

Association between hypothalamus-pituitary adrenal axis activity and anxiety in prepubertal children with Type 1 diabetes

Authors Pascal Barat (1) (2), Julie Brossaud (2) (3), Anne Lienhardt (4), Aurélie Valade (5), Aude Bereron (1), Jean-Benoit Corcuff (2) (3), Marie-Pierre Moisan (6), Aurélie Lacoste (1), Vanessa Vautier (1), Helene Savel (7), Paul Perez (7)

Institutions (1) CHU Bordeaux, Unité d'Endocrinologie et Diabétologie Pédiatrique, Bordeaux, France; (2) Université Bordeaux, NutriNeuro, Bordeaux, France; (3) CHU Bordeaux, Médecine Nucléaire, Bordeaux, France; (4) CHU Hôpital de la mère et de l'enfant, Limoges, France; (5) CHG Cote Basque, Bayonne, France; (6) INRA, NutriNeuro, Bordeaux, France; (7) CHU Bordeaux, Unité de Soutien Méthodologique à la Recherche Clinique et Epidémiologique, Bordeaux, France;

Objectives:

Animal models of insulin-dependent diabetes show hyperactivity of hypothalamus-pituitary adrenal (HPA) axis, independently of hypoglycaemia. Few data exists regarding type 1 diabetes (T1D) in children.

Our objective was to describe HPA axis activity according to the anxiety levels in prepubertal T1D children.

Methods:

Prepubertal T1D children and non-diabetic siblings of T1D children (controls) were included.

State-Trait Anxiety Inventory (STAI)-trait test was performed at inclusion.

Glucocorticoids metabolites (LCMS)/creatinine ratio on nocturnal urines and morning salivary cortisol (SC) were measured at home during 5 consecutive days without identified nocturnal hypoglycaemia.

Expressed results were mean of the five samples for each child.

Tetrahydrocortisol (THF) + allo-THF/tetrahydrocortisone (THE) ratio (ie THFs/THE ratio) was considered as an estimate of type 1 11 β -hydroxysteroid dehydrogenase (11 β -HSD1) activity (Fig 1).

Comparisons between groups have been made with linear regression mixed model. The association between anxiety levels (STAI-TRAIT) and HPA axis activity, adjusted on BMI (and insulin dose in T1D children) was assessed using linear regression model.

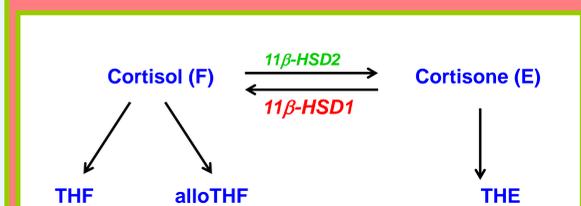


Figure 1: Glucocorticoid metabolites in urine

Results:

Forty-nine T1D children and 26 controls were recruited. Results are expressed in Table 1.

- STAI scores were not statistically different between T1D children and controls with a trend for higher STAI scores in controls group.
- Total glucocorticoid metabolites/creatinine were decreased in T1D children vs controls.
- THFs/THE (HSD1 activity estimate) was increased in TD1 children vs controls.
- Salivary cortisol at awakening and 30 minutes after awakening (SC+30) were not different between groups.

	TD1 Children n=49	Controls n=26	P
Age (yrs)	9.3 (1.4)	9.0 (1.4)	ns
Sex (M/F)	27/22	12/14	ns
BMI (kg/m ²)	16.3 (1.3)	16.0 (1.7)	ns
HbA1c (%)	7.6 (0.7)	5.3 (0.3)	
STAI-TRAIT	29.7 (6.6)	33.0 (7.8)	0.06
F/cr (μg/mmol)	4.9 (2.1)	4.2 (1.4)	0.07
E/cr (μg/mmol)	11.0 (4.7)	10.9 (3.2)	ns
THF/cr (μg/mmol)	93.3 (33.1)	109.7 (38.6)	0.06
Allo-THF/cr (μg/mmol)	22.6 (8.9)	29.2 (10.7)	<0.01
THF + THFs/cr (μg/mmol)	155.0 (45.2)	175.7 (46.3)	0.06
THE/cr (μg/mmol)	260.5 (91.2)	351.4 (101.2)	<0.001
Total GC metabolites/cr (μg/mmol)	551.9 (170.5)	673.3 (170.0)	<0.01
THFs/THE (HSD1 activity estimate)	0.46 (0.10)	0.41 (0.09)	<0.05
SC T0 (nmol/l)	3.5 (1.7)	3.8 (1.5)	ns
SC T30 (nmol/l)	4.5 (1.9)	4.2 (1.8)	ns
SC Δ (0-30) (nmol/l)	1.0 (2.0)	0.5 (1.8)	ns

Results are expressed as mean (SD). STAI: State-Trait Anxiety Inventory; THF: tetrahydrocortisol; THE: tetrahydrocortisone; SC: salivary cortisol

- In DT1 group, higher STAI scores were associated with lower SC+30 ($\beta=-1.0$, $p=0.04$) and higher THFs ($\beta=0.04$, $p=0.01$) and total GC metabolites values ($\beta=0.01$, $p=0.04$) when adjusted for BMI and insulin doses.
- In control group, no significant association was found between STAI scores and any markers of HPA axis activity.

Conclusions:

Subtle changes of HPA axis activity, independently of recognized hypoglycemia, are present in prepubertal children with T1D, particularly for nocturnal glucocorticoid synthesis, 11 β -HSD1 activity and its associations with anxiety.

Disclosure statement

The authors declare no conflict of interest.

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