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SHORT COMMUNICATION

Diurnal cortisol profiles and evening cortisol in post-pubertal adolescents scoring high on the Children's Depression Inventory

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Summary Early-onset mood disorders have become a significant public health problem in recent years. The Children's Depression Inventory (CDI) is a commonly used self-report measure. We studied the relation of CDI cut-offs to biological markers of depression such as the diurnal cortisol rhythm and evening cortisol. In 58 post-pubertal adolescents (29 boys and 29 girls, $M_{age} = 15.1$ years), the diurnal cortisol profile was derived from three saliva samples, collected at awakening, at noon and in the evening on a week-end day. Longitudinal repeated measurements regression revealed that the group with $CDI > 18$ (high depressive symptoms) clearly had a higher and flatter diurnal rhythm with elevated evening cortisol compared to either the group with CDI between 13 and 18 (moderate depressive symptoms) or $CDI < 13$ (low depressive symptoms). Multinomial logistic regression indicated that evening cortisol was useful in classifying the adolescents in the high depressive symptoms group, while awakening and noon cortisol were not. Our results indicate that the type of high flattened profiles sometimes seen in individuals who are clinically depressed according to diagnostic interviews can also be identified with a self-report inventory, at high levels of symptom reporting. Given the complexity of conducting diagnostic interviews, this result bears clinical relevance.

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1. Introduction

Early-onset mood disorders have become a significant public health problem in recent years. Miller (2007) reviewed epidemiological studies involving more than 2500 youngsters and concluded that approximately 2% of young children, 4% of young adolescents and 16% of older adolescents suffer from a major depressive disorder each year. Early-onset depression is a serious burden for an individual's health for the following reasons: (a) the functional problems of depressed youngsters suggest that the disorder can interfere with developmental milestones; (b) these individuals are likely to show symptoms of anxiety and to develop additional co-morbid disorders such as conduct disorders or substance abuse; (c) early-onset depression may persist into adulthood. Therefore, it is clear that the early recognition of mood disorders should be a priority in primary health care (Hyman, 2001) and that more research on depression prevention and intervention is needed (Kovacs, 2006; Adam et al., 2008). Although clinical interviews are obligatory to diagnose depression, in primary health care and research settings other sound yet less complex and time-consuming instruments are often used. The Children's Depression Inventory (Kovacs, 1992), containing 27 items scored from 0 to 2, is a commonly used self-report measure. As an index of severity of depressive symptoms, a cut-off score of 19 has been found to identify major depressive disorder/clinically depressed children and adolescents, whereas levels between 13 and 18 are regarded as a subclinical or minor depressive episode (Kovacs, 1992).

The usefulness of the CDI (and its cut-off scores) has not been studied in relation to important, non-invasive biological markers of depression such as cortisol assessed with saliva samples; our current study is a preliminary investigation of this issue. For example, depression in adolescent outpatients has been associated with a high, flattened diurnal profile (with elevated afternoon/evening cortisol and awakening levels that may be somewhat lower; Shirtcliff and Essex, 2008) or with elevated evening (peri-sleep-onset) cortisol levels (e.g., Dahl et al., 1991; Goodyer et al., 2001; Kaufman and Charney, 2001; Forbes et al., 2006). Our aims were to examine: (1) the association between the degree of depressive symptomatology (i.e., CDI < 13; CDI between 13 and 18 and CDI > 18) and the diurnal cortisol profile, i.e., whether and in what way the CDI can detect a high flattened diurnal cortisol profile (2) the relative importance of awakening, noon and/or evening cortisol in classifying adolescents into the CDI groups.

2. Method

2.1. Participants

The current study involves 58 participants (29 boys and 29 girls, $M_{\text{age}} = 15.1$ years, $S.D. = .26$ years; range = 14.5–15.5), whose mothers were recruited during pregnancy in a prospective follow-up study on the association between maternal anxiety during pregnancy and offspring development (Van den Bergh et al., 2008). Most of them had reached Tanner stage four of pubertal development ($M = 4.13$; $S.D. = .526$). The local ethical committee approved the study and we

obtained informed consent from all adolescents and their parents.

2.2. Measures

The CDI was used to measure the severity of depressive symptoms over the last 2 weeks in this non-clinical sample of post-pubertal adolescents. Adolescents with CDI > 18 formed the high depressive symptoms group (HDSG), those with CDI between 13 and 18 the moderate depressive symptoms group (MDSG), and those with CDI < 13 the low depressive symptoms group (LDSG). The participants were asked to complete the questionnaire on the day they collected saliva. For reasons of feasibility, we planned the saliva collection on a week-end day, at home. We used a short version of the day-time cortisol profile (cf. Wüst et al., 2000) and samples were collected upon awakening (before brushing teeth and having breakfast), around noon and in the evening (approximately 4 and 12 h after awakening, respectively). Samples were collected by spitting in a small plastic tube (Sarstedt, Germany), without using swabs or aids to salivation. Cortisol was analyzed with a revised version of the protocol provided by the manufacturer of the Coat-a-Count Radio-Immuno-Assay Kit (Euro DPC, Llanberis, Wales). The method was sensitive to as low as 0.3 nmol/L; all cases below this threshold were set at zero.

2.3. Statistical analysis

For the first aim, longitudinal repeated measurements (LRM) regression analysis was used. The associations among the cortisol measurements at different times of the day – i.e., at awakening (time = 0 in the analysis), noon (time = 4) and evening (time = 12) – were best modeled using a heterogeneous first-order autoregressive covariance structure (Verbeke and Molenberghs, 2000). We investigated the main effect of CDI groups, the linear and quadratic time effects of cortisol (to investigate how the cortisol level evolves during the day), and the interaction effects of the CDI with the linear and quadratic time effects (to investigate whether the cortisol evolution depends on CDI). Cortisol was log transformed to account for observed skewness in the distribution, mainly for the noon and evening levels. It is useful to mention at this point that the three CDI groups were best modeled as categorical (i.e., LDSG, MDSG, HDSG) rather than numerical (i.e., 1, 2, 3), and that there were no effects (main or interaction) involving gender.

For the second aim, a multinomial logistic regression model was built to predict CDI group. Using the Bayesian information criterion and the likelihood-ratio p -values, variable selection was carried out in order to investigate the importance of morning, noon and evening cortisol. The final model yielded predicted probabilities for each CDI group, and these were used to construct the area under the receiver operating characteristic curve (AUROC) (Lasko et al., 2005). An AUROC of 1 represents a model that perfectly discriminates between two classes of adolescents in the data set (those belonging to that CDI group versus those belonging to the other groups), whereas an AUROC of .5 represents a model with random performance.

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