

Letter to the Editor

The association between overcommitment to work and depressive symptoms is moderated by the polymorphic region of the 5-HTT gene

To the Editors:

Overcommitment (OC) to work is a prevalent personality trait characterized by the inability to withdraw from obligations combined with a high need for control and approval. Over committed individuals are extremely ambitious and tend to repeatedly exaggerate their efforts while at the same time over taxing their resources (Siegrist et al., 2004). Epidemiological studies in apparently healthy employees suggest that OC is associated with depressive symptoms, most likely in a prospective way (e.g. Niedhammer et al., 2004).

Genetic polymorphisms at the serotonin transporter locus have been associated with alterations in brain serotonin turnover in major depressive disorder (MDD). MDD patients carrying the short (s) allele of the 5-HTTLPR showed increased brain serotonin turnover compared to those carrying the long (l) allele at this locus (Barton et al., 2008). Brain serotonin turnover was normalized following medication therapy using selective serotonin reuptake inhibitors (SSRI) accompanied by improvement in depression symptoms (Barton et al., 2008). We investigated whether OC is differentially associated with depressive symptom severity in subjects characterized for 5-HTTLPR gene polymorphisms in a sample including MDD

patients. We hypothesized that the HTTLPR genotype moderates the level of OC and depressive symptom severity in individuals with and without clinical depression.

We recruited 115 consecutively admitted inpatients with recurrent unipolar depression (DSM IV) aged 18–60 years from the Psychiatry Department of the Bonn University and 178 age and gender matched healthy volunteers without psychopathological symptoms from the general population living in the same region. OC was assessed by a uni-dimensional scale composed of six Likert scaled items for which respondents indicated to what extent they personally agreed or disagreed with the given statements on a four-point rating scale ranging from 6 to 24 with higher scores reflecting higher OC (Siegrist et al., 2004). *Depressive symptom severity* was assessed with the 21-item Beck Depression Inventory (BDI) where scores ≥ 10 indicate possible clinical depression. *Effort-Reward imbalance* (ERI) assesses stressful experience at work by means of a 17-item questionnaire consisting of two scales measuring a ratio between perceived efforts and experienced or anticipated rewards (Siegrist et al., 2004). All of the questionnaires have been widely used and showed good internal consistency and validity. We assessed the length polymorphism in the promoter region of the serotonin gene (5-HTTLPR) and the single nucleotide polymorphism rs25531 and reclassified the obtained genotypes into a biallelic model by their supposed level of expression as follows: $L_G/S_{A/G}$, L_G/L_G , and $S_{A/G}/S_{A/G}$ were reclassified as $S'S'$ (lower expression), $L_A/S_{A/G}$ and L_A/L_G

Table 1

Sociodemographic, medical, and psychological characteristics of the study subjects according to their 5-HTTLPR gene polymorphisms.

| | $S'S'$ ^a mean | S.D. | Range | % | Non- $S'S'$ ^a mean | S.D. | Range | % |
|--|--------------------------|------|-----------|------|-------------------------------|------|-----------|------|
| Participants (N) ^b | 75 | | | 25.6 | 218 | | | 74.4 |
| Age (years) | 40.8 | 12.4 | 20–71 | | 40.2 | 11.1 | 20–78 | |
| Gender (men) | 29 | | | 38.7 | 94 | | | 43.1 |
| Overcommitment (OC score) | 14.85 | 4.7 | 6–24 | | 14.79 | 5.2 | 6–24 | |
| Major depression (N) ^b | 24 | | | 32.0 | 91 | | | 41.7 |
| Depression symptoms (BDI score) ^c | 10.49 | 12.9 | 0–41 | | 12.85 | 12.6 | 0–52 | |
| Medication intake | | | | | | | | |
| No medication (N) ^b | 51 | | | 68.0 | 127 | | | 58.3 |
| Remergil (N) ^b | 2 | | | 2.7 | 8 | | | 3.7 |
| Cipramil (N) ^b | 19 | | | 25.3 | 62 | | | 28.4 |
| Noritren (N) ^b | 3 | | | 4.0 | 21 | | | 9.6 |
| Work stress (ERI score) ^d | 0.58 | 0.32 | 0.20–2.01 | | 0.61 | 0.35 | 0.20–2.56 | |
| High school degree (N) ^b | 33 | | | 44.0 | 100 | | | 45.9 |
| Full- or part-time job (N) ^b | 55 | | | 73.3 | 165 | | | 75.7 |
| Weekly work time (hours) | 39.4 | 13.0 | 5–90 | | 38.7 | 12.8 | 1.5–80 | |

Data are presented as mean with standard deviation and range or percentage value.

^a Biallelic reclassification of 5-HTTLPR and rs25531 polymorphisms. $S'S'$ indicates homozygote individuals for presumably lower expressing alleles, non- $S'S'$ indicates individuals for presumably higher expressing alleles (i.e. $L'L$ as homozygote individuals for presumably higher expressing alleles, and $S'L'$ as heterozygous individuals).

^b N, number of subjects.

^c Beck Depression Inventory.

^d Effort–Reward–Imbalance.

were reclassified as L/S', and L_A/L_A was reclassified as L'L' (higher expression) (Parsey et al., 2006). No deviation of Hardy Weinberg equilibrium was observed for any of the groups. We merged the L/S' and L'L' groups into one single group (non S'S', 218 subjects) with probable higher expression levels of the serotonin transporter, leaving 75 subjects for the S'S' group with probable lower expression levels of the serotonin transporter. Statistical analyses of our secondary data analysis were performed using SPSS 19.0.

Subject characteristics are presented in Table 1. OC was significantly associated with higher BDI scores ($\beta=0.46$, $p<0.001$; $R^2=0.21$) even after controlling for age, gender, HTTLPR gene polymorphism group, and work stress (ERI score) ($\beta=0.41$, $p<0.001$; R^2 change=0.11, $R^2=0.28$). This association was confirmed for medication free subjects only ($N=176$), with and without covariates ($p's<0.001$). Moderation testing revealed a differential association between OC and depressive symptoms in subjects with and without S'S' genotype (age, gender, and work stress were controlled): the interaction of OC and S'S' genotype significantly predicted BDI scores while simultaneously controlling for main effects of OC, and S'S' genotype ($\beta=0.36$, $p=0.031$; R^2 change=0.01, $R^2=0.30$). In subjects with S'S' genotype higher OC was associated with higher BDI scores ($\beta=0.48$, $p<0.001$; R^2 change=0.18, $R^2=0.42$). Similar but weaker associations could be observed in subjects without S'S' genotype ($\beta=0.41$, $p<0.001$; R^2 change=0.10, $R^2=0.24$). Restricting to medication free subjects (S'S': $N=51$, non S'S': $N=125$) did not significantly change results ($p's<0.03$).

Our findings suggest a role for OC in increasing depressive symptom severity in MDD patients and controls, especially in subjects with short 5-HTT alleles. The personality trait OC thus seems to be a stronger predictor and thereby risk factor for an increase in depression symptom severity particularly in subjects with short 5-HTT alleles. Underlying mechanisms may involve OC promoted exhaustion and related inflammation that may alter serotonin synthesis (Dantzer et al., 2008) and serotonin turnover leading to a more rapid depletion of neurotransmitter stores in S'S' subjects (Barton et al., 2008). Interestingly, OC scores did not differ between polymorphism groups. Limitations of our study include cross sectional data assessment, the assessment of depressive symptom severity by a self report measure, the composition and size of our study sample, and failure to assess and control for other potential confounders (e.g., alcohol use, smoking).

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