

# Preliminary findings on the association between attachment patterns and levels of growth hormone in a sample of children with non-organic failure to thrive

## *Risultati preliminari sull'associazione tra stili di attaccamento e livelli di ormone della crescita in un campione di bambini affetti da deficit di crescita non organico*

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**SUMMARY. Introduction.** Deficiency of growth hormone (GH) in absence of pituitary injuries is one of the causes of short stature and of the non organic failure to thrive (NOFTT) condition. Advances in developmental psychology have highlighted the role of emotions and caregiving behaviors in the organization of child's personality and psychobiology, with the mother-son attachment bond being considered a fundamental developmental experience. The objective of the present preliminary study was to assess whether there are significant correlations between attachment patterns and GH levels in a sample of subjects with NOFTT. **Methods.** Overall, 27 children (mean age 9.49±2.63 years) with NOFTT were enrolled. Perceived attachment security was assessed through the Security Scale (SS) and its subscales focused on maternal and paternal security. Pearson partial correlation was used to test associations between GH levels and SS measures adjusting for confounding factors (i.e. age, gender and body mass index). **Results.** Across all subjects, GH was significantly positively correlated with general security ( $r=0.425$ ;  $p=0.038$ ) and maternal security ( $r=0.451$ ;  $p=0.027$ ) and not significantly correlated with paternal security ( $r=0.237$ ;  $p=0.264$ ). **Discussion.** These findings preliminarily suggest that the association between GH levels and perceived attachment security may play a role in the pathophysiology of NOFTT and add to the accumulating evidence that attachment patterns may be related with specific psychoendocrine underpinnings.

**KEY WORDS:** growth hormone, non organic failure to thrive, children, attachment style.

**RIASSUNTO. Introduzione.** La riduzione dell'ormone della crescita (GH) in assenza di lesioni ipofisarie è una delle cause di bassa statura e della condizione clinica di deficit di crescita non organico, nota come "non-organic failure to thrive" (NOFTT). I progressi nell'ambito della psicologia dello sviluppo hanno messo in evidenza il ruolo delle emozioni e dei comportamenti del caregiver nell'organizzazione della personalità e della psicobiologia del bambino, considerando il legame di attaccamento madre-figlio come un'esperienza fondamentale nello sviluppo. Il presente studio preliminare si pone come obiettivo quello di valutare l'esistenza di correlazioni significative tra modelli di attaccamento e livelli di GH in un campione di soggetti affetti da NOFTT. **Metodi.** Sono stati arruolati nello studio 27 bambini (età media: 9,49±2,63) con NOFTT. La sicurezza della percezione di attaccamento è stata valutata attraverso la Scala di Sicurezza (SS) e le sottoscale inerenti il grado di sicurezza materna e paterna. La correlazione parziale di Pearson è stata usata per indagare le associazioni tra i livelli di GH e le misure SS, covariando per i fattori confondenti (ossia età, sesso e BMI). **Risultati.** In tutti i soggetti, il valore di GH era positivamente correlato in modo statisticamente significativo alla percezione della sicurezza generale ( $r=0,425$ ;  $p=0,038$ ) e della sicurezza materna ( $r=0,451$ ;  $p=0,027$ ) e non significativamente correlato con la sicurezza paterna ( $r=0,237$ ,  $p=0,264$ ). **Discussione.** Questi dati suggeriscono preliminarmente che l'associazione tra i livelli di GH e la sicurezza nella percezione dell'attaccamento possano svolgere un ruolo nella fisiopatologia del NOFTT, e si aggiungono al filone di evidenze inerenti il fatto che certi modelli di attaccamento possano essere associati a condizioni psico-endocrine specifiche.

**PAROLE CHIAVE:** ormone della crescita, deficit di crescita non organico, bambini, stile di attaccamento.

## INTRODUCTION

The term "failure to thrive" (FTT) includes a heterogeneous range of clinical conditions phenotypically character-

ized by inadequate growth or inability to maintain growth (i.e. <160 cm height in males and <149 cm height in females), usually in early childhood<sup>1</sup>.

Traditionally, the causes of FTT have been divided into

organic (medical) and non-organic (social or environmental)<sup>2</sup>. Increasing evidence suggests that in many children the etiology of FTT is multifactorial, including biological, psychosocial, and environmental contributors<sup>3</sup>. Epidemiological researches have shown that only 20-25% of infants and children with FTT receive the diagnosis of organic FTT (OFTT), while in the majority of cases it is not possible to identify a specific organic cause of FTT (i.e. the so-called non-organic FTT - NOFTT)<sup>4</sup>. The condition of NOFTT does not fulfill the criteria for being considered a medical diagnosis, but rather it represents a standardized description of a pattern of growth<sup>4</sup>.

In absence of clear organic causes, i.e. in the condition of NOFTT, several different psychosocial conditions may play a role in explaining the FTT phenotype, such as children's impaired affect regulation and temperamental characteristics, inadequate children's nutritional intake, a vicious circle of maladaptive behavioral interaction between caregiver and infant, caregivers' unsure attachment styles, psychosocial stress and psychopathology<sup>5</sup>.

Advances in developmental psychology have highlighted the role of emotions and caregiving behaviors in the organization of children's personality and psychobiology, with the mother-son attachment bond being considered a fundamental developmental experience<sup>6,7</sup>. According to the attachment theory, attachment styles have typically been classified into three types: secure, anxious, and avoidant<sup>7,8</sup>. These types not only describe individual's behavioral patterns but also represent the organization through the expectations of others in response to comfort or reassurance seeking<sup>7,8</sup>. The early attachment characteristics have been shown to play an important role in influencing psychopathological outcomes in adulthood<sup>9</sup>, and the presence of insecure attachment (i.e. anxious or avoidant) in children has been suggested to increase vulnerability towards several psychiatric diseases<sup>10</sup>. Further, preliminary studies evidenced a link between attachment styles and certain patterns of endocrine and immune functions<sup>11-15</sup>.

Early studies exploring the conditions of childhood emotional deprivation and mistreatments had identified a syndrome defined as "psychosocial dwarfism" or "reversible hypopituitarism syndrome" characterized by short stature often associated with a reversible deficit of growth hormone (GH) and with a range of psychiatric and behavioural disturbances such as eating disorders, insomnia, depression, bedwetting, poor cognitive performance<sup>16</sup>. The authors postulated that the emotional deprivation could act on the hypothalamus-pituitary gland and alter the release of GH as well as of somatomedins and other endocrine factors<sup>16</sup>.

Reduced levels of GH (i.e. pituitary dwarfism or GH deficiency - GHD) in absence of pituitary injuries are nowadays considered one of the causes of NOFTT<sup>17</sup>. The objective of the present preliminary study was to assess, for the first time in psychoendocrinological research, whether there are significant correlations between patterns of attachment and GH levels in a sample of subjects with NOFTT. A deeper understanding of psychobiological correlates of NOFTT could potentially lead to the development of better diagnostic and therapeutic strategies for individuals with this condition.

## METHODS

### Recruitment procedures and study participants

The institutional review board of Sapienza University of Rome approved the study. All subjects provided written, informed consent prior to commencing their involvement in the trial.

Patients with NOFTT (characterized by short stature or reduced annual growth rate) were recruited among those attending the Centre for the Diagnosis and Therapy of GHD at the Department of Experimental Medicine of Policlinico Umberto I University Hospital (Rome, Italy).

The following auxological criteria were considered as inclusion criteria: (i) age range between 6 and 15 years, (ii) stature  $<3$  SD or stature  $<2$  SD from the mean value, and (iii) annual growth velocity  $<1$  SD from the mean value evaluated after at least 6 months of clinical observation.

The exclusion criteria were: (i) presence of any chronic systemic disease (malabsorption syndrome, Fanconi anemia, cardiac, renal and metabolic disorders), (ii) endocrine and psychiatric disorders diagnosed according to DSM-5<sup>18</sup>, (iii) use of any pharmacological therapy, (iv) presence of brain and pituitary injuries as assessed by cerebral magnetic resonance imaging.

Each patient underwent blood examinations to measure GH levels and psychopathological evaluation (through the Security Scale - SS) to assess attachment. The SS is a self-report measure which assesses children's perceptions of security in parent-child relationships and consists in 15 items<sup>19</sup>. The SS has two sets of specular items focused on the attachment relationship about their mothers and their fathers, in order to get an overall picture of children's attachment perception. The instrument assesses to which degree children perceive their parents as being responsive and available, their tendency to rely on them in times of distress and their ease and interest in communicating with their parents. Each item is scored from 1 to 4, with higher scores representing greater perception of attachment security. The SS has three subscales: the first subscale assesses the degree of security perception in mother-child relationship (SSPSM); the second subscale assesses the degree of security perception in father-child relationship (SSPSP); the third subscale is derived from the sum of the two previously described subscales and assesses the overall perception of security (SSPSC). Serum GH levels were measured using immunoradiometric assays<sup>6</sup>.

### Statistical analyses

All tests were 2-tailed with an  $\alpha=0.05$ . GH was non-normally distributed, thus it was transformed using Ln transformation. Pearson partial correlation was used to test correlations between GH and the assessment measures of attachment (i.e. SSPSM, SSPSP and SSPSC) adjusting for age, gender and body mass index (BMI; weight in kilograms divided by the square of height in meters) because of (i) their known associations with GH secretion and function, and (ii) the significant inverse correlations between age and GH ( $r=-0.485$ ;  $p=0.010$ ) observed in our sample.

## RESULTS

Overall, 21 males and 6 females (mean age  $9.49\pm 2.63$  years) were included in the study. Among them, 19 patients had NOFTT associated with non-organic GHD, while 8 pa-

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tients had NOFTT not associated with GHD. Demographic and clinical characteristics of the subjects are presented in Table 1.

Across all subjects, GH was significantly positively correlated with SSPSM ( $r=0.451$ ;  $p=0.027$ ) and SSPSC ( $r=0.425$ ;  $p=0.038$ ) (Figure 1) and not significantly correlated with SSPSP ( $r=0.237$ ;  $p=0.264$ ).

**DISCUSSION**

To the best of our knowledge, this is the first study testing the association between GH levels and psychological measures of attachment in a sample of children with NOFTT. The

results of this preliminary investigation showed a significant positive correlation between GH levels and perceptions of children’s attachment to their parents in terms of partial scores (attachment to the mother) and of total scores (mother and father). The correlation was not significant for the perception of attachment to the father.

Our findings are consistent with previous evidence suggesting a link between early affective dysregulation, altered physical development and the condition of NOFTT<sup>11,12</sup>, and add specificity to this field of exploration through (i) the quantitative measurement of GH levels and the degree of perceived attachment, and (ii) the enrollment of children who were not using any medication, thus with low levels of biological confounders. Further, our findings add to the accumulating evidence suggesting meaningful associations of attachment patterns with endocrine and immune functions<sup>20,21</sup>.

In the reported significant relationship between GH levels and perceived security of attachment, both the directions of causality may be postulated. On the one hand, it is possible that the degree of perceived attachment towards the parents can contribute to psychobiologically affect the functioning of the hypothalamic-pituitary-adrenal axis with subsequent hormonal alterations of GH levels. On the other hand, it is possible that the conditions of less efficient endocrine functioning and short stature in children can induce anxiety in their parents that might interfere with reliable and consistent parenting and thus facilitate a maladaptive development of inter-personal relationships in children.

The major limitation of the present preliminary study is the small sample size, which partially results from the rarity of the NOFTT clinical condition. Future studies, including ongoing projects of our research team, will need to include a larger number of subjects, a control group, and a more comprehensive set of explored psychopathological and en-

Table 1. Demographic and clinical characteristics of the study participants.

Participants (n)	27
Age (years)	9.49±2.63
Gender (males/females)	21/6
BMI (kg/m <sup>2</sup> )	17.30±3.86
GH (ng/ml)	0.95±1.20
SSPSM	44.81±3.86
SSPSP	43.11±3.39
SSPSC	87.93±6.28

BMI= body mass index; GH= growth hormone; SSPSC= security scale overall; SSPSM= security scale mother-child relationship; SSPSP= security scale father-child relationship.

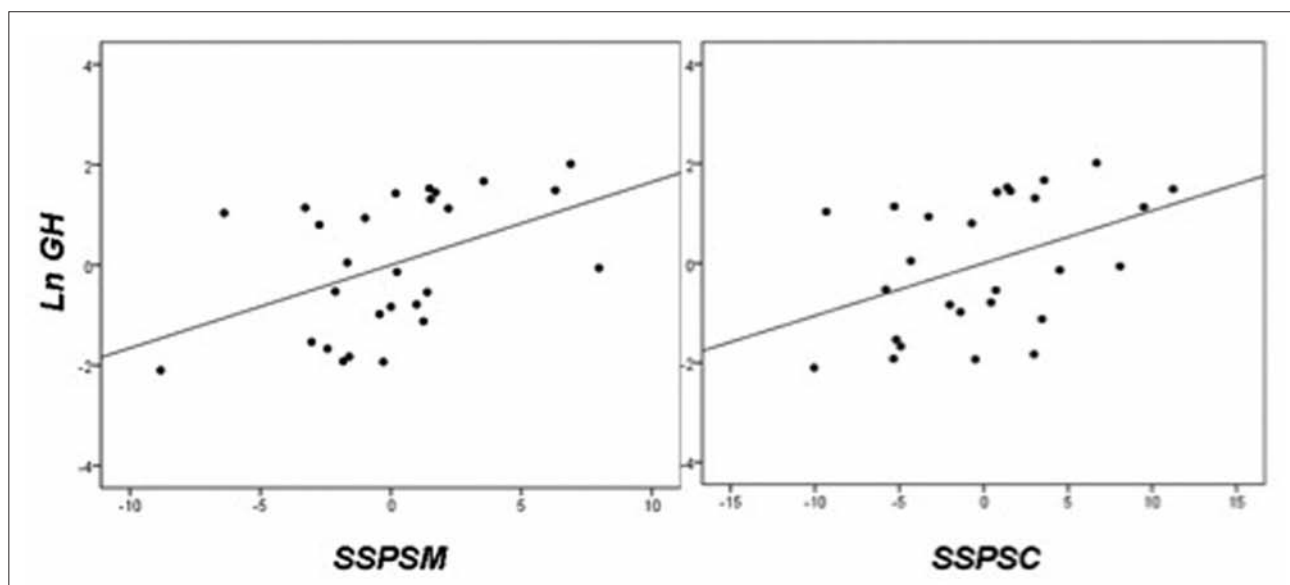


Figure 1. Significant correlations of Ln-transformed levels of growth hormone (GH) with security scale mother-child relationship (SSPSM) ( $r=0.451$ ;  $p=0.027$ ) and security scale overall (SSPSC) ( $r=0.425$ ;  $p=0.038$ ) after covarying age, body mass index, and sex (residuals).

doctrine assessments. Overall, these preliminary findings suggest that the association between GH levels and perceived attachment security may play a role in the pathophysiology of NOFTT and add to the accumulating evidence that attachment patterns may be related with specific psychoendocrine underpinnings.

*Conflict of interest:* none declared.

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