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## Cortisol secretion in children with symptoms of reactive attachment disorder

Eva Kočovská<sup>a</sup>, Philip Wilson<sup>a</sup>, David Young<sup>c</sup>, Alan Michael Wallace<sup>b</sup>, Charlotta Gorski<sup>d</sup>, Michael Follan<sup>d</sup>, Maureen Smillie<sup>d</sup>, Christine Puckering<sup>d</sup>, James Barnes<sup>d</sup>, Christopher Gillberg<sup>a</sup>, Helen Minnis<sup>a,\*</sup>

<sup>a</sup> Institute of Health and Wellbeing, College of Medical, Veterinary, and Life Sciences, University of Glasgow, Caledonia House, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ, UK

<sup>b</sup> School of Medicine, University of Glasgow, Glasgow, Scotland, UK

<sup>c</sup> University of Strathclyde, Glasgow, Scotland, UK

<sup>d</sup> NHS Greater Glasgow and Clyde, Scotland, UK

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### ABSTRACT

Maltreated children with reactive attachment disorder (RAD) have severe problems with social relationships and affect regulation. An association between early maltreatment and changes in the daily rhythm of cortisol secretion has already been reported for maltreated toddlers. We sought to find out whether such changes were apparent in school-age children with symptoms of RAD, who had experienced early maltreatment but were currently adopted in well-functioning families. We recruited 66 children: 34 adopted children, aged 5–12 years, with an early history of maltreatment and with social difficulties such as indiscriminate friendliness; and 32 age- and sex-matched comparison children with no history of maltreatment or social difficulties. Daily rhythms of cortisol production were determined from saliva samples collected over 2 days. The adopted group had significantly lower absolute levels of cortisol compared to the control group, but a typical profile of cortisol secretion. There was no association between cortisol secretion and symptom scores for psychopathology.

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### 1. Introduction

Reactive attachment disorder (RAD) is a serious disorder of social functioning associated with abuse and neglect. The Disinhibited subtype is characterised by indiscriminate friendliness which can be persistent; it has been suggested that this characteristic may be associated with personality problems in adult life (Lyons-Ruth, 2008). We have previously shown that children with indiscriminate friendliness can have complex neurodevelopmental problems and yet are frequently not engaged with therapeutic services (Kocovska et al., 2012). Sufferers can have problems with emotional and behavioural functioning and affect regulation (Zeanah et al., 2002; Green, 2003; Rutter et al., 2010; Gleason et al., 2011), and research with international (mainly post-institutionalized) adoptees has demonstrated an association between indiscriminate friendliness and abnormalities of the hypothalamo-pituitary-adrenal (HPA) axis, which governs the secretion of stress hormones such as cortisol (Johnson et al., 2011).

\* Corresponding author. Tel.: +44 141 201 9239; fax: +44 141 201 0620.  
E-mail address: [Helen.minnis@glasgow.ac.uk](mailto:Helen.minnis@glasgow.ac.uk) (H. Minnis).

RAD is one of only two disorders the other being posttraumatic stress disorder, PTSD) that are directly associated, in the psychiatric classification systems, with aetiology: it is recommended that a diagnosis of RAD should not be made unless there is a history of maltreatment in the first 5 years of life (World Health Organisation, 2007; American Psychiatric Association, 2000). However, not all children who have experienced maltreatment in early life develop RAD, and both genetic and environmental factors contribute to causality (Minnis et al., 2007). Because of the recognised association, in institutionalised children, between indiscriminate friendliness and abnormalities of the HPA axis, we have decided to focus, in this study, on the subgroup of maltreated children who are indiscriminately friendly.

Maltreatment in early life can be associated with long-term changes in regulation of the stress hormone cortisol and we have previously published a systematic review of this literature (Hunter et al., 2011). Our review has demonstrated that studies of adults who have been maltreated show conflicting results regarding the impact of maltreatment on diurnal secretion of cortisol and that there is a gap in the literature as regards cortisol production in maltreated schoolage children (Hunter et al., 2011). Altered function of the HPA axis has been described in depression (Holsboer, 2001), PTSD (Yehuda, 2009), attention

deficit hyperactivity disorder (Freitag et al., 2009; Stadler et al., 2011), conduct disorder and antisocial personality disorder (Vanyukov et al., 1993). Studies of children reared in institutions have shown that lack of caregiver sensitivity and positive regard is associated with a general suppression of the hypothalamic-pituitary axis (Johnson and Gunnar, 2011) and that this can recover if the environment improves. For example, Dozier et al. (2006) reported alterations in the production of salivary cortisol in maltreated toddlers in foster care and substantial recovery has been demonstrated with environmental improvement (Dozier et al., 2006; Tarullo and Gunnar, 2006). There is, however, no available research indicating the extent to which these changes can persist into middle childhood and the issue has not been explored in non-institutionalised school-age children.

During development, cortisol production is modulated in response to the social environment of the child (Tarullo and Gunnar, 2006; Dozier et al., 2008; Hunter et al., 2011). By school-age, under optimal conditions, cortisol levels peak in the morning about 30 min after waking, followed by a gradual decrease towards evening (Gunnar and Donzella, 2002). In an environment of persistent deprivation, neglect or abuse, the development of an infant's daily cortisol rhythm and/or stress reactivity may differ from that of other children in various ways (Brand et al., 2010). When production is persistently elevated or suppressed, or inadequately regulated in response to stress, there may be long-term consequences including effects on brain functioning (Caldji et al., 2000; Hunter et al., 2011). These may be associated with difficulties in handling stressful situations and predispose individuals towards developing mental health problems later in life (Teicher et al., 2003).

In this study, we examined the daytime pattern of cortisol production in previously maltreated children aged 5–12 years with symptoms of Disinhibited RAD who were currently adopted in well-functioning families and comparison children without such difficulties. Our hypothesis was that, in these children, maltreatment in early life may have resulted in differences in cortisol secretion which persisted into school-age.

## 2. Methods

The study protocol was approved by the West of Scotland 2 NHS ethics committee.

### 2.1. Statistical power

An a priori power calculation based on Dozier et al. (2006) indicated that a sample size of 10 in each group would have a 90% power to detect a difference in means of  $-0.2$  assuming that the common standard deviation is  $0.13$  using a two-group *t*-test with a 5% two-sided significance level. In order to ensure this computation was not too conservative and to allow for the suspected non-parametric nature of the data, we recruited a larger sample.

### 2.2. Participants

Because we were interested in potentially persistent effects of early life maltreatment in children with RAD symptoms, we needed to recruit a group of children with RAD symptoms who had experienced abuse and neglect within the early years, but who had not continued to live in these adverse circumstances. In the UK, the mean age of adoption is 4 years (<http://www.gro-scotland.gov.uk/press/news2004/03adopt-press.html>; <http://www.baaf.org.uk/info/stats/england.shtml>) and the overwhelming majority of adopted children have experienced severe abuse and/or neglect in the early years prior to coming into care. In general, they then reside in well-functioning families (Rushton et al., 2006). We therefore considered adopted school-age children with RAD symptoms to be the ideal group within which to test our hypothesis.

Adopted children were recruited via the charity 'Adoption UK'; eligibility criteria were discussed with the Scottish Director who contacted all eligible families known to the charity living within travelling distance of the University. Children were eligible for inclusion if they were aged 5–12 years, had the core

symptom of the Disinhibited form of RAD – indiscriminately friendly behaviour – plus a history of maltreatment. We did not attempt to recruit children with Inhibited RAD because it is thought to be extremely rare (Gleason et al., 2011) and we were unlikely to have enough inhibited children to make a meaningful distinction between the two subtypes in this study. Disinhibited RAD symptoms were verified using the Relationships Problems Questionnaire RPQ; all participating adopted children had at least two disinhibited RAD symptoms on the RPQ (see below). Potentially participating children were excluded if they had moderate or severe intellectual disability (which can itself be associated with disinhibition), current family instability or ongoing maltreatment. Of 43 children who were referred, 40 met inclusion criteria; one female child was subsequently excluded as she had signs of having reached puberty. Two families (five children) withdrew. Thirty-four children (18 boys and 16 girls; mean (S.D.) age 9.4 (1.8) years) were clinically assessed. All adopted children were white British except for one child who was African American by birth. There were 13 sibling pairs and one sibship of three involved in the study. Because, in previous research, we have found that there is a very small correlation in scores between maltreated siblings living in the same substitute family (Minnis et al., 2001), we have not made statistical adjustments for clustering.

Comparison children were included if they were aged 5–12 years and excluded if they had any known child psychiatric diagnosis, moderate or severe intellectual disability, any history (even suspected) of child maltreatment, known contact with social work, child protection registration or any trauma within the last year (assessed using a brief screening instrument for acute stress, the Life Change Scale (Foxman, 2004)). We ensured that no comparison children had high scores suggestive of RAD (i.e. over six on the Relationship Problems Questionnaire—see later). Children were selected through two general medical practices in Glasgow. The practices had 750 children within the age range of 5–12 years, and 615 were eligible according to the inclusion criteria. The general practitioners sent 461 invitation letters: 58 responded, nine withdrew and, because of gender and age mismatches, not all remaining eligible children were invited to participate. In order to address imbalances in age and gender, a further 62 invitation letters were re-sent to non-responders from the original 461, this time only to families with boys aged 6–10 years. Of these, four had moved away, six responded and were assessed. The comparison group eventually comprised 32 children (17 boys and 15 girls; mean (S.D.) age 8.7 (2.4) years) who were clinically assessed. All comparison children were white British.

Children in both the adopted and comparison group were offered a neuropsychiatric assessment using standardised tools for RAD, other diagnoses and measures of cognition and language functioning. These assessments have been described elsewhere (Kocovska et al., 2012).

### 2.3. Procedure

For adopted children, after obtaining consent forms from parents and children, an initial home visit was arranged during which demographic data were collected and parents were interviewed regarding the child's mental health and social functioning. For the comparison group, interviews were carried out either in the child's general practice or at home. Test tubes were delivered and instructions given regarding how to collect saliva samples three times a day over 2 days. A written instruction leaflet was left for each child (Patel et al., 2004).

### 2.4. Measures

Emotional and behavioural symptoms were measured using the Strengths and Difficulties Questionnaire (SDQ), a 25-item scale validated in large-population research that covers conduct problems, emotional problems (depression/anxiety), hyperactivity, problems with peer relations and prosocial (caring, helpful) behaviour. The first four subscales are tallied to produce a Total Difficulties Score (Goodman et al., 2003).

The Relationship Problems Questionnaire (RPQ) is a 10-item parent and teacher-report screening instrument for RAD symptoms. In a large general population twin sample, the RPQ had good internal consistency (Cronbach's alpha 0.85) and factor analysis identified that six items describe Inhibited RAD behaviours and four items describe Disinhibited RAD behaviours (Minnis et al., 2007).

Information about the adopted children's histories of abuse and/or neglect was gleaned from "Form F"—the form completed by the social worker at the time of child placement in the adoptive family, using a standardised checklist developed for this study. Form F is an unstructured form that contains as much detail as the social worker can glean about the child's pre-adoption history. From Form F, we were able to extract information on the various types of abuse and neglect (emotional, physical and sexual), witnessing of domestic violence, and parental history of drug and alcohol misuse.

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