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Frequent cellular phone use modifies hypothalamic–pituitary–adrenal axis response to a cellular phone call after mental stress in healthy children and adolescents: A pilot study

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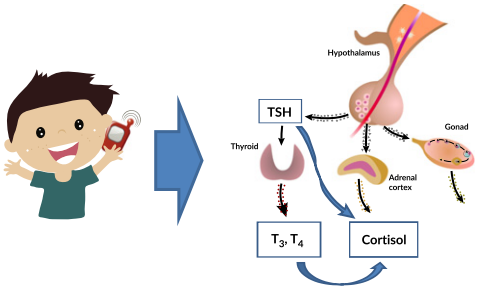
HIGHLIGHTS

- We model two environmental stressors: a cellular phone call and a mental stress.
- Frequent versus sporadic cellular phone users demonstrate different HPA-axis response.
- Baseline thyroid hormones predict HPA response to environmental stressors in children.

GRAPHICAL ABSTRACT



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ABSTRACT

Objective: The hypothalamic–pituitary–adrenal (HPA) axis is the main "gate-keeper" of the organism's response to every somatic or mental stress. This prospective study aims to investigate the HPA-axis response to a cellular phone call exposure after mental stress in healthy children and adolescents and to assess the possible predictive role of baseline endocrine markers to this response.
Subjects and methods: Two groups of healthy school-age children aged 11–14 (12.5 ± 1.5) years were included in the study, the one comprising those who are occasional users of a cellular phone (Group A) while the second those who do regularly use one (Group B). Blood samples were obtained from all participants at 8.00 am after a 12-hour overnight fasting for thyroid hormone, glucose, insulin, and cortisol levels determination. The participants performed the Trier Social Stress Test for Children (TSST-C) (5 min oral task followed by 5 min arithmetic task). Salivary cortisol samples were obtained at baseline, 10′ and 20′ min after the TSST-C and 10′ and 20′ after a 5 minute cellular phone call.
Results: Significant changes in the salivary cortisol levels were noted between 10′ and 20′mins after the cellular phone call with different responses between the two groups. Baseline thyroid hormone levels seem to predict the cortisol response to mental stress mainly in group A, while HOMA had no impact on salivary cortisol response at any phase of the test, in either group.

Abbreviations: HPA, hypothalamic–pituitary–adrenal axis; TSST-C, Trier Social Stress Test for Children; T4, thyroxine; T3, tri-iodothyronine; TSH, thyroid stimulating hormone; BMI, body mass index; Hs-CRP, high sensitivity C-reactive protein; ACTH, adrenocorticotropic hormone; HOMA, homeostasis model assessment.

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Conclusions: HPA axis response to cellular phone after mental stress in children and adolescents follow a different pattern in frequent users than in occasional users that seems to be influenced by the baseline thyroid hormone levels.

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1. Introduction

Environmental insults have repeatedly been reported to have a negative impact on public health. Children and adolescents grow nowadays in a different environment in comparison to their parents since electromagnetic field exposure is, nowadays, diffuse and inevitable. The electromagnetic exposure to "close to the body" sources include cellular phone usage which is a common part of daily life even among children.

Potential endocrine effects from this technology expansion in pediatric and adolescent populations is suggested by the European Health Risk Assessment Network on Electromagnetic Fields Exposure in its 2012 report (EHFRAN, 2012; Sadetzki et al., 2014): "These groups represent the first generation of Europeans to be exposed to diffuse EMF fields since conception and birth, thus, are expected to be more sensitive to these fields".

Certain research groups sought to find possible endocrine effects of 900 MHz radiation exposure (Bortkiewicz, 2001; Djeridane et al., 2008; Eskander et al., 2012; Koyu et al., 2005; Mortavazi et al., 2009). In fact, there is growing evidence that people and animals exposed to 900 MHz radiation present thyroid function and morphology alterations (Djeridane et al., 2008; Riccioni et al., 2004; Bergamaschi et al., 2004; Eskander et al., 2012; Hackney and Gulledge, 1994; Koyu et al., 2005; Shahryar et al., 2009). The effect of cellular phone use on fasting glucose is established in the literature (Meo and Al Rubeaan, 2013), while scarce data exist on insulin secretion or insulin resistance to cellular phone call response.

On the other hand, the hypothalamic–pituitary–adrenal (HPA) axis, which constitutes the stress response system of the organism, when activated, as documented by altered salivary or plasma cortisol levels, may affect several systemic responses including those of the nervous, cardiac and immune systems (Chrousos and Gold, 1992; Heim et al., 2000; Hench et al., 1950; Holsboer, 1989; Raison and Miller, 2003; Sternberg et al., 1992; Stratakis and Chrousos, 1995; Tsigos and Chrousos, 1994). Salivary cortisol constitutes a non invasive and sensitive stress biomarker (Aardal-Eriksson et al., 1998; Laudat et al., 1988; Safar Zadeh et al., 2005; Schmidt, 1998; Vining et al., 1983a, 1983b) that is repeatedly used in Trier Social Stress Test for Children (TSST-C) (Beetz et al., 2012; Pesonen et al., 2012; Sherzai et al., 2012). Trier Social Stress Test is a standardized experimental tool for stress assessment independent of individual's confounding factors such as personality, education, income, etc. (Buske-Kirschbaum et al., 1997; Gunnar et al., 2009; Kudielka and Wust, 2010). It consists of a brief preparation period (3 min) followed by a test period in which the subject has to deliver a free speech (5 min) and perform a mathematical task (5 min) in front of an audience. With this, the total exposure time adds up to no more than 13 min (Kudielka et al., 2007a, 2007b). As already reported, stress has repeatedly been demonstrated to trigger metabolic and systemic cascades affecting the function of the nervous, cardio-respiratory or immune system, while little is known concerning the impact of other hormones besides the HPA axis, namely of the thyroid hormones, on the HPA axis response to mental stress. On the other hand, little is known on the HPA axis response to cellular phone call after mental stress The aim of the current study was to investigate how HPA axis response changes over time in every day stimuli, in other words, the HPA response to cellular phone call exposure after mental stress in healthy children and adolescents (this generation is the first to be exposed since conception) as well as the possible predictive role of baseline endocrine and biochemical markers such as thyroid hormones levels, glucose and insulin levels to this HPA response.

2. Subjects and methods

2.1. Study population

Twenty eight healthy primary school graders and high school attendants aged 11–14 (12.5 ± 1.5 years), were recruited from schools from January 2011 to February 2011 for participation in the study. The exclusion criteria included the presence of an infection during the previous month, cardiac or other chronic disease, obesity or chronic medication. They were divided into two groups: those who do not possess and regularly use a cellular phone (occasional users) (n = 16) (Group A) and those who do possess and regularly use (n = 12) (Group B). The participants were asked to give more details about their behavior towards the cellular phone use irrespective of whether they possessed a cellular phone or not: a. Daily frequency of cellular phone use and b. Minutes of use per day.

The participants health status was confirmed by a careful clinical examination (including weight, height,) and personal history data collection including intrauterine life events. Venous blood sampling was then undertaken after an overnight fasting at 8.00 am for tri-iodothyronine (T3), thyroxin (T4), thyroid stimulating hormone (TSH), insulin and glucose determination. The insulin resistance was assessed by the calculation of the homeostasis model assessment-insulin resistance index according to the initial formula [HOMA-IR = insulin (expressed in mU/L) glucose (expressed in mg/dL) / 405] (Levy et al., 1998; Wallace et al., 2004). The study was conducted at the Biomedical Research Foundation of the Academy of Athens.

2.1.1. Ethical issues

The study protocol adhered to the Helsinki Guidelines of Good Clinical Practice and was approved by the Ethics Committee of "Aghia Sophia" Children's Hospital. Written informed consent was obtained from the parents/guardians of all participants before the children were enrolled in the study.

2.2. Methods

2.2.1. Mental stress: Trier Social Stress Test for Children

Details on the procedure are previously described by Buske-Kirschbaum et al. (1997), consisting of public speaking and mental arithmetic tasks in front of an audience with two modifications: the investigator was leaving the room during intervals as modified by Dedovic et al. (2005). b. The story details (but not the concept) were adapted to the Greek children's habits and temperament. Upon arrival in the laboratory, the participants rested in calm for 20 min. At time + 15 min the researcher re-entered the room asking the participant to introduce himself. The child was told that he/she should complete the following story as exciting and plausible as possible — better than all other children. "You have decided to make a Sunday trip to a forest with your friends. The sun was shinning and you climbed the mountain Taygetos (a mythical Greek mountain with dangerous itineraries and unexplored forests). In the afternoon just before you decided to return, clouds appeared in the sky, and soon afterwards, a tremendous rain began. The pathways disappeared under the unexpected rainfall and you

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