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The hypothalamic-pituitary-thyroid axis and personality in a sample of healthy subjects

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ABSTRACT

Thyroid hormones influence various brain pathologies, including psychiatric disorders. However, the relationship between these hormones and the psychological state in the normal, non-clinical population is poorly understood. We aimed to test whether serum levels of thyroid hormones are associated with personality in the healthy population. Thyrotropin (TSH), free T3 (FT4), total and free T4 (TT4 and FT4) concentrations were measured in the blood of 104 healthy participants (44% men) aged 18–59 (M = 35 ± 9). Personality traits were assessed using the revised short versions of the Temperament and Character Inventory (TCI-140) and the NEO Five-Factor Inventory (NEO-FFI). The data were analysed by correlational, regression, extreme groups and graphical techniques, which showed significant correlations between inter-individual variations in serum thyroid hormone levels and specific aspects of personality. In particular, high serum TSH was strongly associated with higher Persistence and Self-Directedness, and negatively correlated with Harm Avoidance on the TCI-140 and Neuroticism on the NEO-FFI, thus representing a more adaptive personality profile. Furthermore, increased FT4 was associated with lower Reward-Dependence, and increased TT4 was associated with lower Cooperativeness, representing a deficit in social attachment. Our data indicate that the relationship between thyroid hormones and personality in the healthy population might be rather more complex than the results obtained in clinical samples suggest.

1. Introduction

The study of the relationship between hormones and personality dates back to Antiquity, when Hippocrates and Galen proposed the first notions of humoral typologies based on the deficit or excess of body fluids. Today, according to Netter (2004), the hormones most frequently studied in relation to personality are the ones associated with the hypothalamo-pituitary-adrenal (HPA) axis such as cortisol, the ones in the gonadal-pituitary-adrenal (HPG) axis such as testosterone, and the ones in the adrenomedullary axis such as the catecholamines noradrenaline, adrenaline and dopamine. The most significant results of the study of HPA axis hormones and personality show a positive relationship between cortisol and Neuroticism (anxiety and depression), and a negative relationship with Novelty/Sensation seeking and Aggressiveness. For its part, testosterone has also been associated with Dominance, Aggressiveness and Novelty/sensation seeking. Likewise, higher levels of noradrenaline have been associated with Anger and Aggressiveness, while adrenaline levels are more related to Fear and serotonin levels to Anxiety (Gray, 1993). In contrast, the dopaminergic system has been fundamentally associated with Novelty/Sensation seeking, and the serotoninergic system with Harm Avoidance (Cloninger, 2000). In addition, the adrenomedullary axis (the catecholaminergic system) in interaction with the HPG axis has been considered as the regulatory mechanism of emotions, social behavior and clinical conditions (Zuckerman, 1997).

Thyroid hormones appear to be less studied in the relation to personality. However, there is a lot of background data. A variety of mechanisms of thyroid hormone uptake into brain tissues and hormone activation and their influences on neurotransmitter generation have been described (for a review, see Schroeder and Privalsky, 2014). Thyroid hormones are also involved in neurogenesis and neuron-astrocyte communication (Morte and Bernal, 2014; Préau et al., 2014; Sánchez-Huerta et al., 2016). Thyroid-stimulating hormone (TSH) serum level predicts response to selective serotonin reuptake inhibitors in depressive patients, suggesting a relationship between thyrotrophic hormone and serotoninergic system susceptibility (Gitlin et al., 2004).

TSH secretion is exerted by classical negative feedback loop, thus elevated TSH is believed to indicate low peripheral thyroid function. An

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association between hypothyroidism and depression has been long accepted by scientists and clinical specialists. Indeed, many studies suggest that the hypothalamic–pituitary–thyroid axis (HPTA) is involved in pathogenesis of psychiatric disorders, especially mood disorders such as depression (Hein and Jackson, 1990) and bipolar disorder (Sierra et al., 2014; Bauer et al., 2014). Hypothyroidism and depression share some symptoms (Jackson, 1998) and many patients with depression have abnormal thyroid hormone levels (Kirkegaard and Faber, 1998).

However, larger studies on the relationship of thyroid hormones and depression conducted over the last 15 years in normal populations, including studies with prospective and community approaches, have unexpectedly shown serum TSH to be inversely associated with anxiety and depression (Forman-Hoffman and Philibert, 2006; Williams et al., 2009; Medici et al., 2014). Furthermore, a negative correlation has been found between serum TSH and Neuroticism (Frey et al., 2007).

Regarding peripheral thyroid hormones, several studies (Roca et al., 1990; Sim et al., 2002; Steiblienė et al., 2012; Akiibinu et al., 2012) have reported elevated T4 in patients with cluster A personality disorders (e.g., Schizoid and Schizotypal). Stalenheim et al. (1998; cited by Sinai et al., 2009) found that elevated T3 levels were associated with psychopathy and antisocial disorder, whereas serum levels of FT4 were negatively related to these disorders. Sinai et al. (2009) also mention other studies (Arqué et al., 1987; Balada et al., 1992) suggesting a negative correlation between TSH and T4 with sensation seeking, and a positive correlation between T4 and scores on depression-anxiety scales in healthy females with no psychiatric history.

As can be seen from the above, despite the long history of investigation, the relationship between thyroid hormones and psychological and psychiatric functions is not clearly defined. Most of the studies in the area dealt with thyroid pathology or psychiatric illness. However, we believe that better and more fundamental understanding of the problem might be obtained by studying the role of HPTA in health, i.e. by investigating the role of thyroid hormones in normal regulation of psychological functions, such as personality, in subjects with no thyroid disease. In the present study we aimed to explore in detail whether personality dimensions in mentally healthy individuals might be related to physiological concentrations of serum thyroid hormones.

2. Methods

2.1. Participants

A total of 104 healthy volunteers (46 male, 58 female, aged 18–55 years, M35 ± 12) from the Moscow region in Russia were recruited for this study via a social network advertisement containing a brief description of the study, which was posted in the online communities of students at the biology and psychology faculties and on the personal webpages of researchers. The advertisement invited students and researchers to participate in the study and asked them to share the invitation with their peers. As an incentive to take part, prospective participants were told that they would be given information on their blood hormone levels and psychological measures. Before enrollment, participants completed an online medical history in order to assess the presence of any clinical syndrome (DSM, Axis I; American Psychiatric Association, 2013), medical condition or any thyroid or psychotropic drug intake, all of which were considered as exclusion criteria. After a complete description of the study to the subjects, written informed consent was obtained. The study was approved by the local ethics committee of the N.N. Burdenko Neurosurgical Institute.

Participants were asked not to come for blood sampling if they had slept poorly the night before, and not to drink alcohol in the preceding days before in order to mitigate the influence of these factors on thyroid hormone plasma levels (Ylikahri et al., 1980; Kessler et al., 2010). On the day of blood sampling, participants were asked to state when they had last drunk alcohol, how they had slept the previous night (recorded on a 1–5 Likert scale with «5» corresponding to «slept perfectly» and «1» «did not sleep at all») and how they felt at the present moment. Seven participants were excluded from the data analysis: one who reported feeling unwell, four who had drunk alcohol the day before, and two who had slept very poorly or not at all the previous night.

2.2. Psychological measures

Two models for assessing personality were used: the NEO Five Factor Inventory (NEO-FFI; Costa and McCrae, 1992) and the short version (TCI-140) of the revised Cloninger's Temperament and Character Inventory (Cloninger, 1999). The NEO-FFI is based on a lexical analysis of trait adjectives and the TCI-140 is based on a psychobiological model that accounts for individual differences in personality traits by integrating neurochemical systems, learning, and social influences. Personality measures from these models correlate to problem behaviors and psychiatric diagnoses. Personality dimensions assessed with both the NEO-FFI and the TCI-R demonstrate broad-sense heritability in excess of 30% (Johnson et al., 2008).

All participants completed the short version of the revised 5-point Likert scale version of TCI-140, which allows valid personality assessment over four dimensions of temperament (NS: Novelty Seeking, HA: Harm Avoidance, RD: Reward Dependence, PS: Persistence) and three dimensions of character (SD: Self-Directedness, C: Cooperativeness, ST: Self-Transcendence). The NEO-FFI was performed in 71 subjects (70%). The participants completed the short 60-item version of the NEO-FFI, which allows reliable and valid assessment of personality along the dimensions Neuroticism (N), Extraversion (E), Openness to experiences (O), Agreeableness (A), and Conscientiousness (C) (Kudryashev, 1992; Baturina and Aidman, 2010). If not indicated as a raw score, each dimensional score is presented as a T-score with a mean of 50 and a standard deviation of 10. Table 1 shows descriptive statistics and reliability data for TCI-140, and Table 2 shows descriptive statistics for NEO-FFI. Since we used a commercial version of the questionnaire that does not provide scoring keys or raw items data, we were unable to calculate Cronbach's alphas and so reliability data on NEO-FFI are not presented here.

2.3. Thyroid hormone measurements

All analyses were performed in accordance with accredited routines at the Laboratory for Clinical Biochemistry of the Burdenko Neurosurgical Institute. Blood was collected in the morning between 8:00 a.m. and 10:30 a.m. after an overnight fast using separating gel tubes. Serum was separated by centrifugation at 3000*g* for 15 min. The levels of thyrotropin (TSH), total and free thyroxin (TT4 and FT4) and free triiodothyronine (FT3) were determined using automated chemiluminescence immunoassay ("Immulite2000", Siemens, USA).

2.4. Statistical analysis

We used correlations, extreme groups, graphical and regression techniques to investigate the relationships between serum thyroid hormones and personality traits. Each type of analysis complemented

Table 1
TCI-140 descriptive statistics and alpha internal consistency.

	Mean	SD	S	K	alpha
Novelty Seeking	62.3	9.08	0.19	0.16	0.71
Harm Avoidance	55.2	12.7	0.13	−0.47	0.87
Reward Dependence	62.3	10.9	−0.24	0.25	0.81
Persistence	68.1	10.0	0.08	0.72	0.84
Self-Directedness	65.7	10.4	−0.55	0.44	0.80
Cooperativeness	72.3	11.2	−0.70	0.34	0.84
Self-Transcendence	46.7	8.2	−0.22	0.04	0.71

K − kurtosis, S − skewness, n = 104.