



# Serotonergic functioning correlates with positive and negative affect in psychiatrically healthy males

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## Abstract

A large animal literature implicates serotonin (5-HT) in the modulation of positive and negative affective behavior. In contrast, data from human studies almost exclusively emphasize 5-HT modulation of negative emotional processing. However, no previous studies have directly assessed the relation between 5-HT functioning and positive (PA) and negative (NA) affect. The present investigation tested whether individual differences in 5-HT functioning correlate with PA and NA ratings in a group of healthy subjects. Thirty-one psychiatrically healthy males completed separate assessments of affect and 5-HT functioning. Affect was examined with the Positive and Negative Affect Schedule rated three times a day for two work-weeks. 5-HT functioning was indexed by the maximum prolactin response to d,l-fenfluramine. The prolactin response to d,l-fenfluramine demonstrated a significant inverse correlation with mean ratings of both PA ( $r = -0.49$ ;  $p < 0.005$ ) and NA ( $r = -0.42$ ;  $p < 0.05$ ). These data provide evidence that 5-HT exerts an inhibitory influence over both PA and NA in humans, such that individual differences in 5-HT functioning inversely correlate with ratings of affect. © 2000 Elsevier Science Ltd. All rights reserved.

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## 1. Introduction

A large body of research with animals demonstrates that serotonin (5-HT) modulates the expression of multiple classes of behavior, including locomotor activity, reactivity to reward, sexual activity, affective and irritable aggression, active avoidance and escape latencies to aversive stimulation, and reactivity to sensory stimuli (Depue & Collins, 1999; Depue & Spoont, 1986;

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Depue & Zald, 1993; Lucki, 1992; Soubrie, 1986; Spont, 1992). In most cases, 5-HT appears to exert an inhibitory influence on behavior, whereby reductions of 5-HT result in exaggerated behavioral responding (Depue & Collins, 1999; Depue & Spont, 1986; Soubrie, 1986; Spont, 1992). The broad range of functions modulated by 5-HT suggests that, in most cases, 5-HT does not mediate any specific behavioral, emotional, or motivational system. Accordingly, we and others have proposed that serotonergic functioning modulates both positive and negative affective processing, as well as other motor, and cognitive processes (Depue & Collins, 1999; Depue & Spont, 1986; Depue & Zald, 1993; Panksepp, 1986; Soubrie, 1986; Spont, 1992; Zuckerman, 1991).

Data from human studies of psychiatrically healthy and personality disordered subjects also indicate that 5-HT modulates many behavioral and motivational systems, including aggression, “violent” suicidal behavior, irritability, generalized impulsivity and risk-taking behavior (Cleare and Bond, 1997; Coccaro & Kavoussi, 1996; Coccaro, Kavoussi, Cooper & Hauger, 1997; Coccaro et al., 1989; Depue & Collins, 1999; Manuck et al., 1998; Spont, 1992). However, the human literature has emphasized 5-HT’s specific influence over negative emotions and aggression (Coccaro & Kavoussi, 1996; Coccaro et al., 1997; Coccaro et al., 1989; Knutson et al., 1998). This has led to a narrow view of 5-HT’s influence on affective processing which conflicts with the animal literature indicating that 5-HT influences both negative and positive affective behavior.

Unfortunately, little research has directly assessed the relationship between 5-HT functioning and affect. Instead, researchers have tended to examine personality factors that are theoretically or empirically related to affect. To more directly address this issue, we examined the association between 5-HT functioning, indexed by fenfluramine activation of prolactin secretion, and positive affect (PA) and negative affect (NA) ratings taken three-times daily over a period of two weeks in 31 psychiatrically-healthy male subjects.

## 2. Method

### 2.1. Subjects

Subjects were recruited through the distribution of notices to graduate students and staff of several large academic departments and by advertisement in the university newspaper. Only males were included in this study due to the complex hormonal influences on prolactin levels in females (Josimovich et al., 1987; O’Keane, O’Hanlon, Webb & Dinan, 1991). Of the 45 male subjects who attended an initial group meeting, 41 (91%) agreed to participate in the study. These subjects were screened using the structured clinical interview for DSM-III-R (Nonpatient version 1.0) (Spitzer, Williams, Gibbon & First, 1990), and excluded if they had any current or past DSM-III-R Axis I diagnoses, or if they reported high levels of current life stressors which might affect emotional reactivity in a relatively ongoing manner. No subject manifested marked personality disorder. Subjects completed a medical screening questionnaire and a physical examination. Potential subjects who reported use of any prescribed medication during the past six months, any form of substance abuse, endocrinopathies or other relevant medical conditions were excluded from the study. This left 34 psychiatrically and medically healthy male subjects ranging in age from 19 to 37 years ( $M = 25$ ;  $s.d. = 3.1$ ). All subjects completed written informed consent as approved by the Institutional Review Board of the University of Minnesota.

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