Elevated central serotonin levels inhibit emotional crying

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Abstract

Previous research has suggested a possible role of serotonin in emotional expressions, such as crying. We have found that a transient increase of central serotonin levels by means of oral administration of paroxetine reduces crying in response to emotional movies in healthy female volunteers. This is the first direct evidence of an important role of serotonin in this uniquely human emotional response.

Crying is a uniquely human emotional response. The utility of crying for newborns is well established, but little is known about the functions, determinants, and consequences of crying in adults. Factors such as age, gender, attachment style, and personality (e.g., neuroticism and empathy) play a role, but little is known about the underlying neurobiological mechanisms[1]. It has been reported that pathological crying can be successfully treated with selective serotonin reuptake inhibitors (SSRIs), implicating serotonin as being a potential modulator of crying[2]. Furthermore, some studies have shown that tryptophan, which is the precursor of 5-HT, is reduced in women in the postpartum period[3], which is characterized by emotional lability and a high crying proneness[4]. Finally, preliminary data suggest that being in love is accompanied by low 5-HT levels[5]. Together, this evidence suggests that 5-HT levels might influence the emotional threshold for crying. Therefore, we directly examined whether acute increases in central 5-HT levels by means of the SSRI paroxetine increases the crying threshold.

Twenty-five healthy female volunteers were tested in a double-blind randomized placebo-controlled single-dose cross-over design. Placebo or paroxetine (20 mg) were orally administered on two days, separated by a one-week interval. On both days, participants watched an emotional movie (either 'Brian's Song' or 'Once Were Warriors') five hours after medication administration, the time at which the effect of paroxetine on central 5-HT levels is maximal[6]. Directly after the movie, the crying of the participants in response to a number of specific scenes was measured with a validated questionnaire[7]. In order to control for possible effects on mood and the evaluation of emotional stimuli, mood was measured directly before administration of the pill and after the movie by means of the profile of mood scales (POMS)[8], whereas valence and arousal ratings were obtained using a subset of the International Affective Pictures System[9]. Four categories of 10 pictures each were selected on the basis of their valence (high/low) and arousal (high/low) norm ratings.

Analysis of variance showed that paroxetine strongly affected the intensity of self-reported crying behavior (three-way interaction treatment x movie x order, $F_{1,21} = 16.9$, $P < 0.0005$, $\eta^2 = .446$; Figure 1). A follow-up analysis showed that crying was reduced on the paroxetine day ($T = 3.97$, $P < .005$).

<<Insert Figure 1 about here>>

Paroxetine did not affect mood or overall appraisal of emotional pictures. Arousal and valence ratings of specific categories of the emotional pictures, however, were affected (arousal: treatment x high/low valence category, $F_{1,21} = 7.6$, $P < 0.05$, $\eta^2 = 0.25$; valence: treatment x high/low arousal category, $F_{1,21} = 5.5$, $P < 0.05$, $\eta^2 = 0.19$). More precisely, paroxetine decreased arousal ratings in the high arousal/low valence category and valence ratings of the high arousal/high valence category (see Figure 2). This raised the question whether the altered evaluation of specific subgroups of emotional stimuli could be responsible for the reduced crying response to the movies, observed in the paroxetine condition. To examine this, correlations between the ratings and crying were computed. It was found that the arousal score for the high arousal/low valence category in the paroxetine condition was significantly correlated with crying ($r = .52$, $P < .01$), with higher arousal scores going together with more crying. The valence scores in the high valence/high arousal category did not show an association with crying. A further analysis on individual differences revealed that paroxetine has a stronger inhibiting effect on the crying of women with high neuroticism scores (correlation between neuroticism scores and crying on paroxetine day, $r = -.63$, $P < .001$). No significant relation was found with romantic love, attachment style or sleep quality.

<<Insert Figure 2 about here>>

The finding that paroxetine heightens the crying threshold clearly supports our hypothesis that 5-HT is involved in crying. However, this effect can partially be attributed to the changed appraisal of emotional stimuli. Although only the arousal ratings of a subgroup of

pictures were affected, the effect was in the expected direction and the affected category of pictures was most comparable to the movie scenes in terms of emotional content. In addition, arousal ratings were associated with crying behavior only on the paroxetine day. The effect of paroxetine on the evaluation of emotional pictures was not in line with the results of previous studies[10, 11], which failed to show an effect of different SSRIs on valence ratings of emotional pictures. It should be noted, however, that these studies failed to differentiate between subcategories of pictures in terms of arousal.

The association between neuroticism and crying behavior corroborates previous findings demonstrating a relation between 5-HT and neuroticism[12]. Neuroticism has been associated with a polymorphism of the gene that regulates the 5-HT transporter, which is associated with higher central 5-HT levels and a greater anti-depressive response to paroxetine[13]. Therefore, it could be argued that among the participants with high neuroticism scores, on average the potential effect of paroxetine is larger, which could explain the found relation between neuroticism and crying behavior after paroxetine.

In conclusion, this is the first study that shows a direct relation between central 5-HT levels and crying behavior in healthy volunteers. This study shows that SSRIs can have a major effect on the expression of emotions, which can have serious consequences for both the measured and experienced treatment effects of SSRIs. Further research is necessary to show whether the role of 5-HT is restricted to crying behavior or whether it extends to other (including positive) emotional expressions as well. There is some evidence that suggests that 5-HT also is involved in laughing[14], but direct evidence in healthy volunteers is lacking. More research is also necessary to further elucidate the underlying neurophysiological processes and specify the precise role of 5-HT in this positive emotional expression. Taken together this would lead to a better insight into the underlying neurobiological mechanisms of this mysterious and important, but scientifically ignored and poorly understood human behavior.

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Figure 1 Effect of paroxetine or placebo on subjective crying as expressed in z-scores for 'Once were Warriors' presented as the first or second movie (warriors1, warriors2) and 'Brian's song' presented as first or second movie (Brian1, Brian2).

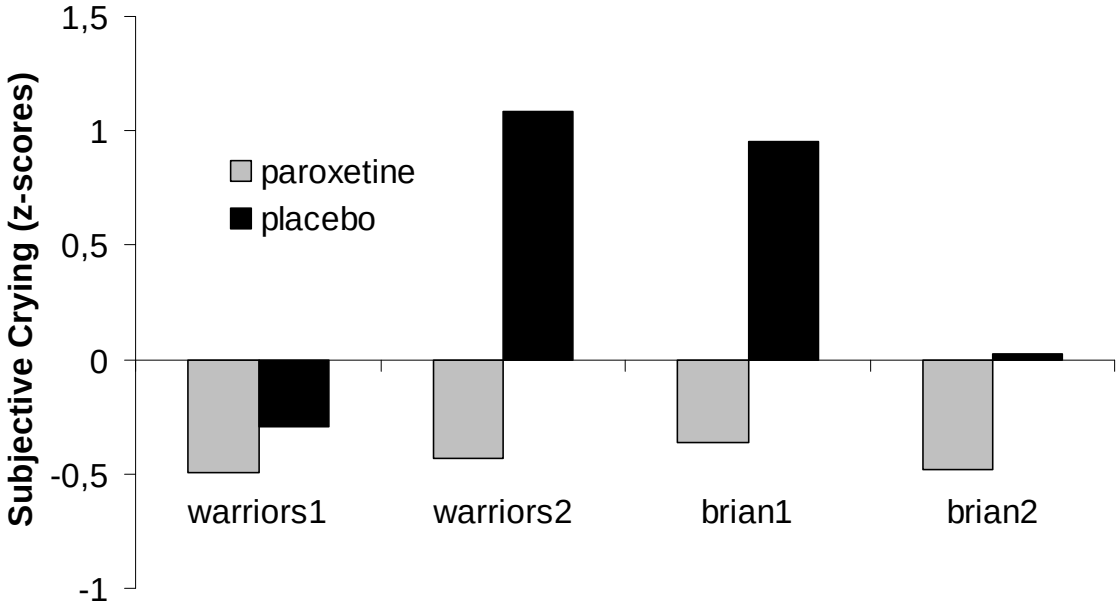

Figure 2 Scatter plot of subjective crying expressed in z-scores and arousal ratings as measured on a 9-point scale (r=.52, P<.01).