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Relationship between rapheal echogenicity and personality as possible markers of a disposition to develop depressive and anxiety disorders

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ABSTRACT

Early diagnosis of anxiety and depression may be facilitated by the use of neurobiological markers. In depression and panic disorder, transcranial sonography (TCS) has revealed decreased echogenicity of the brainstem raphe (BR). The aim of the present study was to detect whether decreased echogenicity of the BR correlates with personality features described in the five-dimension model, especially neuroticism. We examined 100 healthy volunteers using quantitative and qualitative TCS, the five-dimension revised NEO Personality Inventory, Beck´s scales of anxiety and depression, and the Social Re-adjustment Rating Scale (SRRS). Visual BR anechogenicity was found in 11 subjects, BR hypoechogenicity in 29 subjects, and normal BR echogenicity in 60 subjects. The visual assessment correlated with the digital assessment. Comparing the groups with visual BR anechogenicity and BR normoechogenicity, only increased SRRS score and increased agreeableness z-score were significant. Our hypothesis that BR hypoechogenicity reflects an inclination for depression and anxiety characterized by the personality dimension neuroticism was not supported. However, this disposition may be present in a different state, such as stress.

1. Introduction

Mood disorders and anxiety disorders classified according to the ICD-10 (World Health Organization, 1992) are the two most frequent categories of mental disorders. The 12-month prevalence of anxiety disorders in Europe is estimated to be 14% and the prevalence of depressive disorder in the same region 6.9%. Both groups of mental disorders have negative economic consequences apart from serious health problems and decreased quality of life for patients (Wittchen et al., 2011). From this point of view, an early diagnosis of anxiety and depression is important. A modern trend is to use neurobiological markers of disease, which broadens the descriptive diagnostics of subjective symptoms with objective criteria (Singh and Rose, 2009).

Transcranial brain sonography in the B-mode (TCS) is a novel imaging method applied mostly in neurology. This procedure was developed over the last 20 years and has offered important assistance, especially in the diagnosis of Parkinson´s disease (PD) and other movement disorders (Walter and Školoudík, 2014). TCS has also been used in the field of mental disorders, where it focused mostly on mesencephalic brainstem raphe (BR) echogenicity. The rapheal zone of the examined area consists of the raphe nuclei (RN) and a group of ascendant and descendent neural projections connecting the brainstem and cerebellar nuclei with subcortical and cortical areas (Becker et al., 2001). RN are the major source of serotonin innervation in the mammalian brain (Azmitia and Segal, 1978). Serotonin is an important neurotransmitter in the pathogenesis of depressive disorder (Coppen, 1967) and anxiety disorders (Kahn et al., 1988).

TCS has repeatedly revealed decreased or extinct BR echogenicity in 37–65% of depressed patients (Becker et al., 1994, 1995; Budisic et al., 2010; Ghourchian et al., 2014; Hoeppner et al., 2009; Walter et al.,

Abbreviations: BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BR, brainstem raphe; DICOM, Digital Imaging and Communications in Medicine; EI, Echogenicity Index; NEO-PI-R, revised NEO Personality Inventory; PD, Parkinson´s disease; RN, raphe nuclei; ROI, region of interest; SRRS, Social Re-adjustment Rating Scale; TCS, transcranial sonography

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2007), with a few exceptions (Steele et al., 2005). BR hypoechogenicity has been reported in patients with panic disorder (Šilhán et al., 2015), as well as a trend of BR hypoechogenicity in obsessive-compulsive disorder (Mavrogiorgou et al., 2013). Most of these studies did not discover an association between rapheal hypoechogenicity and the seriousness or course of the disorder, so the sonographic findings were interpreted as a marker of vulnerability (Budisic et al., 2010; Krogias et al., 2011; Mijajlovic, 2010; Walter et al., 2007).

The patient´s personality is an important factor that may predispose them to depression. Personality can be assessed using the five-factor model developed by Costa and McCrae (1992), the revised NEO Personality Inventory (NEO-PI-R). This model covers the items neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. A recent meta-analysis detected an association between depressive disorder and increased neuroticism, decreased extraversion, and decreased conscientiousness. This personality profile is also associated with a prospective depressive disorder (Hakulinen et al., 2015). Similar personality features were reported in another meta-analysis of depressive and anxiety disorders (Kotov et al., 2010).

The aim of the present study was to ascertain whether decreased BR echogenicity, which is usually found in 10–20% of healthy volunteers (range 0–35.7%) (Becker et al., 1994, 1995; Budisic et al., 2010; Ghourchian et al., 2014; Hoeppner et al., 2009; Steele et al., 2005; Walter et al., 2007), as a potential trait marker of depressive and anxiety disorders, is associated with personality features that possibly predispose an individual to depression and anxiety according to the NEO-PI-R, especially neuroticism.

2. Methods

2.1. Subjects

Students of medical science and non-medical subjects at the University of Ostrava School of Medicine voluntarily participated in this study. The subjects were examined at the Laboratory of Neurosonology at University Hospital Ostrava between January 2014 and June 2015. The inclusion criteria were age 18–65 years and written informed consent. The exclusion criteria were any mental or neurological disorder or use of psychotropic medication any time during the potential subject's lifetime as assessed by an anamnestic questionnaire. Participation in the study was not remunerated, but interested subjects were informed of their study results with professional advice.

2.2. Applied assessment scales

The study subjects filled in the self-reported Beck Depression Inventory (BDI) (Beck et al., 1961), Beck Anxiety Inventory (BAI) (Beck et al., 1974), and Social Re-adjustment Rating Scale (SRRS) (Holmes and Rahe, 1967) to assess the extent of major stressful life events. Personality was evaluated using the five-factor model based on the Czech version of the 240-item NEO-PI-R questionnaire (Costa and McCrae, 1992; Hřebíčková, 2004). All participants also completed a basic anamnestic questionnaire about their personal data, demographic data, health status, regular medication, and trouble-free childhood (yes or no).

2.3. Transcranial sonography

Transcranial sonography was performed using the Esaote MyLab Twice ultrasound machine (Esaote S.p.A., Genova, Italy) with a 2.5-MHz phased-array transducer (PA240). Brainstem structures were examined through both the right and left temporal bone window using the following parameters: a penetration depth of 16 cm, penetration high, dynamic range 7 (50 dB), frequency 1–4 MHz, enhancement 3, density 2, view 9, persistence 7, dynamic compression 0, gain 36%, gray map 0, S view off, 2 focuses at 5 and 10 cm, mechanical index 0.9, tissue index (TI) 1.0, TIB 1.0, and TIC 2.1. The butterfly-shaped structure of the mesencephalic brainstem and BR region were depicted as clearly as possible from the transversal plane. Videos and images of the BR were acquired in the standard transverse planes, saved in avi and Digital Imaging and Communications in Medicine (DICOM) format, and subsequently encoded. Personal data and examination times were deleted and all acquired images encoded as anonymized data using a unique key before manual measurement or digital analysis. Subjects with an insufficient temporal bone window were excluded from the analysis.

Examinations were performed by an experienced sonographer (DŠ) with 20-year TCS experience. The visual evaluation of BR was performed by two experienced sonographers (DŠ and MJ) by consensus. A 3-grade scale was used for visual evaluation of the BR: 1 = non-visible BR (BR1), 2 = disrupted BR line (BR2), 3 = normal echogenic BR (BR3). Digitized image analyses with an assessment of the Echogenicity Index (EI) of the BR were performed using the B-Mode Assist System (Blahuta et al., 2014). For all subsequent steps of the digital analysis and measurements, images were converted to 8-bit grayscale. The designed algorithm allowed region of interest (ROI)-based processing of grayscale images with intensities (I) of 0–255 and computation of the area inside the specific elliptical ROIs (28 mm^2 for BR). A predefined ROI was manually placed in the echogenic region. For statistical purposes, the greater of two BR measurements was used for the analysis.

Neurosonological examination and assessment scales were always performed the same day in every participant.

2.4. Statistical analysis

The necessary number of subjects to be examined was determined to be 111, which reflects the demand of the sample size using the one-factor ANOVA with three groups at a power of 0.8, significance level of 0.05, and Cohen´s d effect size of 0.3. Statistical assessments were performed using IBM SPSS software, version 22 (IBM Corporation, USA). Continuous variables are described as mean ± standard deviation. Normal distribution was verified by the Shapiro-Wilk test. Individual scores were compared between genders using the Mann-Whitney test and among visually set groups in the case of data normality using the t-test with Bonferroni correction ($p < 0.025$) considering the BR3 group as a control. The differences among groups with different BR echogenicity among variables with a non-normal distribution were analyzed by the Kruskal-Wallis test. Categorical variables were compared by the χ^2 test or Fisher´s exact test if necessary. The correlation analysis was performed using Pearson´s (r) and Spearman´s (rs) correlation coefficients.

2.5. Ethical issues

The study was approved by the ethics committee of University Hospital Ostrava. The work was carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) and good clinical research practice as postulated by the European Agency for the Evaluation of Medicinal Products in 2002. Informed consent was obtained from every participant in the study.

3. Results

A total of 111 subjects were examined, but 11 were excluded (8 mental or neurological disorder or use of psychotropic medication; 2 temporal window inaccessibility; 1 non-compliance in completing the questionnaires). Thus, 100 subjects completed the study (18 males, 82 women). The average age of the participants was 25.7 ± 7.1 years (males 25.4 ± 6.3 years, women 25.8 ± 7.2 years). The quantitative results from the whole study sample are presented in Table 1, and the quantitative and qualitative results of the visual BR assessment are presented in Table 2.