Serotonin and the Neurochemistry of Intimacy

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Human beings have a fundamental need to belong (1), and it is well-known that social isolation can be detrimental to mental and physical well-being (2–4). Despite the well-established connection between close relationships and heath, we are only beginning to understand the biological factors that might mediate this relationship in humans. The burgeoning field of social neuroscience and, in particular, the use of pharmacological interventions in conjunction with cognitive and/or behavioral paradigms has produced a number of intriguing neurochemical candidates, including the neuropeptide oxytocin (5) as well as some less obvious contenders like proinflammatory cytokines (6) and, finally, serotonin. With respect to the latter, research has shown that serotonin has been associated with impulsivity, aggression (specifically, reactive aggression), social isolation, dominance, quarrelsomeness, and heightened reactivity to emotional events (see Crockett [7] for review), but a new study by Bilderbeck *et al.* (8), published in this issue of *Biological Psychiatry*, suggests that serotonin might also modulate perceptions of close relationships.

Bilderbeck *et al.* used a well-established acute tryptophan depletion procedure to look at the effects of central serotonin levels on cognitive appraisals of close personal relationships. Specifically, male and female healthy volunteers ingested an amino acid drink with tryptophan (T+) ($n = 22$) or without tryptophan (T−) ($n = 19$) in this between-subject, double-blind study. Approximately five hours after ingesting the amino acid drink, participants completed a novel "Couples Appraisal Task" in which they viewed photographs of heterosexual couples (a mixture of real and posed) who were either: 1) standing apart, or 2) making affiliative gestures (e.g., putting their arms around each other or holding hands). Participants then rated the couples in terms of 10 descriptors that were thought to reflect "perceived stability of romantic relationships" (e.g., "committed," "intimate," "trusting," "supportive") as well as in terms of relative dominance of the partners, their independence, and their ability to solve conflicts.

Results showed a significant effect of tryptophan treatment on relationship appraisals; post hoc analyses revealed that tryptophan specifically altered intimacy and romance judgments but had no effect on the other relationship descriptors. One should be cautious when interpreting these observations, given the novelty of the task and that norms have not been established. Nevertheless, it is interesting to think about the selective effects of tryptophan on intimacy and what that might mean about potential mechanisms.

Definitions of "intimate" include "associated in close personal relations," "very private/closely personal," "warmly cozy," and "inmost/deep within." In the context of close relationships, Collins and Stroufe (9) nicely illustrate the complex emotional, motivational, and behavioral aspects of intimacy:

> "To achieve intimacy, one must first be oriented to value and seek closeness. Second, one must be able to tolerate and even embrace the intense emotions that are inextricably part of close relationships and be able to share emotional experiences freely. Finally, one must be capable of self-disclosure, mutual reciprocity, sensitivity to the feelings of the other, and concern for the other's well-being." (p. 127).

In essence, intimate relationships are those in which the boundary between self and other is perhaps the most blurred and thus those in which we are especially vulnerable.

Why would serotonin selectively bias intimacy (and romance) perceptions? As noted, (low) serotonin has been implicated in aggressive and/or quarrelsome behavior (10) and emotional reactivity (7), all of which are antithetical to the interdependence, reciprocity, and vulnerability that intimacy entails. One way to interpret the relationship appraisals measured in this study is as examples of motivated cognition (11)—that is, participants' perceptions of the photographed couples are biased by and thus can be considered to reflect their underlying goal state(s). Viewed in this light, the effects of tryptophan depletion on intimacy and romance ratings in this study might reflect peoples' desire to create distance between themselves and significant others in an effort to regulate feelings of quarrelsomeness and heightened emotional reactivity induced by low serotonin levels.

Indeed, it is noteworthy that tryptophan depletion had the same effect on relationship appraisals as that of chronic fearful attachment without treatment (i.e., both selectively predicted lower intimacy and romance ratings). According to adult attachment theory (12), fearful attachment is associated with mixed feelings about close relationships: fearful individuals desire closeness but feel extremely uncomfortable with emotional intimacy. Fearful attachment is also characterized by high degrees of anger and hostility (possibly due to their chronic conflict about closeness) (12). There are, of course, many reasons why someone might rate the photographed couples as less intimate and romantic, but because fearful attachment is associated with anger and heightened emotional reactivity and low serotonin is also associated with these states, it is possible that low serotonin could induce a temporary state of fearful attachment (at least in the context of closeness), or could exacerbate chronic feelings of fearful attachment. The authors emphasize that the effects of tryptophan remained statistically significant when attachment was included as a covariate, but one wonders whether individual differences in attachment anxiety and/or avoidance might have interacted with treatment. Indeed, there is evidence that traits—possibly reflecting variability in the serotonin system—can interact with state changes in serotonin to influence behavior (13,14). Future research, with larger samples, could address whether fearful individuals are more sensitive to the effects of tryptophan depletion or whether tryptophan depletion could have an additive effect on attachment avoidance or attachment anxiety, in effect shifting them to a fearful state. More specifically, tryptophan depletion could make dismissive individuals (who tend to suppress emotions) more fearful by increasing emotional reactivity or could make preoccupied, "enmeshed" individuals more fearful by making them more angry and hostile.

In addition to looking at factors related to the stability of romantic relationships, the authors also looked at the effects of serotonin on dominance. Importantly, the dominance measure used in this study captures relational dominance (i.e., the dominance of the

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woman relative to the dominance of the man) rather than dominance per se (e.g., physical size). Here, results showed an effect of treatment on dominance ratings, but this effect was qualified by gender. The T− women rated men as more dominant (and women as less dominant) than T+ women, whereas both T− and T+ men rated men as more dominant. Although perception of dominance have been associated with serotonin in prior research (14), it is unclear why the effects of tryptophan on dominance perceptions were specific to women in this study. One possibility might have to do with the tendency for men, in general, to identify with traits associated with agency, including dominance and power (15). Because agency is more central to the self-concept of men, it might be less likely to fluctuate in response to phasic manipulations like tryptophan depletion.

Finally, results also revealed an intriguing three-way interaction among gender, treatment, and touch (i.e., whether or not the photographed couples were touching each other) predicting conflict resolution abilities; here again, T− women but not men judged touching couples as more able to resolve conflict. At first glance, this observation seems at odds with their results showing that tryptophan depletion negatively biased intimacy and romance ratings. The authors propose an intriguing hypothesis that tryptophan depletion might enhance sensitivity to social cues. The salience hypothesis is consistent with research linking low serotonin to heightened emotional reactivity; that T− women in this study showed both the highest conflict resolution ratings for touching couples and the lowest conflict resolution ratings for non-touching couples supports salience modulation. That being said, it is not clear why the salience effects were specific to women. Moreover, one wonders why the effects of treatment on intimacy and romance appraisals were not also moderated by the touch manipulation, which cues closeness.

In conclusion, this is an intriguing preliminary investigation that points to the potential role of serotonin in the well-established but complex relationship between close relationships and well-being. Research has shown that altering serotonin can significantly influence interpersonal behavior (7,10,14), but these data suggest that serotonin might also bias interpersonal perceptions. Numerous psychiatric disorders are marked by serotonergic dysfunction—for example, depression, anxiety, schizophrenia, and borderline personality disorder. Perhaps not uncoincidentally, these same disorders have also been associated with interpersonal disturbance and feeling of loneliness and isolation. These data suggest one neurochemical candidate that might help explain this association: low serotonin levels might negatively bias intimacy perceptions (and/or induce a state in which intimacy is undesirable) and, in this way, perpetuate perceived (and possibly actual) isolation—a particularly unfortunate situation, since individuals with chronically low serotonin levels are amongst those who could most profit from the mental and physical benefits that close relationships can bestow.

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