



Thyroid hormones and adult interpersonal violence among women with borderline personality disorder



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ABSTRACT

Elevated T3 levels have been reported in men with antisocial behavior. The aim of the present study was to investigate the relationship between thyroid hormones and expressed adult interpersonal violence in female patients with borderline personality disorder (BPD). Furthermore, expressed adult interpersonal violence in female BPD patients was compared to healthy female controls. A total of 92 clinically euthyroid women with BPD and 57 healthy women were assessed with the Karolinska Interpersonal Violence Scales (KIVS). Baseline thyroid function was evaluated by measuring plasma free and bound triiodothyronine (FT3 and T3), thyroxine (FT4 and T4), and thyroid-stimulating hormone (TSH) with immunoassays in patients. Plasma cortisol was also measured. Among females with BPD, expressed interpersonal violence as an adult showed a significant positive correlation with the T3 levels. The mean expression of interpersonal violence as an adult was significantly higher in BPD patients as compared to healthy controls. The multiple regression model indicated that two independent predictors of KIVS expressed interpersonal violence as an adult: T3 and comorbid diagnosis of alcohol abuse. Association between T3 levels and violent/aggressive behavior earlier reported exclusively in male samples may be valid also in females with BPD.

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1. Introduction

The risk of violent behavior is elevated in both individuals with personality disorders (Berman et al., 1998; Johnson et al., 2000; Coid et al., 2006) as well as in the context of hazardous drinking. Borderline personality disorder (BPD) has been associated with violent acts (Fountoulakis et al., 2008), especially if combined with antisocial personality disorder (Howard et al., 2008; Látalová and Praško, 2010), even though the association may not be that evident in all groups of BPD patients (Allen and Links, 2012). Impulsive aggression, a heritable trait (Olweus, 1979; Coccaro et al., 1993), is a core feature of “cluster B” personality disorders, particularly antisocial personality disorders as well as BPD.

Thyroid hormones, in relation to violent behavior, have been studied mostly in male forensic settings. Elevated mean T3 levels have been reported in young criminally active and institutionalized male recidivists, as compared to non-delinquent controls,

although the two groups did not differ in TSH levels (Levander et al., 1987). In line with that finding, young men with persistent criminal behavior had higher mean T3 levels, as compared to both men with previous but no current antisocial behaviors and controls (Alm et al., 1996). In addition, Stålenheim (2004) found positive associations between T3 levels and Psychopathic Check List scores of Detachment and Irritability, in a group of violent male criminal recidivists. Suicidal and violent behaviors are interlinked and may share common neurobiological underpinnings. We have reported that high scores on aggressiveness were associated with a low T3/T4 ratio in male suicide attempters (Sinai et al., 2009). Stress reactions have also been associated with the thyroid function (Kioukia-Fougia et al., 2002), and basal hypothalamic pituitary adrenal (HPA) axis activity has been reported to be negatively related to provoked aggressive behavior (Böhnke et al., 2010).

No prior study has assessed the association between thyroid hormones and expressed interpersonal violence in women. Studies in the general population have reported that men are more violent than women, but this has not been found to be the case among psychiatric inpatients (Krakowski and Czobor, 2004).

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The aim of the present study was to assess the relationship between thyroid hormones and expressed adult interpersonal violence in female patients with borderline personality disorder. Furthermore, we compared expressed adult interpersonal violence in female BPD patients with violence scores of female healthy volunteers. It is not known if the same kind of association between thyroid hormones and violent behavior, earlier reported in anti-social male populations, could be found in women with BPD and severe suicidal behavior. We hypothesized higher scores of expressed interpersonal violence in individuals with BPD, and that thyroid hormones and comorbid substance abuse would be associated with adult violent behavior in patients with BPD.

2. Methods

2.1. Study setting

The participants were recruited between 1999 and 2004 for a clinical psychotherapy trial: "Stockholm county council and Karolinska Institute Psychotherapy project for suicide-prone women" (SKIP). The SKIP project is a randomized controlled trial, comparing the efficacies of two forms of psychotherapy, and general psychiatric care (treatment as usual). Inclusion criteria were BPD diagnosis according to DSM-IV, a history of at least two suicide attempts (defined as a self-destructive act with some degree of intent to die), a fair capacity to communicate verbally and in writing in the Swedish language, and age between 18 and 50 years. Exclusion criteria were schizophrenia spectrum psychosis, melancholia, mental retardation, drug abuse and severe anorexia. The Regional Ethical Review Board in Stockholm approved the study protocol (Dnr. 95–283) and the participants gave their written informed consent to the study.

2.2. Participants

2.2.1. Patients

A total of 162 women with BPD were invited to take part in the SKIP project. Of these individuals, 14 declined to join the study, 41 were excluded due to not fulfilling inclusion criteria or to fulfilling exclusion criteria and one completed suicide before joining the study. Thus, out of 162 women, 106 (65%) took part in the SKIP study. The mean age of the patients was 29.5 years (S.D.=7.6; range 19–50). We obtained laboratory data for 97 of 106 individuals. 92 patients were euthyroid (TSH reference range: 0.4–3.5 mE/l, Karolinska University Hospital) and thus included in the statistical analyses. The study population has recently been described in more detail (Sinai et al., 2014). This SKIP-cohort is practically independent (except two patients who also participated in an earlier study; Sinai et al., 2009), and not overlapping with other clinical studies on suicide attempters. All self-rating scales were completed under the supervision of a research nurse. The participants were interviewed by a trained psychiatrist, using the SCID I research version interview to establish the DSM-IV diagnoses (First et al., 1997). Trained clinical psychologists established Axis II diagnoses by DIP-I-interviews (Ottosson et al., 1995). Ninety (98%) of the participants had at least one current Axis I psychiatric diagnosis. Among the Axis I diagnoses, 78 (85%) of the patients met the criteria for mood disorders (unipolar major depressive disorder, single episode or recurrent, bipolar disorder, depressed or dysthymic disorder), 76 (83%) for anxiety disorders. Fifty-two (57%) patients met the criteria of posttraumatic stress disorder (PTSD). Twenty-four (26%) had a comorbid eating disorder; of whom 16 (17%) with bulimia and 8 (9%) with anorexia nervosa. Eight women (9%) had a diagnosis of alcohol abuse. Fifty women had an additional personality disorder (PD); avoidant PD ($n=24$), paranoid PD ($n=15$), obsessive-compulsive PD ($n=12$), histrionic PD ($n=10$), dependent PD ($n=9$), narcissistic PD ($n=4$). Twenty-two (24%) women had three or more personality disorders. The criteria for conduct disorder were met in seven of the women. Medication records were obtained for 68 (74%) of the patients, of whom seven patients were medication free. Three patients were treated with lithium. The most frequent medications were venlafaxine ($n=12$), fluoxetine ($n=11$), sertraline ($n=9$) and citalopram ($n=4$). Two patients had a combination of two antidepressants. In the medical records, there were no prescriptions of thyroid supplementation, anti-arrhythmic medications or opioids.

2.2.2. Healthy controls

Fifty-seven healthy women were recruited for another study (Jokinen et al., 2010). They were screened by a psychiatrist to verify the absence of current mental disorder. The mean age for healthy volunteers was 39.4 years (S.D.=10.7; range, 18–54).

2.3. Neuroendocrine testing

Baseline thyroid function was evaluated by measuring plasma free and bound T3, T4 and TSH levels. Venous blood was drawn and immediately frozen in aliquots

at -70°C or below until analyzed. The samples were thawed and analyzed by immunoassays (Unicel Dxl 800 Beckman Coulter, for FT4, FT3 and TSH and AutoDelfia, for T4 and T3) in the year 2010. No prior thawing of the frozen plasma samples had been performed. The Karolinska University Laboratory in Solna, Stockholm, performed all analyses according to accredited routines. The reference range for TSH was: 0.4–3.5 (mE/l) and for T3 1.1–2.5 (nmol/l), Karolinska University Hospital. The intra-assay coefficient of variation (CV) for TSH was 3.85–5.56%, for FT4 2.74–4.4%, for FT3 5.1–6.6%, for T4 2.7–3.6% and for T3 2.9–3.1%. The interassay CV for TSH was 3.02–3.68%, for FT4 3.34–8.08%, for FT3 1.3–8%, for T4 1.4–2.2% and for T3 1.2–2.1%. Analytical interferences in thyroid hormone testing are estimated to occur in less than 0.1%, at the Karolinska University Laboratory. Cortisol CV was within the range 43 (15%)–690 (6%) nmol/l, analyzed by Modular Analytics 170, Roche Diagnostics, Switzerland. Pre-analytical variation was minimized by performing the venipuncture in a standardized manner for all participants, of which a great majority was sampled at noon.

2.4. Assessments of adult used interpersonal violence

The Karolinska Interpersonal Violence Scale (KIVS) (Jokinen et al., 2010) contains four subscales with direct questions with concrete examples of exposure to violence and expressed violent behavior in childhood (between 6 and 14 years of age) and during adult life (15 years or older). The ratings (0–5 for each subscale, in total maximum of 20) were completed by the interviewing trained psychiatrist during a structured interview, to gather a comprehensive lifetime trauma and victimization history, as well as history of lifetime expressed violent behavior. The KIVS scale has been validated against several other rating scales measuring aggression and acts of violence and the inter-rater reliability of the KIVS subscales was high ($r > 0.9$) (Jokinen et al., 2010). The KIVS-subscale used adult interpersonal violence, is shown in Table 1.

2.5. Statistical analysis

Group differences in expressed adult interpersonal violence were analyzed with the Mann–Whitney U test. Correlation analyses (Spearman's rho, two tailed test) were used to determine associations between the clinical ratings and the biological variables. The significance of association between the categorical variables comorbid alcohol diagnosis (current and/or remitted versus no lifetime alcohol diagnosis) and diagnosis of PTSD was tested with a χ^2 test. Based on the results of the bivariate analyses, the association between T3 and expressed interpersonal violence among patients was analyzed with multiple regression analysis, adjusted for age, cortisol, sample storage time, and comorbid alcohol diagnosis. The selected covariates showed significant correlations with either T3 levels (age, cortisol, sample storage time) or with expressed interpersonal violence (comorbid alcohol diagnosis).

The residual scatterplots were examined to check the assumptions of normality, linearity and homoscedasticity between the predicted dependent variable scores and errors of predictions, and the assumptions were deemed to be satisfied. Furthermore, the Durbin–Watson test statistic expressed no correlation in adjacent residuals. The alpha level was set on $p < 0.05$. Missing data was handled by pairwise exclusion in the statistical analyses, in order to preserve degrees of freedom. The statistical analysis was performed using the SPSS statistical software package (IBM, SPSS™, version 22).

3. Results

3.1. Clinical assessments

KIVS ratings for adult expression of interpersonal violence were available from 91 euthyroid participants with BPD and 57 healthy controls. The mean expression of interpersonal violence as an adult was significantly higher in BPD patients (mean=1.3, S. D.=1.3, median=1, range 0–4), as compared to healthy controls (mean=0.4, S.D.=0.8, median=0, range 0–3), $p=0.001$. None of the patients or the controls did score the highest level (KIVS score: 5) of expressed adult interpersonal violence. Among patients 23% reported score 3 or 4, in contrast to the controls, among whom only 2% scored on the same rating levels. KIVS ratings of expressed adult interpersonal violence in patients and healthy controls are depicted in Fig. 1. Since the patients were significantly younger than the controls ($t_{(d.f.=90,8)}=6.6$, $p=0.0001$), the correlations between age and the KIVS ratings of expressed violence as an adult were analyzed and found to be non-significant in both patients ($p=0.23$) and healthy controls ($p=0.89$). The mean total score of KIVS among the patients was 7.3 (S.D.=3.8, median=7,

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