The effect of acute tryptophan depletion on performance and the BOLD response during a Stroop task in healthy first-degree relatives of patients with unipolar depression

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Previous research has shown that low central serotonin, induced by acute tryptophan depletion (ATD), results in depressed mood and impairs cognition in healthy volunteers with a predisposition for depression. It remains unknown whether ATD affects emotional processing via mood changes or directly. In the present study we investigated the interaction between vulnerability for depression and the effect of ATD on mood, cognition and the associated brain activation. In a previous functional MRI study, we tested the effect of ATD during a combined cognitive and emotional Stroop task in healthy women without a family history of depression (FH−). In this study, we present the data of an additional group of 12 healthy women with a positive family history of unipolar depression (FH+). The effect of ATD on mood and Stroop performance was different for the FH+ group as compared with the FH− group. Scores on the depression sub-scale of the Profile of Mood States (POMS) did not correlate with performance changes, but did correlate with the anterior cingulate cortex response during Stroop interference. This study showed that a family history of unipolar depression interacts with the effect of ATD.

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1. Introduction

Major depression, a disorder characterized by depressed mood and cognitive dysfunction, has been associated with disturbed serotoninergic functioning (Risch and Nemeroff, 1992). To gain more insight into the etiology and symptoms of depression, acute tryptophan depletion (ATD), a model for reduced central serotonin (e.g. Hood et al., 2005), has been used (e.g. Neumeister, 2003; Salomon et al., 1993; Van der Does, 2001). ATD is a well-established method to temporarily lower central serotonin (5-HT) (Nishizawa et al., 1997; Williams et al., 1999; Young et al., 1999), in line with the cognitive disturbances found in depressed patients, ATD impaired memory consolidation (Riedel et al., 1999; Schmitt et al., 2000) and cognitive flexibility (Park et al., 1994; Rogers et al., 1999) in healthy volunteers. In addition, ATD has been used to study individual vulnerability of the 5-HT system (e.g. Jans et al., 2006; Booij et al., 2005a; Walderhaug et al., 2007). Previous studies showed that risk factors for developing depression (e.g. the serotonin transporter (5-HTTPR) short allele polymorphism, previous depressive episodes, being female, a positive family history of affective disorder) are associated with a depressed mood after ATD (Benkelfat et al., 1994; Booij et al., 2002; Ellenbogen et al., 1996; Klaassen et al., 1999; Neumeister et al., 2002; Riedel et al., 2002, 2003). Participants without a susceptibility to depression do not show a depressed mood after ATD (for review see Van der Does, 2001). Only a few studies have investigated the association between depressed mood induced by ATD and emotional processing (Booij et al., 2005b; Munafo et al., 2006; Merens et al., 2008). Booij et al. (2005b) showed that ATD induced a depressed mood and impaired the processing of positive words on an emotional Stroop task in remitted depressed patients. Merens et al. (2008) showed that a mood response in remitted depressed patients after ATD tended to increase accuracy of sadness recognition. Furthermore, Munafo et al. (2006) showed that ATD induced a depressed mood and increased interference from social threat words in recovered depressed patients on medication during an emotional Stroop task. It remains unclear, however, whether individual changes in depressed mood after ATD are related to individual changes in emotional processing. To gain more insight into the association between a transient lowering of
central 5-HT, mood and emotional processing we examined the effect of ATD on healthy women with a first-degree family member who has been diagnosed with unipolar depression (FH+). During a combined cognitive and emotional Stroop task. These data were statistically compared with published data from healthy women without such family history (FH−; Evers et al., 2006). A major strength of this study is that by studying unaffected relatives we are able to study vulnerability markers without the confounding influence of symptoms related to the illness.

Previous ATD studies showed inconsistent effects of ATD on Stroop performance in healthy volunteers. Some previous studies showed that ATD improved (Coull et al., 1995; Rowley et al., 1997; Rosse et al., 1992; Scholes et al., 2007), whereas other studies showed that ATD did not change Stroop performance (Gallagher et al., 2003; Horacek et al., 2005; Sobczak et al., 2002). Also neuroimaging studies are inconclusive. In an event-related fMRI study, Horacek et al. (2005) showed that ATD increased the activation in the bilateral medialfrontal cortex, anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex during Stroop interference without affected performance. In an earlier report about the FH− data (Evers et al., 2006), we showed that ATD decreased the interference score and increased the activation in the anterior cingulate cortex (ACC) during Stroop interference in the first Stroop block. Factors like a susceptibility to depression may influence not only the effect of ATD on mood, but also the effect of ATD on Stroop performance and brain activation.

In this study we tested the following hypotheses: 1) ATD triggers depressed mood in FH+ but not in FH− participants, 2) ATD affects Stroop performance and the associated brain activation patterns differently in FH+ and FH− participants, and 3) depressed mood is associated with the effect of ATD on Stroop performance and brain activation.

2. Methods

Fifteen healthy FH− women performed a combined cognitive and emotional Stroop task in a balanced (BAL) and a tryptophan depleted (TRP−) session (Evers et al., 2006). In the present study, we report the data of an additional group of healthy FH+ women that was recruited and tested in the same time period as the FH− group (exact same paradigm), and statistically compare the results of these two groups.

2.1. Participants

Fifteen healthy FH− women were successfully tested (19–33 years old; mean age 22.1 (S.D.= 3.5); mostly university students). In the FH+ group, fourteen healthy women (19–42 years old; mean age 23.5 (S.D.= 5.7); mostly university students), with a first-degree relative who had been diagnosed with unipolar depression, were included. The family members (12 mothers, 1 father and 1 sister) gave permission to check their medical history with their general practitioner or psychologist, who received a small payment for this. No patient was Asian, the rest was Caucasian. The participants were recruited by local psychiatrists and nursing homes, and thereafter the TRP− or BAL amino acid (AA) drink was administered. After a four and a half hour break they filled out another set of questionnaires and a second blood sample was taken. Then the participants were scanned at the Maastricht University Hospital radiology department. In each scan session the participants performed two blocks of the Stroop task (9 min each) and halfway through a structural scan was made (10 min). In addition, the participants performed a facial recognition task (Van der Veen et al., 2007). Before the first test session the participants were trained in a dummy scanner.

2.2. Experimental design

Participants were tested in a double-blind placebo-controlled within-subject design. The researchers were blind to the composition of the drinks, but not to the FH status of the participants. Due to a lack of personnel the first author both recruited and tested the participants. When the participants arrived at the laboratory they first completed mood and health complaints questionnaires, then a blood sample was taken and thereafter the TRP− or BAL amino acid (AA) drink was administered. After a four and a half hour break they filled out another set of questionnaires and a second blood sample was taken. Then the participants were scanned at the Maastricht University Hospital radiology department. In each scan session the participants performed two blocks of the Stroop task (9 min each) and halfway through a structural scan was made (10 min). In addition, the participants performed a facial recognition task (Van der Veen et al., 2007). Before the first test session the participants were trained in a dummy scanner.
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