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None of the authors have any conflicts of interest to declare

## Introduction and objectives

Attention-deficit/hyperactivity disorder (ADHD) is the most prevalent neurodevelopmental disorder worldwide. Evidence suggests dysfunction of the fronto-subcortical pathways and the dopaminergic and noradrenergic systems, as well as dysregulation of the stress system, i.e., the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS).

The aim of the study was to examine i) the diurnal secretion patterns of salivary cortisol and salivary  $\alpha$ -amylase, as peripheral biomarkers of the HPA axis and the SNS, respectively and ii) the stress response to a physical stressor, the venipuncture, in both ADHD and typically developing children.

## Methods

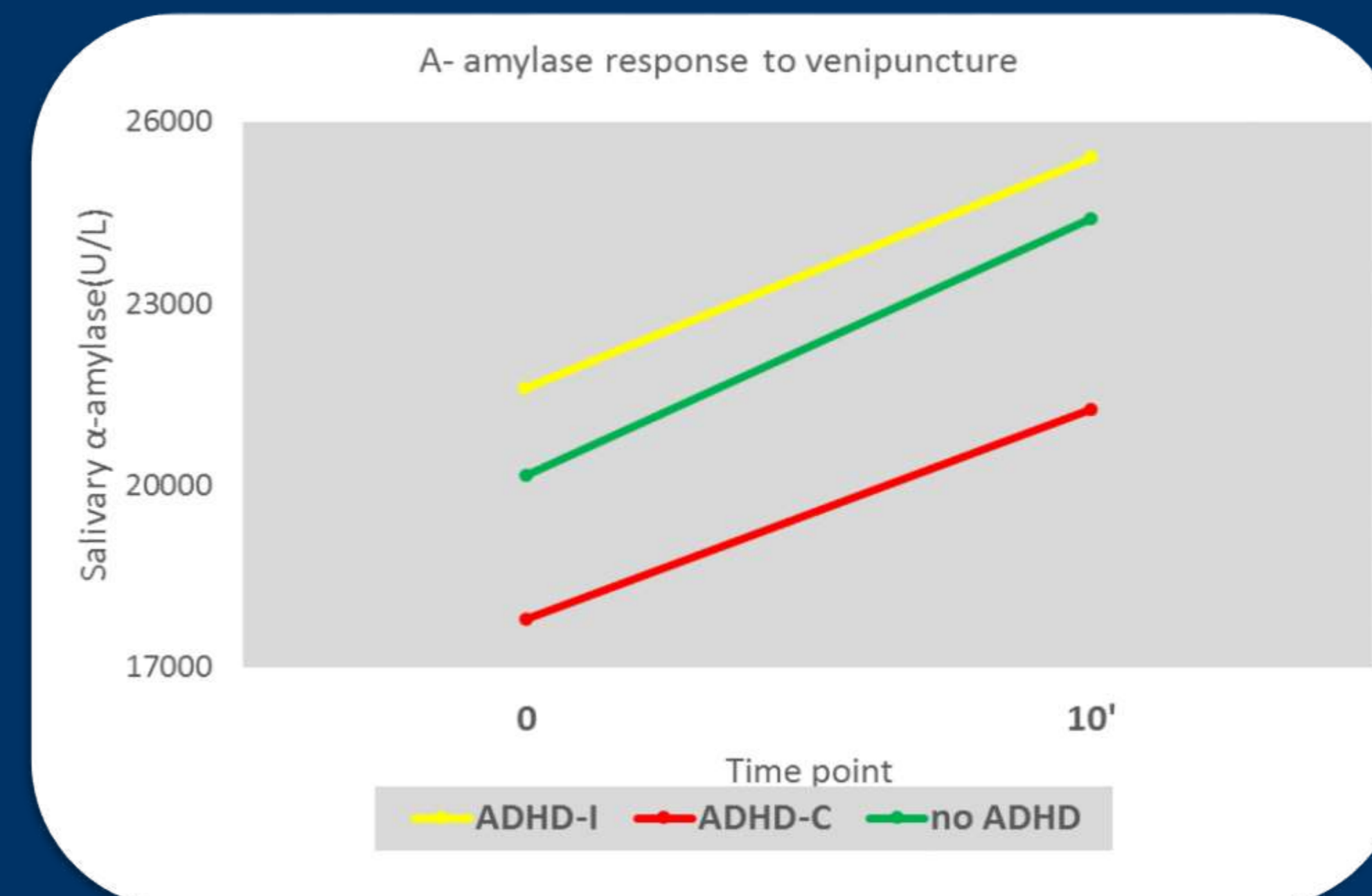
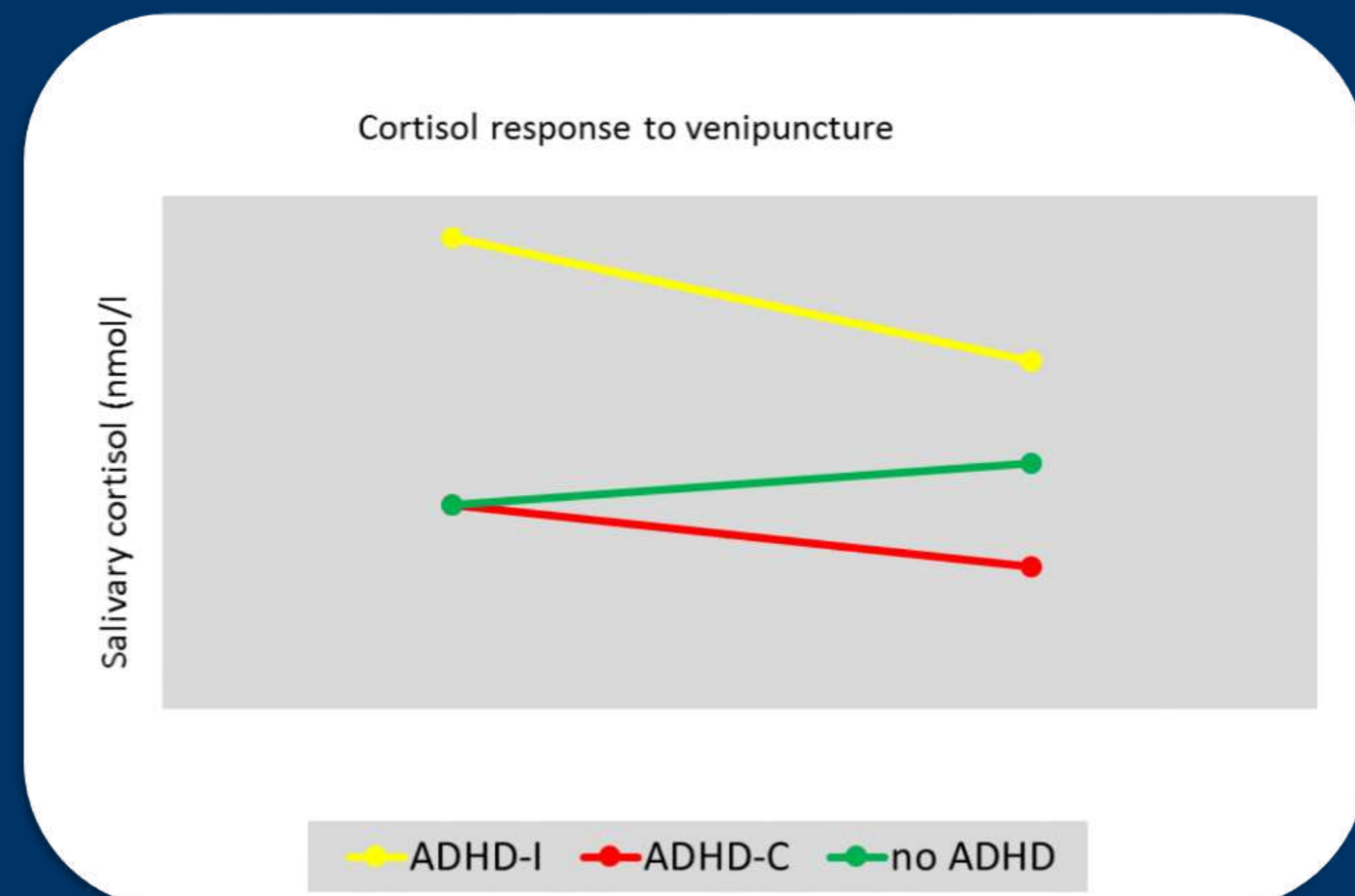
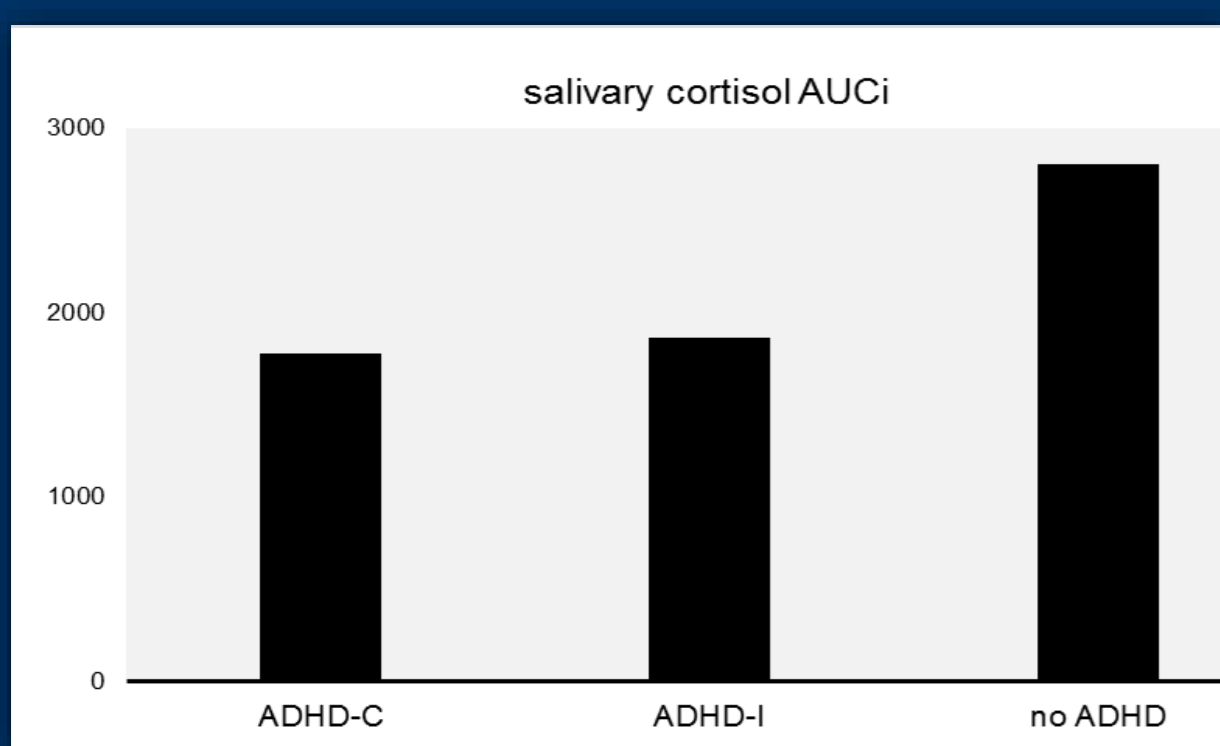
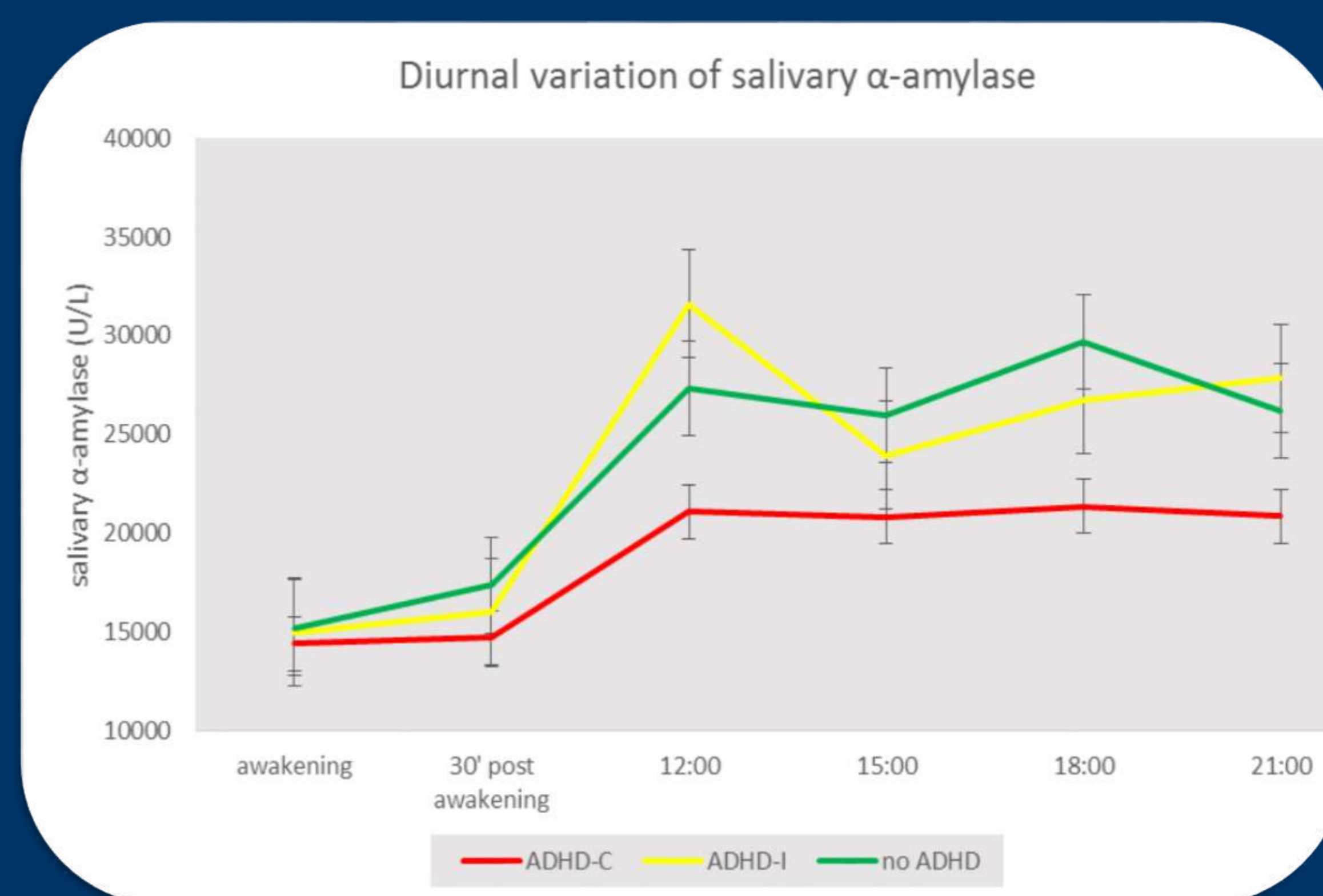
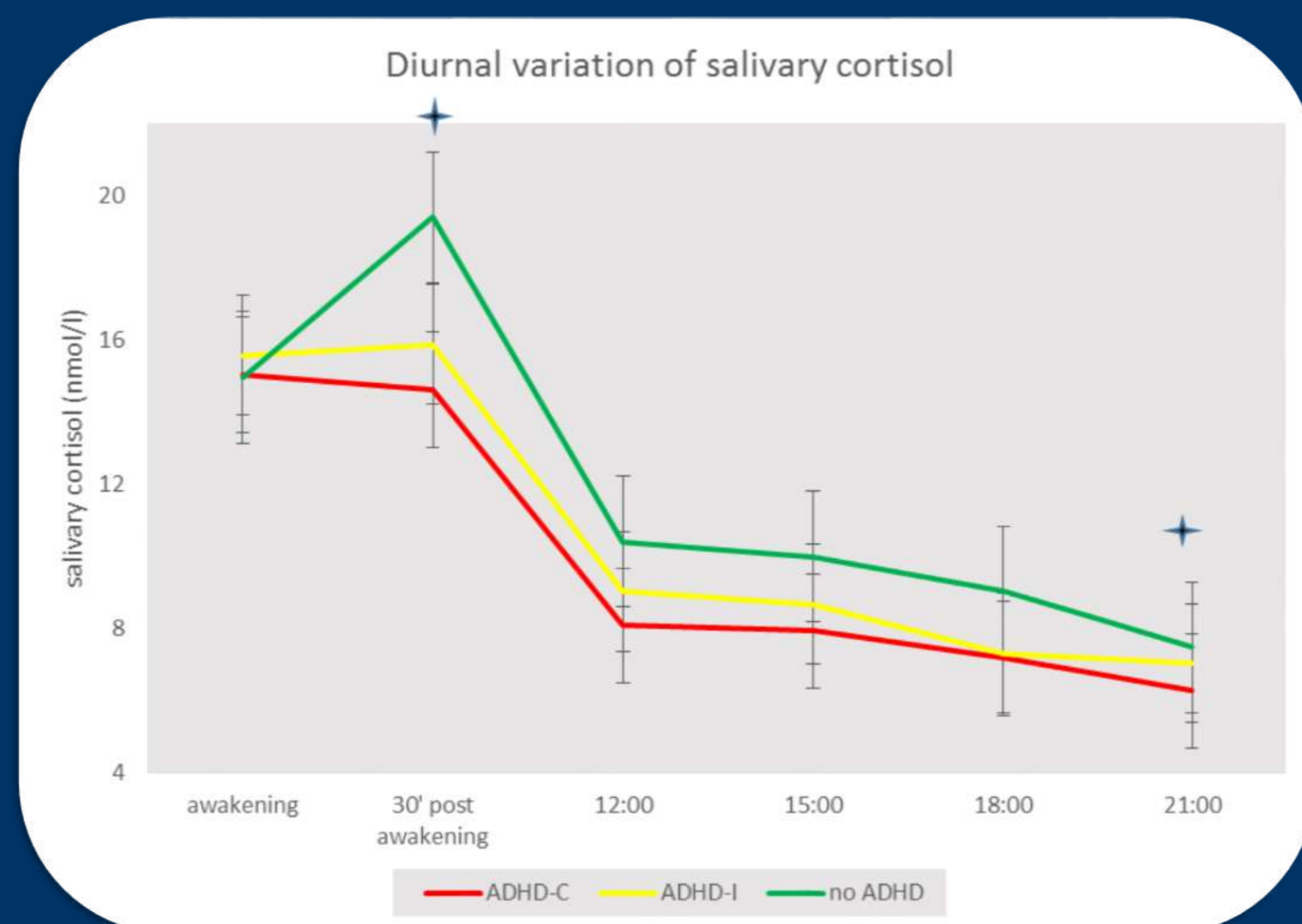
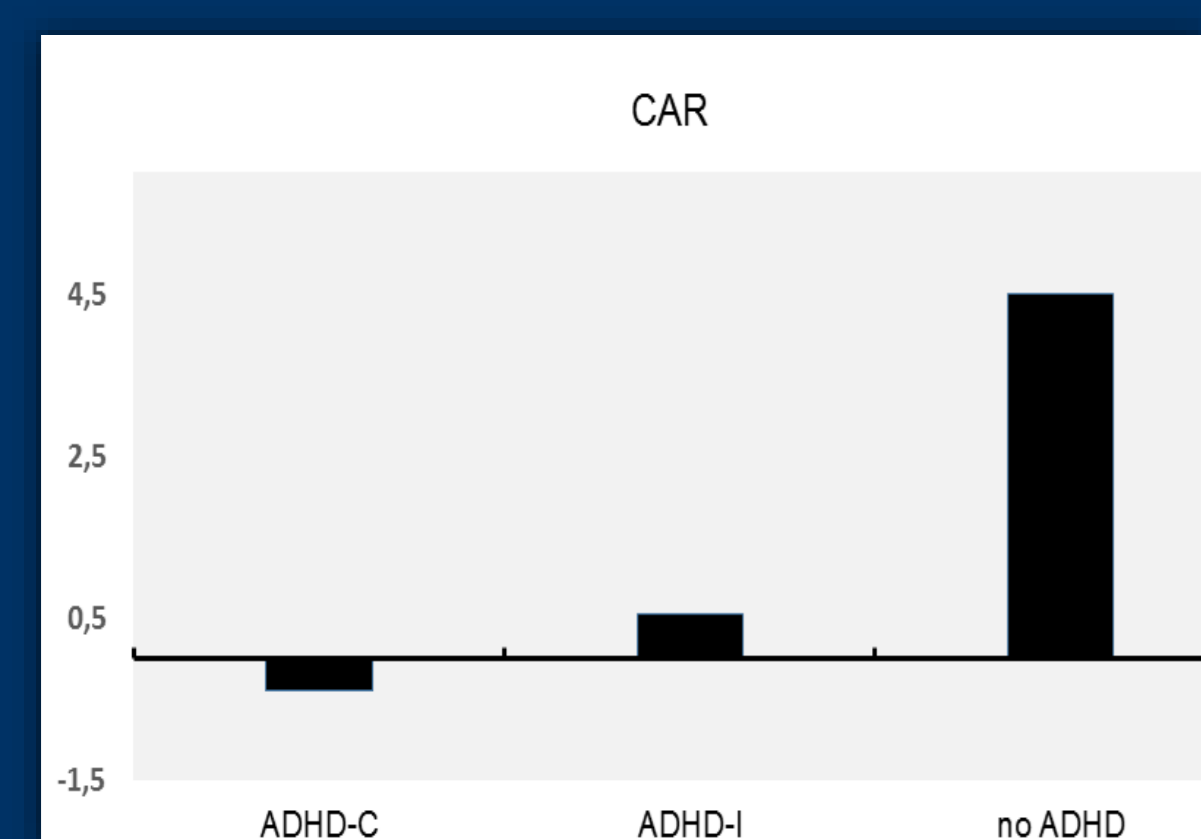
Sixty-two prepubertal children (30.2% girls; mean age  $8.63 \pm 2.27$ ) with a clinical diagnosis of ADHD (combined or inattentive subtype) were compared with 40 typically developing children (35.9% girls; mean age  $8.1 \pm 1.7$ ). Saliva was collected at six time points over one weekend day as well as before and 10 min after a scheduled morning venipuncture. Chemilluminescence immunoassay and kinetic-reaction assay were used for the determination of cortisol and  $\alpha$ -amylase in saliva, respectively.

## Results and conclusions

i) Both groups demonstrated the typical circadian cortisol rhythm with highest levels in the morning and lowest in the evening. Significantly lower cortisol concentrations were observed in children with ADHD across the day compared to controls ( $P < 0.05$ ). Moreover, children with ADHD had significantly lower CAR and cortisol AUC ( $P < 0.001$ ). In both groups, the secretion pattern of  $\alpha$ -amylase showed lowest levels in the morning and highest in the afternoon.

ii) Venipuncture-induced salivary cortisol concentrations tended to increase in controls, and decrease in ADHD children. The venipuncture-induced increase in salivary  $\alpha$ -amylase tended to be more pronounced in controls.

Differences in salivary cortisol and  $\alpha$ -amylase diurnal rhythms and responses to venipuncture suggest altered stress system activity in children with ADHD.



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