

CARRIERS OF 21-HYDROXYLASE DEFICIENCY DEMONSTRATE INCREASED PSYCHOLOGICAL VULNERABILITY TO STRESS



Eleni Magdalini Kyritsi¹, Georgia Koltsida¹, Ioanna Farakla¹, Aikaterini Papanikolaou², Gerasimos Kolaitis², Emilia Mantzou¹, Evangelia Charmandari^{1,3}

¹Division of Endocrinology, Metabolism and Diabetes, First Department of Pediatrics, University of Athens Medical School, 'Aghia Sophia' Children's Hospital, Athens, 11527, Greece;

²Department of Child Psychiatry, University of Athens Medical School, 'Aghia Sophia' Children's Hospital, Athens, 11527, Greece;

³Division of Endocrinology and Metabolism, Biomedical Research Foundation of the Academy of Athens, Athens, 11527, Greece

The authors have no financial relationship(s) to disclose relevant to this poster presentation

BACKGROUND

Carriers of congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21-OHD) demonstrate increased secretion of cortisol precursors following ACTH stimulation, suggestive of impaired cortisol production and compensatory increases in hypothalamic CRH secretion. Both cortisol and CRH have behavioral effects, and hypothalamic CRH hypersecretion has been associated with chronic states of anxiety and depression.

OBJECTIVE AND HYPOTHESES

To perform endocrinologic and psychologic evaluation in carriers of 21-OHD and matched control subjects.

METHODS

Twenty-nine parents of children with classic CAH [14 males, 15 females; age (mean ± SEM): 41.76 ± 1.07 yr], and hence obligate 21-OHD carriers, and 13 normal subjects (5 males, 8 females; age: 43.77 ± 1.69 yr), were recruited to participate in the study. The carrier state of 21-OHD was confirmed by genotype. All subjects underwent a formal oCRH test for measurement of ACTH, cortisol, 17-hydroxyprogesterone (17-OHP) and androstenedione concentrations, which was preceded by determination of 24-hour urinary free cortisol (UFC) excretion. Psychometric assessment was performed by administering the State-Anxiety Inventory (STAI), Beck Depression Inventory, Symptom Checklist-90R, and Temperament and Character Inventory. The study was approved by the Ethics Committee and written informed consent was obtained in

Table 1. Comparison of psychometric parameters between CAH carriers and controls

	CAH Carriers (n=29)	Controls (n=13)	p-value *
State Anxiety Inventory (STAI)			
State anxiety (STAI 1)	47.6 ± 1.1	43.3 ± 1.5	0.023
Trait anxiety (STAI 2)	47.8 ± 1.1	47.9 ± 1.0	NS
Total STAI score	95.4 ± 1.6	91.2 ± 2.3	NS
Beck Depression Inventory (BDI)			
Depression score	7.7 ± 1.1	8.4 ± 1.1	NS
Symptom Checklist – 90R (SCL-90R) ¶			
Somatization	7.3 ± 1.5	8.0 ± 1.7	NS
Obsessive-compulsive	9.8 ± 1.1	10.9 ± 1.7	NS
Interpersonal sensitivity	6.4 ± 1.0	7.0 ± 0.7	NS
Depression	9.8 ± 1.6	13.8 ± 2.1	NS
Anxiety	6.2 ± 0.9	6.7 ± 1.1	NS
Hostility	4.5 ± 0.9	5.6 ± 1.3	NS
Phobic anxiety	2.2 ± 0.7	1.2 ± 0.5	NS
Paranoid ideation	6.1 ± 0.8	5.9 ± 1.0	NS
Psychoticism	3.3 ± 0.6	3.2 ± 0.8	NS
Total SCL-90R	61.1 ± 7.7	67.8 ± 7.8	NS
Temperament and Character Inventory (TCI)			
Novelty seeking	22.2 ± 0.6	20.5 ± 1.2	NS
Harm avoidance	16.3 ± 0.8	13.6 ± 1.0	NS
Reward dependence	13.4 ± 0.4	13.8 ± 0.4	NS
Persistence	3.2 ± 0.2	3.5 ± 0.4	NS
Self-directedness	20.5 ± 1.1	22.0 ± 1.5	NS
Cooperativeness	23.7 ± 0.6	24.2 ± 1.0	NS
Self-transcendence	15.2 ± 0.8	15.6 ± 1.4	NS

Continuous variables presented as mean ± SEM; *Mann-Whitney p-value
 ¶ SCL-90R conducted among n=37 (CAH carriers: n=27 vs Controls: n=12)

RESULTS

Carriers of 21-OHD had significantly higher peak, mean and area under the concentration curve (AUC) 17-OHP concentrations in response to oCRH stimulation (peak 17-OHP: 3.97 ± 0.62 vs. 1.9 ± 0.26 ng/mL, P<0.001) (Figure 1A), and significantly higher STAI 1 scores (47.6 ± 1.1 vs 43.3 ± 1.5; P=0.023) compared with healthy matched subjects (Table 1). Carriers of CAH had significantly higher mean androstenedione concentrations 15 minutes prior to stimulation (Androstenedione -15 min: 2.4 ± 0.3 vs. 1.5 ± 0.2 ng/mL, P=0.036) (Figure 1B). ACTH, cortisol and peak androstenedione responses were similar in the two groups. Peak 17-OHP concentrations were positively correlated with STAI 1 (state anxiety) responses (r=0.364; P=0.027). Mean UFC concentrations were significantly correlated with the SCL-90R subscale responses relating to paranoid ideation (r=0.435; p=0.023) and psychoticism (r=0.454; P=0.017), as well as to the TCI subscale of self-transcendence (r=0.371; P=0.048). Finally, stepwise multiple linear regression analyses revealed that the single independent predictor of state anxiety (STAI 1) was peak concentration of 17-OHP (R²: 0.290; P=0.031).

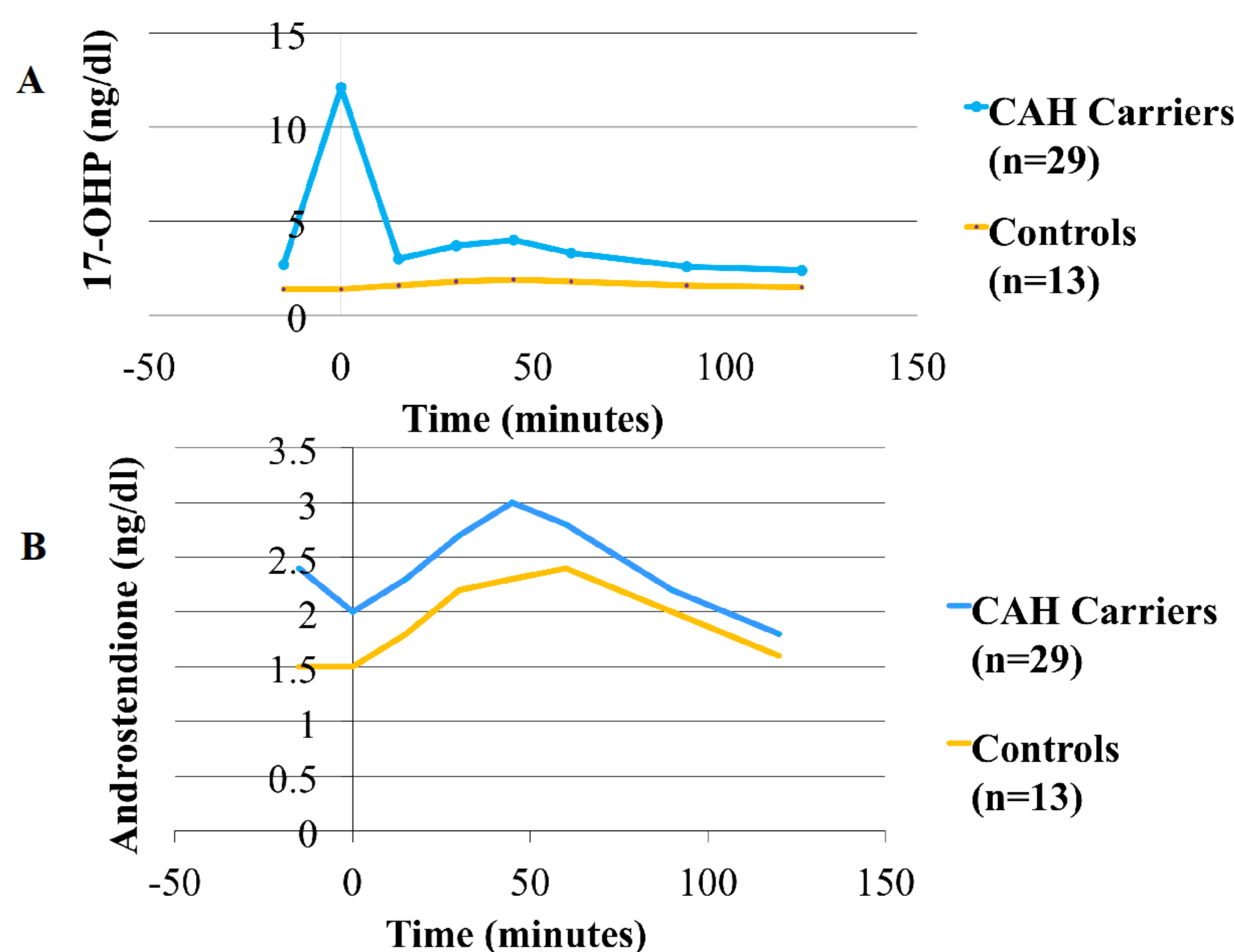


Figure 1. Responses of 17-OHP (A) and androstenedione (B) concentrations to oCRH in carriers of 21-OHD and controls

CONCLUSIONS

Carrier state of 21-OHD may predispose subjects to psychopathology. The severity of anxiety-related symptoms may be associated with the degree of impairment of cortisol biosynthesis.

References

- Charmandari E et al. J Clin Endocrinol Metab 2004;89(5):2228-2236.
- Hori H et al. J Psychiatr Res 2010;44(14):865-873.
- Penninx BW et al. Am J Geriatr Psychiatry 2007;15(6):522-529.
- Gold PW, Chrousos GP. Mol Psychiatry 2013;18(6):632-634.

