____ active
_____ proud	_____ afraid

RBQ-A

In this questionnaire we are interested in whether certain events have happened to you in the **PAST MONTH**. Please indicate how often the following events have happened to you in the **PAST MONTH**.

Scale: (0) Never
(1) Almost Never (1 Time Per Month)
(2) Sometimes (2-4 Times Per Month)
(3) Almost Always (2-3 Times Per Week)
(4) Always (4 or More Times Per Week)

		Never	Almost Never	Sometimes	Almost Always	Always
1.	Have you destroyed property (other than your own)?	0	1	2	3	4
2.	Have you been unfaithful to your boyfriend or girlfriend?	0	1	2	3	4
3.	Have you been in a physical fight?	0	1	2	3	4
4.	Have you bullied, threatened, or intimidated a peer(s)?	0	1	2	3	4
5.	Have you been binge drinking and/or drinking to get drunk?	0	1	2	3	4
6.	Have you used illegal drugs?	0	1	2	3	4
7.	Have you sold illegal drugs?	0	1	2	3	4
8.	Have you skipped class (or entire days of school)?	0	1	2	3	4
9.	Have you cheated or plagiarized?	0	1	2	3	4

		Never	Almost Never	Sometimes	Almost Always	Always
10.	Have you shoplifted?	0	1	2	3	4
11.	Have you stolen money?	0	1	2	3	4
12.	Have you had unsafe sex?	0	1	2	3	4
13.	Have you verbally harassed someone?	0	1	2	3	4
14.	Have you made attempts to cut or burn yourself?	0	1	2	3	4
15.	Have you purged or binged?	0	1	2	3	4
16.	Have you gambled?	0	1	2	3	4
17.	Have you lied to your family members (e.g., grandparents, parents, siblings)?	0	1	2	3	4
18.	Have you driven (a bicycle, a moped, and/or a car) recklessly (e.g., at fast speeds, under the influence of a substance)?	0	1	2	3	4
19.	Have you used cigarettes?	0	1	2	3	4
20.	Have you engaged in acts of revenge?	0	1	2	3	4

Kiddie-Schedule for Affective Disorders and Schizophrenia – Present and Lifetime (KSADS)

Please note that the Kiddie-Schedule for Affective Disorders and Schizophrenia – Present and Lifetime (KSADS; Kaufman et al., 1997) is freely available at http://www.psychiatry.pitt.edu/sites/default/files/Documents/assessments/ksads-pl.pdf

SHAPS – Snaith-Hamilton Pleasure Scale

INSTRUCTIONS: This questionnaire is designed to measure your ability to experience pleasure. It is important to read each statement carefully. Circle the answer that corresponds to how much you agree or disagree with each statement.

		RESPONSE			
1.	I would enjoy my favorite television or radio program.	**Strongly Disagree**	**Disagree**	**Agree**	**Strongly Agree**
2.	I would enjoy being with my family or close friends.	**Definitely Agree**	**Agree**	**Disagree**	**Strong Disagree**
3.	I would find pleasure in my hobbies and past-times.	**Strongly Disagree**	**Disagree**	**Agree**	**Strongly Agree**
4.	I would be able to enjoy my favorite meal.	**Definitely Agree**	**Agree**	**Disagree**	**Strongly Disagree**
5.	I would enjoy a warm bath or refreshing shower.	**Definitely Agree**	**Agree**	**Disagree**	**Strongly Disagree**
6.	I would find pleasure in the scent of flowers or the smell of a fresh sea breeze or freshly baked bread.	**Strongly Disagree**	**Disagree**	**Agree**	**Strongly Agree**
7.	I would enjoy seeing other people's smiling faces.	**Definitely Agree**	**Agree**	**Disagree**	**Strongly Disagree**
8.	I would enjoy looking smart when I have made an effort with my appearance.	**Strongly Disagree**	**Disagree**	**Agree**	**Strongly Agree**
9.	I would enjoy reading a book, magazine or newspaper.	**Definitely Agree**	**Agree**	**Disagree**	**Strongly Disagree**
10.	I would enjoy a cup of tea or coffee or my favorite drink.	**Strongly Disagree**	**Disagree**	**Agree**	**Strongly Agree**
11.	I would find pleasure in small things, e.g. bright sunny day, a telephone call from a friend.	**Strongly Disagree**	**Disagree**	**Agree**	**Strongly Agree**
12.	I would be able to enjoy a beautiful landscape or view.	**Definitely Agree**	**Agree**	**Disagree**	**Strongly Disagree**
13.	I would get pleasure from helping others.	**Strongly Disagree**	**Disagree**	**Agree**	**Strongly Agree**
14.	I would feel pleasure when I receive praise from other people.	**Definitely Agree**	**Agree**	**Disagree**	**Strongly Disagree**

Appendix E

Participant Information Sheet

UNIVERSITY OF EXETER
MOOD DISORDERS CENTRE

(Version 5.0, 31/03/2015)

Information Sheet - Participant

Understanding feelings and behaviour in young people with different life experiences

Principal Researcher: Dr. Pia Pechtel
Supervisors: Professor Edward Watkins, Dr. Anna Adlam

My name is Dr. Pia Pechtel and I am a Trainee Clinical Psychologist. You will find my contact details below on page 7.

I would like to invite you to take part in a study to better understand the thoughts, feelings, and behaviour of young people who had different early life experiences. We aim that the findings of this study will ultimately help us to find better ways to support young people who experienced childhood abuse.

- To find out how life experiences affect young people's feelings and behaviour we will both invite *young people **without a history** of childhood abuse* **AND** *young people **with a history** of childhood abuse.*

Before you decide whether you would like to take part, please read through the information, which will explain why the study is being conducted, and what your involvement would be. Take time to decide whether or not you would like to participate.

If you have any questions about the research or about this form, please ask us. If you decide to take part in this study, you must sign a form to show that you want to take part. If you are younger than 16 years, the form you will sign to agree to participate is called an 'assent form'. In this case, your parent will also be asked to sign a form as you are considered a minor. If you are 16 years or older, the form you will sign to agree to participant is called a 'consent form'. We will give you a copy of this information sheet and the consent or assent forms to keep.

What is the purpose of the study?

Young people show a range of feelings and behaviour that are specific to their developmental stage and that may change as they become adults. Some of these behaviours, however, are linked to negative early life experiences and may be maintained throughout life possibly leading to mental health difficulties.

- *In this study we try to **understand how mood and behaviour differ** depending of whether young people had a **protected upbringing** compared to those young people who were **exposed to childhood abuse.***

In the UK, 1 in 4 individuals (25.3%) experience childhood abuse such as verbal, sexual or physical abuse (NSPCC, 2013). The effects of Childhood Abuse (CA) can affect a young person's mood (e.g., major depressive disorder) and may be related to engaging in risky behaviour in adolescence (e.g., self-harm, dysfunctional eating). We hope that understanding how CA affects mood and behaviour can help to inform better psychological treatments for supporting young people in need and prevent high-risk behaviour.

The study is part of a Doctorate of Clinical Psychology, which is being carried out by the Principal Researcher, Dr. Pia Pechtel (see contact details on page 5). A small team of postgraduate researchers and graduate and undergraduate students will help to conduct the study.

Why have I been chosen?

We are asking you to take part in this research because you are a female between the ages of 13 and 19 years. You can participate if you:

(1) have **not** experienced any form of childhood abuse

OR

(2) are currently experiencing low mood (major depressive disorder)

OR

(3) have experienced childhood abuse such as verbal, physical or sexual abuse and are currently experiencing low mood (major depressive disorder)

About 48 individuals will take part in this study over the next year. Funding has been awarded to Dr. Pia Pechtel by the Brain and Behavior Research Foundation (NARSAD).

Do I have to take part?

It is entirely up to you if you wish to take part. If you do decide to take part, you are free to change your mind at any time and you can withdraw during the study by simply letting the researcher know. Withdrawal from the study is immediately effective and can be expressed verbally. In this case, your data will be destroyed and not included in the study's findings.

What if I do not want to carry on with the study?

Nothing will happen! If you no longer wish to be part of the study, you can withdraw at any time without any loss of current treatment or any other negative consequences. It will not affect any services that you will receive in the future. You will still be reimbursed for the study session you attended but not completed.

What does participation involve?

If you think that you would like to participate and would like to know more, the Principal Researcher can organize to contact you by telephone. Of course, you can also call or email the Principal Researcher, Dr Pia Pechtel, at any time (contact details on page 5). Please note that if you are younger than 16 years, we will first need verbal consent from one of your parents to talk to you about the study on the phone. If you are 16 years or older, we do not need your parent's permission to talk to you about the study.

If consent is given, we will explain the purpose and the study procedures to you. We will also complete a brief screening questionnaire (10 minutes) to make sure it is safe and appropriate for you to participate.

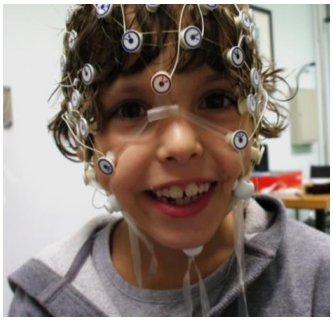
If you would like to participate, we will arrange dates for you to attend two sessions at the University of Exeter. The first visit will take 2 hours and the second visit will take1.5 hours. Not everyone will meet study criteria, but you will still be reimbursed for your time and travel.

All study procedures are **safe, painless and non-invasive:**

Session 1:

- During the first visit, you will be asked to complete **six brief questionnaires (15 min) and an interview (35-40 min).**
  - One questionnaire to measure your mood at the beginning and at the end of the session.
  - Three questionnaires to ask about your recent mood, thoughts and the ability to enjoy things.
  - Two questionnaires to ask if you have experienced difficult events in childhood (yes/no) and behaviours you may have engaged in.
  - The interview will ask about your past and current mental well-being.

- Then you will be asked to play a **"Picture Game"** on a computer for **20 minutes while we are recording an electroencephalography (EEG)**. The EEG is a safe and painless procedure and involves putting a cap with 64 small sensors on the scalp to measure electrical brain activity.



For the EEG, each little sensor will be moistened with paste to improve the cap's ability to measure your brain electrical activity. The EEG sensors can be removed in less than a minute and the gel can be easily wiped and/or washed off. You may want to wash and blow-dry your hair after the session and this can be done in our lab.

You will be sitting in a chair in front of the computer to play the "Picture Game". **We will also show you the brain waves and explain how the EEG works!** You can ask us questions and ask to stop the recording at any time.

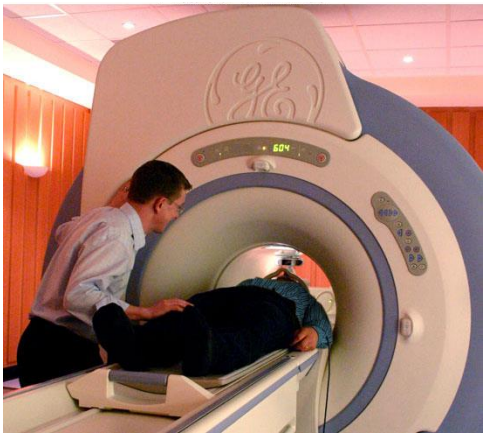
In the "Picture Game", you will see pairs of images (e.g., chair and toothbrush) on the screen and are asked to press a key to the image that has the highest chance of being correct. For the first four blocks of the Picture Game, you will be given feedback for each of your

responses. During the final block of the game, you will be asked to respond without receiving feedback. This will allow us to assess how well you learn from feedback. Once you have finished the Picture Game, we will remove the cap and the session ends. We are curious to learn about your thoughts regarding the session and will answer any of your questions.

Session 2:

- During the second visit, we would invite you to participate in a **magnetic resonance imaging (MRI)** scan to take a picture of your brain while you are **playing a "Card-Guessing Game".** We will measure your **mood** at the beginning and the end of the session.

The MRI scanner has a field strength of 1.5T and will be conducted at the Exeter MR Research Centre in presence of certified technicians. We are able to see and hear you at all times. Your can communicate with the researcher throughout the scan using an intercom system that works like a telephone. This means that you can stop the scan at any time.



The magnetic resonance (MR) scanner looks like a large donut (cylinder) with a tube running down the centre. You will be asked to lie down on your back on a foam-padded table and place your head into a special holder. The table will slide you inside the "hole" of the scanner. Soft foam rubber sponges may be placed on both sides of your head for comfort and to help keep your head from moving. Because the scanner contains a strong magnet, your will be asked to remove all metal objects including, but not limited to: watches, rings, necklaces, bracelets, earrings and other body piercings, belts, loose change, wallet (with credit cards), items of clothing containing magnetic materials (for example, underwire bras, certain types of zippers), and shoes. These items will be secured in a safe place until your scan is completed.

In the scanner, we will take images of your brain anatomy and function during which you can relax (15 minutes). We will also invite you to play the "Card-Guessing Game" (20 minutes). In this game, you can guess if a card with a possible value of 1-9 is higher or lower than 5 by pressing buttons on the response box in the scanner. Once you have made your choice, you will see if this round is a "reward", "loss" or "no-change" trial. Finally, you will see the actual numerical value of the card and a feedback screen showing if you received a monetary reward (green upward-facing arrow), lost a reward (red downward-facing arrow) or nothing changed (yellow circle). This game will examine what your brain is doing as you receive rewards. As we are taking picture of your brain during the game, we will ask you to remain as still as possible.

You may feel cramped inside the scanner, but a mirror has been placed so your can look out through the scanner "hole" into the scanning room. The approximate time that you will be in the scanner is about 45 minutes (getting you comfortable in scanner (10 min), relaxing (15 min), and playing the game (20 min)).

When you have finished the scan you will be moved out of the scanner and assisted from the table. You will have time to talk to the researcher about the study and about your experience.

We will also explain how the brain works using a picture of your own brain that you can take home after the study.

More detailed information about the MRI scan can be found on the MRI information sheet that the researcher has given you. Please do not hesitate to ask questions at any time.

What do I have to do before the sessions?

There are no restrictions on lifestyle or diet before taking part in this study. However, you may wish to use the toilet before the sessions.

What are the possible benefits of taking part?

There are no direct benefits for you; however, the information we get from the study may help to learn more about how different life experiences affect young peoples feelings and behaviour. This can help us to **develop better psychological treatment for young women who were exposed to childhood abuse.**

If you decide to take part, we also hope that you will find the experience interesting and enjoyable. We are very happy to **talk to you about the way the brain works and what we are expecting to find.**

As a **thank you** for volunteering your time for the study, you will receive a picture of your brain. We will also reimburse your time and travel costs with **gift vouchers** (£20 for session 1; £26 for Session 2).

It is important to note, that this study involves the recording of typical brain function. The EEG and brain scans are not intended to provide a medical diagnosis or a clean 'bill of health' – and the person conducting the scan will not be able to comment on the results of your scans.

Are there disadvantages of taking part in this study?

There are no known disadvantages associated with taking part in the study. The measurement of brain activity and bodily responses will be done using safe and well-established procedures.

- ***Potential for distress***: Taking part in a study has the potential of eliciting some distress. This may be due to answering questions or noises experienced during the MRI. The researcher will regularly ask about your level of comfort and well-being. If you feel distressed, you can choose to stop the study at any time. A clinical psychologist is available throughout the study if needed.
- ***Questionnaires and Interview:*** Some of the questions asked about your feelings or experiences could elicit some feelings. A clinical psychologist is available throughout the study to speak to you if this seems appropriate.
- ***Computer games***: The games played during the sessions are engaging and pleasant; most people feel that time goes by easily when doing them. The games do not contain distressing images or negative content.
- ***EEG***: The sensors can be removed in less than a minute and the gel can be easily wiped and/or washed off. You may want to wash and blow-dry your hair after the session and this can be done in our lab.

- ***MRI scan***: The MRI scan is a painless and non-invasive procedure. Our MRI scanner does not use x-rays or other harmful radiation, and there is **no known risk** even if you have a very large number of scans. For more information, please see the separate MRI information sheet.

All assessments, including the EEG and MRI, can be stopped at any time if you wish to do so.

What happens if you find something unusual on the scan?

The researchers involved in the study do not have expertise in MRI diagnosis, as they are psychologists or allied scientists and are not medical doctors. These research scans cannot be regarded as a medical screening procedure. Occasionally when we scan participants, the researchers may be concerned that a potential abnormality may exist on the scan. In this case, we will ask for your consent to forward the scans to your GP for further investigation.

It is important that you realise that these scans will not provide information that may help in the diagnosis of any medical condition. If you do have any health concerns, you should contact a qualified medical practitioner in the normal way.

What happens if I feel upset after completing the study?

It is unlikely that any part of the study will cause you harm. However, two clinical psychologists will be available throughout the course of the study to speak to you if needed. In the unlikely event that you feel upset after the study has been completed, you can contact one of the 24-hour helpline numbers provided below. A member of the research team will also call you approximately one week after the study was completed to hear how you are doing. If you continue to feel upset following the study, we do advise that you contact your GP and/or mental health professionals. We would be happy to assist you in contacting your GP or mental health professional if you have given us permission (consent).

Helplines:

ChildLine
0800 1111
www.childline.org.uk
Call to talk to a ChildLine counsellor at any time (it's free, even from a mobile).

Get Connected:
0808 808 4994
www.getconnected.org.uk
Free telephone and email helpline finding young people the best help whatever the problem, can connect a child or young person to any UK helpline where appropriate.

Samaritans (24 hours a day)
www.samaritans.org
08457 909090

Will my taking part in the study be kept confidential?

- All information, which is collected during the research, would be kept strictly confidential

within the limits of the law.

- You will be allocated your own unique study code number, ensuring that all information that you give will contain your number rather than your actual name. Only immediate members of the research team will be able to link the number to her name.
- Identifiable information will be stored in a locked cabinet and/or password protected computer and only the researchers of this project will have access to it.

The only exception would be if the interview revealed a significant risk to you of harm to yourself or others. In this case, information may be fed back to your GP and, if applicable, your mental health professional but normally only after discussion with you (and your parent if you are under the age of 16). Therefore, we ask for your GP and mental health professional's details in the consent form. If you wish we can inform your GP and mental health professional about your participation in the study.

In accordance with British Psychological Society research guidelines, all data for the study will be securely stored away for 5 years and will be destroyed after this time.

What will happen with the results of the research study?

The data obtained during the study will be combined with that from other participants to be written up to appear in scientific journals or be shared with other professionals at scientific conferences. This will help to inform clinicians and researchers who are working to support young people who have experienced childhood abuse. Any write-up of the findings for this study will not mention the participants personally. No names or identifiable information will be published with the results. If you would like to obtain a copy of the findings, we will be more than happy to send them to you when they become available.

Who is organising and funding the research? Who has reviewed the study?

Funding for this study is provided by the Brain and Behavior Research Foundation (NARSAD) awarded to Dr. Pia Pechtel following the approval by a scientific committee. The appropriate ethical committees have also approved the research to ensure the highest ethical standard.

What if there is a problem?

If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, you can contact the Study Supervisor, Professor Edward Watkins (contact details on page 5).

Contact Details:

If you require further information or would like to ask any questions, please do not hesitate to contact the Principal Researcher using the details below.

We look forward to speaking to you!

Appendix F

Consent Form: Participant

UNIVERSITY OF EXETER
MOOD DISORDERS CENTRE

(Version 4.0 02/03/2015)

Consent – Young Adult (16 years or older)

Title: Understanding feelings and behaviour in young people with different life experiences

Researcher:

Dr. Pia Pechtel
Mood Disorder Centre
Sir Wellcome Building for Mood Disorder Research
School of Psychology
College of Life and Environmental Sciences
University of Exeter
Exeter
EX4 4QG
Phone: 07827 984314
Email: pp293@exeter.ac.uk

Supervisor:

Professor Edward Watkins
Mood Disorder Centre
Sir Wellcome Building for Mood Disorder Research
School of Psychology
College of Life and Environmental Sciences
University of Exeter
Exeter
EX4 4QG
Phone: 01392 724692
Email : E.R.Watkins@exeter.ac.uk

Please read statement and initial box

1) I confirm that I have read and understood the Information Sheet for the above study dated 02/03/2015 (Version 4.0). I have had the opportunity to consider the information and ask questions, and have had these answered satisfactorily. ☐

2) I am aware that my participation in this study is voluntary and that I can withdraw my consent for participation at any point during the study without giving any reason, and without my legal rights or medical care being affected. ☐

3) I understand that my data will be confidential unless it indicates a risk of harm to myself or harm to others in which case information will be shared with appropriate health professionals. ☐

4) I understand that I have the right to obtain information about the findings of the study after it is completed. A summary letter with the group findings of the study will be sent to me following the completion of the study. The summary letter will not contain identifiable data or individual results. I can let the researcher know if I do not wish to receive a summary letter. ☐

5) I understand that sections of the data collected during the study may be looked at by relevant individuals of the University of Exeter (i.e. the research supervisors) and from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data. ☐

6) I agree to take part in the above study. ☐

7) I would like my name and contact details to be kept on a secure and confidential database so that I can be contacted about taking part in other studies within the Mood Disorders Centre (**optional**). ☐

8) I agree that my General Practitioner is informed about my study participation. The GP will also be contacted in case data collected during the study will require medical follow-up or if long-term emotional support is advised. ☐

Please give your GPs contact details:

……..

……..

……..

9) If applicable: I agree that my mental health professional is informed about my study participation and contacted if further emotional support is advised. Data collected during the study is shared with the practitioner. ☐

Please give your mental health professional's contact details:

……..

……..

……..

Name of participant (print)	**Date:**	**Signature**
Name of researcher (print)	**Date:**	**Signature**

One copy for participant, one copy for researcher

Appendix G

Consent Form: Caregiver

UNIVERSITY OF EXETER
MOOD DISORDERS CENTRE

(Version 4.0 02/03/2015)

Parental Consent

Title: Understanding feelings and behaviour in young people with different life experiences

Researcher:

Dr. Pia Pechtel
Mood Disorder Centre
Sir Wellcome Building for Mood Disorder Research
School of Psychology
College of Life and Environmental Sciences
University of Exeter
Exeter
EX4 4QG
Phone: 07827 984314
Email: pp293@exeter.ac.uk

Supervisors:

Professor Edward Watkins
Mood Disorder Centre
Sir Wellcome Building for Mood Disorder Research
School of Psychology
College of Life and Environmental Sciences
University of Exeter
Exeter
EX4 4QG
Phone: 01392 724692
Email : E.R.Watkins@exeter.ac.uk

Please read statement and initial box

1) I confirm that I have read and understood the Information Sheet for the above study dated 02/03/2015 (Version 4.0) I have had the opportunity to consider the information and ask questions, and have had these answered satisfactorily. ☐

2) I am aware that participation in this study is voluntary and that I can withdraw my consent for my daughter's participation at any point during the study without giving any reason, and without her legal rights or medical care being affected. ☐

3) I understand that my daughter's data will be confidential unless it indicates a risk of harm to herself or harm to others in which case information will be shared with appropriate health professionals and with me as one of her parents (legal guardian). ☐

4) I understand that I have the right to obtain information about the findings of the study after it is completed. A summary letter with the group findings of the study will be sent to my daughter following the completion of the study. The summary letter will not contain identifiable data or individual results. I can let the researcher know if I do not wish for my daughter to receive a summary letter. ☐

5) I understand that sections of the data collected during the study may be looked at by relevant individuals of the University of Exeter (i.e. the research supervisors) and from regulatory authorities, where it is relevant to my daughter's taking part in this research. I give permission for these individuals to have access to my daughter's data. ☐

6) I agree for my daughter to take part in the above study. ☐

7) I would like my daughter's name and contact details to be kept on a secure and confidential database so that she can be contacted about taking part in other studies within the Mood Disorders Centre (**optional**). ☐

8) I agree that my child's General Practitioner is informed about the study participation. The GP will also be contacted in case data collected during the study will require medical follow-up or if long-term emotional support is advised. ☐

Please give your child's GPs contact details:

……..

……..

……..

9) If applicable: I agree that my child's mental health professional is informed about the study participation and contacted if further emotional support is advised. Data collected during the study is shared with the practitioner. ☐

Please give your child's mental health professional contact details:

……..

……..

……..

Name of participant (print)	**Date:**	**Signature**
Name of researcher (print)	**Date:**	**Signature**

One copy for participant, one copy for researcher

Appendix H

Assent Form: Minors

UNIVERSITY OF EXETER
MOOD DISORDERS CENTRE

(Version 5.0 31/03/2015)

Assent Form for individuals Younger than 16 Years of age

Title: Understanding feelings and behaviour in young people with different life experiences

Researcher:

Dr. Pia Pechtel
Mood Disorder Centre
Sir Wellcome Building for Mood Disorder Research
School of Psychology
College of Life and Environmental Sciences
University of Exeter
Exeter
EX4 4QG
Phone: 07827 984314
Email: pp293@exeter.ac.uk

Supervisor:

Professor Edward Watkins
Mood Disorder Centre
Sir Wellcome Building for Mood Disorder Research
School of Psychology
College of Life and Environmental Sciences
University of Exeter
Exeter
EX4 4QG
Phone: 01392 724692
Email : E.R.Watkins@exeter.ac.uk

Please read statement and initial box

1) I confirm that I have read and understood the Information Sheet for the above study dated 31/03/2015 (Version 5.0) I have considered the information and had the chance to ask questions. The research team has answered all of my questions. ☐

2) I am aware that my participation in this study is my choice and that I can stop taking part in the study at any point without giving any reason. This does not affect how I will be treated in the future (e.g., my legal rights, my medical care) ☐

3) I understand that my data will be confidential (private) unless I am at risk of harming others or myself. In this care the researcher will share this information with my health professionals and one of my parents. ☐

4) I understand that I have the right to learn about the outcomes and findings of the study after it is completed. A summary letter with the group findings of the study will be sent to me following the completion of the study. The summary letter will not contain identifiable data or individual results. I can let the researcher know if I do not wish to receive a summary letter. ☐

5) I understand that some of my results may be looked at by individuals of the University of Exeter (i.e. the research supervisors) and from regulatory authorities, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my data. ☐

6) I agree to take part in the above study. ☐

7) I would like my name and contact details to be kept on a secure and confidential database so that I can be contacted about taking part in other studies within the Mood Disorders Centre (**your choice**). ☐

8) I agree that my GP is informed about me taking part in the study. The GP will also be contacted in case data collected during the study will require medical follow-up or if long-term emotional support is advised. ☐

Please give your GPs contact details:

.....

.....

.....

9) If applicable: I agree that my mental health professional is informed about me taking part in the study and will be contacted if I need emotional support. Results from this study are shared with the practitioner. ☐

Please give your mental health professional's contact details:

.....

.....

.....

Name of participant (print)	**Date:**	**Signature**
Name of researcher (print)	**Date:**	**Signature**

One copy for participant, one copy for researcher

Appendix I

Regression Analysis

Table I1

Hierarchical Regression Analysis for Activation in Region-of-Interests during Anticipatory Reward Period

	B	SE B	β	Variance Explained
Left Putamen				
Model 1				
Constant	-.01	.12		
Age	-.001	.007	-.03	
BDI	-.002	.001	-.37*	R^2 = .15, $R^2_{adjusted}$ = .10
Model 2				
Constant	-.10	.15		
Age	-.003	.008	-.06	
BDI	-.003	.001	-.44*	
CTQ_{log}	.10	.09	.20	ΔR^2 = .03, $\Delta R^2_{adjusted}$= .001
Right Putamen				
Model 1				
Constant	-.02	.11		
Age	.00	.007	-.007	
BDI	-.002	.001	-.33	R^2 = .11, $R^2_{adjusted}$ = .06
Model 2				
Constant	-.10	.14		
Age	-.002	.007	-.04	
BDI	-.002	.001	-.40*	
CTQ_{log}	.09	.08	.20	ΔR^2 = .03, $\Delta R^2_{adjusted}$= .03
Left Pallidum				
Model 1				
Constant	.09	.15		
Age	-.008	.009	-.16	
BDI	-.001	.001	-.11	R^2 = .05, $R^2_{adjusted}$ = -.01
Model 2				
Constant	.05	.18		
Age	-.008	.009	-.17	
BDI	-.001	.001	-.14	
CTQ_{log}	.04	.10	.06	ΔR^2 = .01, $\Delta R^2_{adjusted}$= -.02
Right Pallidum				
Model 1				
Constant	.12	.14		
Age	-.008	.009	.16	
BDI	-.001	.001	.19	R^2 = .08, $R^2_{adjusted}$ = .03
Model 2				
Constant	-.03	.17		
Age	-.01	.009	-.20	
BDI	-.002	.001	-.29	
CTQ_{log}	.15	.10	.27	ΔR^2 = .06, $\Delta R^2_{adjusted}$= .03

Left Caudate				
Model 1				
Constant	-.17	.17		
Age	.004	.01	.07	
BDI	-.003	.001	-.32	R^2 = .09, $R^2_{adjusted}$ = .04
Model 2				
Constant	-.25	.21		
Age	.003	.01	.05	
BDI	-.003	.002	-.34	
CTQ_{log}	.07	.12	.12	$^{\Delta}R^2$ = .01, $^{\Delta}R^2_{adjusted}$= -.02
Right Caudate				
Model 1				
Constant	-.25	.15		
Age	.01	.009	.18	
BDI	-.002	.001	-.26	R^2 = .07 and $R^2_{adjusted}$ = .01
Model 2				
Constant	-.34	.19		
Age	.008	.009	.16	
BDI	-.002	.001	-.31	
CTQ_{log}	.09	.11	.15	$^{\Delta}R^2$ = .02 and $^{\Delta}R^2_{adjusted}$= -.007

Note. * p<.05, ** p<.01; BDI = Beck Depression Inventory; CTQ_{log} = Log transformed Childhood Trauma Questionnaire

Table I2

Hierarchical Regression Analysis for Activation in Bilateral Putamen, Caudate and Pallidum During Consummatory Reward Period

	B	**SE B**	β	**Variance Explained**
Left Putamen				
Model 1				
Constant	.04	.12		
Age	-.002	.007	-.05	
BDI	.001	.001	.25	R^2 = .06, $R^2_{adjusted}$ = .00
Model 2				
Constant	.02	.15		
Age	-.002	.008	-.05	
BDI	.001	.001	.23	
CTQ	.02	.09	.04	$^{\Delta}R^2$ = .001, $^{\Delta}R^2_{adjusted}$= -.03
Right Putamen				
Model 1				
Constant	.07	.12		
Age	-.054	.007	-.12	
BDI	.002	.001	.28	R^2 = .07 and $R^2_{adjusted}$ = .02
Model 2				
Constant	.13	.14		
Age	-.004	.007	-.10	
BDI	.002	.001	.33	
CTQ	-.07	.08	-.15	$^{\Delta}R^2$ = .02 and $^{\Delta}R^2_{adjusted}$= -.02

Left Pallidum				
Model 1				
Constant	-.13	.18		
Age	.006	.01	.10	
BDI	.002	.001	.24	R^2 = .08 and $R^2_{adjusted}$ = .03
Model 2				
Constant	-.16	.21		
Age	.005	.01	.10	
BDI	.002	.002	.22	
CTQ	.04	.12	.06	$^{\Delta}R^2$ = .01 and $^{\Delta}R^2_{adjusted}$= -.02
Right Pallidum				
Model 1				
Constant	-.06	.18		
Age	.005	.01	.08	
BDI	.000	.002	.02	R^2 = .01 and $R^2_{adjusted}$ = -.05
Model 2				
Constant	.02	.22		
Age	.006	.01	.10	
BDI	.001	.002	.07	
CTQ	-.08	.13	-.12	$^{\Delta}R^2$ = .01 and $^{\Delta}R^2_{adjusted}$= -.02
Left Caudate				
Model 1				
Constant	-.05	.17		
Age	.005	.01	.09	
BDI	.000	.001	-.05	R^2 = .01 and $R^2_{adjusted}$ = -.05
Model 2				
Constant	.03	.21		
Age	.006	.01	.11	
BDI	8.05	.002	.001	
CTQ	-.08	.12	-.13	$^{\Delta}R^2$ = .01 and $^{\Delta}R^2_{adjusted}$= -.02
Right Caudate				
Model 1				
Constant	.09	.16		
Age	-.006	.01	-.11	
BDI	.002	.001	.31	R^2 = .09 and $R^2_{adjusted}$ = .03
Model 2				
Constant	.09	.20		
Age	-.006	.01	-.11	
BDI	.002	.002	.31	
CTQ	.001	.11	.002	$^{\Delta}R^2$ = .00 and $^{\Delta}R^2_{adjusted}$= -.03

Note. * p<.05, ** p<.01; BDI = Beck Depression Inventory; CTQ_{log} = Log transformed Childhood Trauma Questionnaire

Table I3

Results of Hierarchical Regression Analysis of Region-of-Interest Activation during Reward Anticipation and Reward Outcome Predicting High-Risk Behaviour

	B	SE B	β	**Variance Explained**
Anticipatory Reward				
Model 1				
Constant	6.04	1.33		
Left Putamen	-24.93	11.93	-.33*	R^2 = .11*, $R^2_{adjusted}$ = .09
Model 2				
Constant	2.93	1.44		
Left Putamen	-9.74	11.15	-.13	ΔR^2 = .24**, $\Delta R^2_{adjusted}$= .31
BDI	.25	.07	.53**	
Model 1				
Constant	6.18	1.18		
Right Putamen	-32.23	12.76	-.39*	R^2 = .15**, $R^2_{adjusted}$ = .13
Model 2				
Constant	2.86	1.38		
Right Putamen	-18.35	11.71	-.22	ΔR^2 =.23**, $\Delta R^2_{adjusted}$= .22
BDI	.23	.07	.51**	
Model 1				
Constant	6.98	1.79		
Left Caudate	-6.31	9.61	-.11	R^2 = .01, $R^2_{adjusted}$ = -.02
Model 2				
Constant	3.73	1.67		
Left Caudate	4.10	8.33	.07	ΔR^2 = .33**, $\Delta R^2_{adjusted}$= .32
BDI	.28	.07	.61**	
Model 1				
Constant	8.88	1.65		
Right Caudate	7.61	10.56	.12	R^2 = .02, $R^2_{adjusted}$ = -.01
Model 2				
Constant	4.79	1.58		
Right Caudate	15.93	8.55	.25	ΔR^2 =.38**, $\Delta R^2_{adjusted}$= .37
BDI	.29	.06	.63**	
Model 1				
Constant	6.86	1.49		
Left nACC	-8.52	8.64	-.16	R^2 = .03, $R^2_{adjusted}$ =-.001
Model 2				
Constant	2.79	1.59		
Left nACC	-4.58	7.24	-.09	ΔR^2 = .32**, $\Delta R^2_{adjusted}$= .31
BDI	.26	.06	.57**	
Model 1				
Constant	6.98	1.41		
Right nACC	-9.37	9.61	-.16	R^2 = .03, $R^2_{adjusted}$ = -.001
Model 2				
Constant	2.71	1.56		
Right nACC	-6.28	7.99	-.11	ΔR^2 =.33**, $\Delta R^2_{adjusted}$= .31
BDI	.26	.06	.57**	

Consummatory Reward				
Model 1				
Constant	7.72	1.09		
Left Putamen	8.02	13.38	.10	R^2 = .01, $R^2_{adjusted}$ = -.02
Model 2				
Constant	3.29	1.40		
Left Putamen	-2.84	11.38	-.04	ΔR^2 = .33**, $\Delta R^2_{adjusted}$= .32
BDI	.27	.07	.59**	
Model 1				
Constant	7.77	1.03		
Right Putamen	13.83	13.48	.17	R^2 = .03, $R^2_{adjusted}$ = .002
Model 2				
Constant	3.31	1.40		
Right Putamen	2.70	11.60	.03	ΔR^2 = .31**, $\Delta R^2_{adjusted}$= .30
BDI	.27	.07	.58**	
Model 1				
Constant	8.10	1.08		
Left Caudate	-4.32	9.81	-.07*	R^2 = .006, $R^2_{adjusted}$ = -.02
Model 2				
Constant	3.42	1.43		
Left Caudate	-3.88	8.08	-.07	ΔR^2 = .34**, $\Delta R^2_{adjusted}$= .33
BDI	.27	.06	.58**	
Model 1				
Constant	7.61	1.03		
Right Caudate	12.87	9.54	.22	R^2 = .05, $R^2_{adjusted}$ = .02
Model 2				
Constant	3.32	1.40		
Right Caudate	3.87	8.37	.07	ΔR^2 = .30**, $\Delta R^2_{adjusted}$= .33
BDI	.26	.07	.57**	
Model 1				
Constant	7.77	1.28		
Left NAcc	1.48	6.48	.04	R^2 = .001, $R^2_{adjusted}$ =-.03
Model 2				
Constant	2.77	1.57		
Left NAcc	3.72	5.34	.10	ΔR^2 = .35**, $\Delta R^2_{adjusted}$= .34
BDI	.27	.06	.59**	
Model 1				
Constant	7.98	1.26		
Right NAcc	-.30	6.42	-.008	R^2 = .00, $R^2_{adjusted}$ = -.03
Model 2				
Constant	3.58	1.46		
Right NAcc	-3.62	5.32	-.10	ΔR^2 = .35**, $\Delta R^2_{adjusted}$= .34
BDI	.28	.06	.60**	

Note. * p<.05, ** p<.01; BDI = Becks Depression Inventory

Appendix J

Extended Data Analysis

Separate simple linear regression was calculated to predict neural anticipation in the region-of-interests during reward anticipation and reward outcome based on depressive symptoms (BDI scores). Significant regression equations were found in which BDI scores predicted significant activation in the left putamen ($F(1, 35) = 5.93$, $p = .02$) and in the right putamen ($F(1, 35) = 4.35$, $p = .04$) during reward anticipation. Results of the two regression models are displayed below in Table A1. All other regression models were not significant.

Table J1

Results of Simple Regression Analyses for Depressive Symptoms Predicting Neural Activation to Anticipation of Reward in the Left and Right Putamen

	B	SE B	β	**Variance Explained**
Left Putamen				
Constant	-.04	.02		
BDI scores	-.002	.001	-.38*	$R^2 = .15$*, $R^2_{adjusted} = .12$
Right Putamen				
Constant	-.02	.02		
BDI scores	-.002	.001	-.33*	$R^2 = .11$*, $R^2_{adjusted} = .09$

Note. * p<.05, ** p<.01

Appendix K

Dissemination Statement

Dissemination of results will take place on multiple levels. First, where consent was provided, outcomes from clinical questionnaire data were shared with participants' mental health practitioners within days of participating in the study. This allowed clinical information to be immediately utilized in practice.

Secondly, following the data collection, group results will be presented with local services that contributed to the research (e.g., Joint Agency of Child Abuse Team, Child and Adolescent Mental Health Service, Wellbeing Service). A talk at Exeter University been scheduled for June 2016 to present the findings to a colleagues and other professionals.

Thirdly, revised versions of the literature review and empirical findings will be submitted for publication to a peer-reviewed journal. We will revaluate the journal choices but initially had planned to submit the empirical study to *Biological Psychiatry* and the systematic review to the *Journal of Child and Adolescent Psychiatry* (pre-approval of review topic is required as journal only publishes invited reviews). Moreover, study outcomes will be submitted for presentation at professional conferences (e.g., *Biological Psychiatry,* May 18th - 20th, 2017).

Most importantly, a letter describing the results in lay terms will be shared with the participants. The relevant ethics committees (e.g., NHS, VirginCare) will be sent a summary of the findings and notified that the study is now completed.

Appendix L

Preparation and Submission Requirements for *Biological Psychiatry*

Archival Reports are original research papers reporting novel results on a broad range of topics related to the pathophysiology and treatment of major neuropsychiatric disorders. Clear explication of methods and results is critical to facilitate review of papers and replicability of findings. The main text must be no more than 4000 words, and be structured with sections entitled and ordered as follows: Introduction, Methods and Materials, Results, Discussion. Abstracts should be 250 words or less, structured with sections entitled as follows: Background, Methods, Results, Conclusions. Figures, tables, and references should be included as necessary.

Manuscript. Manuscripts should be structured with sections entitled and ordered as follows: Title Page, Abstract, Text, Acknowledgments, Financial Disclosures, References, Footnotes, and Table/Figure Legends. Begin all sections on separate pages. The text of research papers should be organized into sections titled Introduction, Methods and Materials, Results, and Discussion. Tables may also be included in a text format at the end of the manuscript file. Manuscripts should be double-spaced. Pages must be numbered and include the first author's name. Acronyms must be spelled out on first use in both the abstract and the text, and where used in tables or figures, in each of their legends. American spellings should be used. Accepted manuscripts are copyedited to conform to the *AMA Manual of Style*.

Title Page. On the title page, include the full names of all authors and their academic or professional affiliations, along with the corresponding author's complete contact information. Six key words, used for indexing, should also be

included. Separately list the number of words in both the abstract and article body (excluding abstract, acknowledgments, financial disclosures, legends and references), and the number of figures, tables, and supplemental information (if zero, state zero for each item). Article titles may not contain acronyms, and should be less than 100 characters. For full-length articles (Archival Reports, Priority Communications, Reviews), a short title of 55 characters or less (including spaces) must also be included.

Abstracts. Abstracts should be formatted according to the article type and should not exceed the word limits as detailed above. The Methods section should explicitly state the sample size of the trial. For those manuscripts that require clinical trials registration (see Clinical Trials Registration section, below), the registry name, URL, and registration number should be included at the end of the abstract.

Acknowledgments. This section should include acknowledgments for non-author contributors/collaborators and individuals who provided personal and technical assistance, in addition to detailed information regarding all sources of funding, including grant and other material or financial support. The role of study sponsor(s), if any, should also be provided. If a research group is listed as an author, then the individual members of the research team must be named here. Written permission should be obtained from all individuals named in this section. Data that was published previously, such as in an abstract or poster, should also be identified.

Financial Disclosures. This section must include the required conflict of interest statements for each author (see section on disclosure, below).

References. References should be numbered and listed by their order of appearance in the text. Refer to references in the text with the appropriate

number in parentheses. References in tables and figures should also be numbered. List all authors; if there are more than seven authors, list the first six then *et al*. Periodical abbreviations should follow those used by Index Medicus.

Figures and Tables. Figures and tables should be cited in the text, numbered consecutively (i.e., 1, 2, 3) in the order of their mention, and have brief descriptions. If not included in the manuscript file, tables should be uploaded individually in an editable text format, such as DOC. Table footnotes should use superscript lowercase letters, rather than symbols.