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

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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 11β-hydroxysteroid dehydrogenase (11β-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.

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 T1D children vs controls.
- Total glucocorticoid metabolites/creatinine were decreased in T1D children vs controls.
- THFs/THE (HSD1 activity estimate) was increased in T1D children vs controls.
- Salivary cortisol at awakening and 30 minutes after awakening (SC+30) were not different between groups.

- In DT1 group, higher STAI scores were associated with lower SC+30 (β=-1.0, p=0.04) and higher THFs (β=-0.04, p=0.01) and total GC metabolites values (β=-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 hypoglycaemia, are present in prepubertal children with T1D, particularly for nocturnal glucocorticoid synthesis, 11β-HSD1 activity and its associations with anxiety.

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