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Original article

Increased cortisol awakening response after completing the summer treatment program in children with ADHD

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Abstract

Objective: Little is known about the cortisol awakening response (CAR) in children with attention deficit hyperactivity disorder (ADHD). Here, we examined the CAR in children with ADHD and their mothers before, immediately after, and 4 months after an intensive summer treatment program (STP).

Methods: Participants were 37 children aged 7–12 years who completed the STP in 2009 and 2010, and their mothers. Daily saliva samples for cortisol measurement were collected twice daily at awakening and 30 min afterwards at pre-STP, post-STP, and during a follow-up measurement period. ADHD symptom scores were evaluated by parents, and participants completed the Kid-KINDL^R QOL questionnaire.

Results: CAR was low in children with ADHD before the STP, and increased to the control range 4 months after STP. Maternal CAR also tended to increase after STP. Changes in the CAR in children tended to correlate with an improved ADHD inattention scores ($p = 0.091$), physical health ($p = 0.070$), and school life subscales scores in the Kid-KINDL^R ($p = 0.079$).

Conclusion: We demonstrated that STP improved the behavior and QOL of children with ADHD. Our results indicate that STP could lead to improvements in HPA axis function, as reflected by increased CAR after STP.

Keywords: Attention deficit hyperactivity disorder; Cortisol awakening response; Summer treatment program; QOL; Psychosocial treatment

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common childhood psychiatric disorders. Globally, it affects about 5% of children and about 2.5% of adults [1]. Children with ADHD show symptoms of inattention, hyperactivity, and impulsivity that

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is inappropriate for their developmental level [1]. In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), ADHD is categorized as a neurodevelopmental disorder involving brain dysfunction.

Based on differing symptoms, ADHD type has been classified according to three clinical presentations: predominantly inattentive, predominantly hyperactive-impulsive, and combined. Comorbid disorders, such as autism spectrum disorders (ASD), learning disorders (LD), anxiety disorders (AxD), oppositional defiant disorders (ODD), and conduct disorders (CD) are frequently observed. ADHD can affect all aspects of a child's life, and can also have a strong influence on the lives of parents and siblings.

The hypothalamic–pituitary–adrenal (HPA) axis is a major homeostatic system that is involve in the maintenance of equilibrium between an organism and its environment [2]. The HPA axis is the primary mammalian system associated with stress responses, and the endpoint of HPA-axis activation is the release of glucocorticoid cortisol [3]. Cortisol secretion is governed by a diurnal rhythm such that levels are at their highest in the morning and gradually decrease during the night. In addition to circadian variation, an acute increase in cortisol secretion occurs after awakening [4]. Although cortisol is often used as a measure of HPA activation, several studies have indicated that this cortisol awakening response (CAR) may be a more appropriate measure for assessing HPA activation in relation to psychosocial factors [4,5].

Our research team has conducted multiple experiments in which we sampled and measured salivary cortisol in individuals ranging in age from neonates to adults [5–7]. In these previous studies, we reported that salivary CAR was associated with mood status in healthy female children [5] and that plasma cortisol levels were linearly correlated with salivary cortisol in neonates [7]. These findings indicate that salivary cortisol is a useful surrogate marker for plasma cortisol that can be collected in a non-invasive way.

Salivary cortisol levels and HPA axis activity in individuals with ADHD have been previously assessed within the framework of the behavioral inhibition system [8]. Previous studies have reported an altered cortisol response [9] or lower CAR in children with ADHD compared with healthy control children [9]. Compared with control children, children with ADHD had lower levels of cortisol both when they awoke and 30 min thereafter, and a smaller CAR [10,11]. However, these findings have not been replicated in other studies. Corominas et al. conducted a large-scale review of studies that examined the involvement of cortisol in ADHD [12], and observed two diverse patterns: (1) dampened cortisol responses to stress were associated with comorbid disruptive behavior disorder (DBD), and (2) high cortisol responses were associated with comorbid AxD [12,13]. These results remain controversial. Discrepancies between studies may be due to different participant characteristics (e.g., medication, comorbidities, age) or different assessment methods (e.g., saliva, plasma).

There are three evidence-based treatments for ADHD: medication with a central nervous system stimulant, behavioral modification, such as the summer treatment program (STP) and parent training programs, and a combination of medication and behavioral modification [14]. Numerous studies in North America have reported on the efficacy of the STP over the past decade. These studies have documented substantial STP-related improvements in multiple domains, including peer relationships, compliance with adult requests, and classroom functioning, as assessed via direct behavioral observation and rating scales [15]. We modified the American STP into a 2-week program, which we have administered since 2005 in Kurume, Japan. In a previous report, we demonstrated that our program had a short-term effect on behavioral and cognitive function that lasted up to 4 months after completion [16]. However, previous study lacked objective evaluation techniques, such as measurements of salivary cortisol as a biomarker. Therefore, in the present study, we sought to clarify the influence of STP on the CAR in both children with ADHD and their mothers. We hypothesized that the CAR would be lower in children with ADHD prior to the treatment program, and that it would increase after intensive STP, with specific improvements in behavioral function and QOL.

2. Participants and methods

2.1. Participants

Participants included 48 school children (41 boys and 7 girls) aged 7–12 years who participated in the STP in 2009 and 2010. Diagnoses for these patients were based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (DSM-IV-TR) [17] and were determined by three experienced pediatric neurologists (YY, SN, and TM) who, together with multiple clinical psychologists, reviewed detailed participant data [16]. Each participant met the criteria for IQ level, i.e., an IQ greater than 70, as per the Wechsler Intelligence Scale for Children-Third edition.

As a control group, 16 age and sex matched children were recruited from an elementary school in the same area. We obtained information about the developmental history and medical status of the children via questionnaires completed by their parents. The parents also completed a questionnaire focused on the symptoms of ADHD based on the DSM-IV-TR [17]. This enabled us to rule out the possibility that members of our control group had ADHD. The control group did not participate in the STP.