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The effect of tryptophan on quarrelsomeness, agreeableness, and mood in everyday life

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Abstract. In humans there is an association between low serotonin levels and aggressive behavior, and drugs that increase serotonin function have been used to treat aggression. In monkey alterations in serotonin function seem to influence behavior along the agonistic–affiliative axis, with increases in serotonin function not only decreasing aggression but also increasing the grooming of other animals. Measurement of human social behavior in everyday life has advanced to the stage where it is possible to measure behavior along the agreeable–quarrelsome axis. Therefore we performed two double-blind cross-over studies to compare the effects of tryptophan, the serotonin precursor, with placebo on the social behavior of healthy people. In the first study tryptophan decreased quarrelsome behaviors. In the second study on irritable people tryptophan not only decreased quarrelsome behaviors but also increased agreeable behaviors and improved mood. Our studies suggest that increasing serotonin synthesis with tryptophan moves behavior along the axis that encompasses aggressive, quarrelsome, and agreeable behaviors towards more positive social behavior in healthy people in everyday life. Irritability is a risk factor for various mental and physical disorders. It remains to be seen whether increasing serotonin function in irritable people improves their mental and physical health.

Keywords: Tryptophan; Serotonin; Social interaction; Agreeableness; Quarrelsomeness; Mood

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1. Introduction

1.1. Serotonin and aggression in animals

Research on experimental animals suggest that serotonin is part of the system that modulates the response to a number of different stimuli [1,2]. For example, low serotonin will enhance startle responses, pain responses, food intake, sexual activity and aggression. Work in rodents has shown that serotonin inhibits a variety of different types of aggression [3–5]. The situation in monkeys is a bit more complex. Lowering serotonin in monkeys increases aggression [6–8], while increasing serotonin not only decreases aggression but increases affiliative behaviors such a grooming another animal [6,7]. In monkeys serotonin is also involved in regulating hierarchy [9]. In many species of monkeys, increasing serotonin function can help a male animal to achieve dominance. This is in part because increasing serotonin function increases social affiliation and a male will achieve dominance in part through affiliative interactions with high ranking females [9,10]. Dominance is also achieved or maintained through strategic episodes of aggression, and although increasing serotonin may decrease aggression overall this is not necessarily true for the instrumental aggression sometimes needed in establishing hierarchy [9]. Low serotonin, as indicated by low levels of the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid (CSF), is associated with impulsive aggression in monkeys [11,12] rather than with instrumental aggression. Impulsive aggression is often inappropriate in the social context and monkeys with low CSF 5-HIAA tend be driven out of their social group [13] and to die earlier than other members of their group [14].

1.2. Serotonin and aggression in humans

A review of studies in which CSF 5-HIAA was measured in aggressive people concluded that low serotonin is associated with aggression, but not necessarily in all diagnostic groups [15]. This may be due in part to the fact that in humans as in monkeys low serotonin may be associated primarily with impulsive aggression. For example, in one study CSF 5-HIAA was low in impulsive violent offenders, but this was not true for the offenders who had premeditated their violent acts [16]. Drugs that increase serotonin function have been used to treat aggression. In aggressive schizophrenics tryptophan, relative to placebo, decreased uncontrolled behavior in one study [17] and decreased the need for neuroleptics and sedatives in aggressive psychiatric inpatients in another study [18]. Selective serotonin reuptake inhibitors (SSRIs) have been used to treat aggressive patients with a variety of different diagnoses [19–26].

In healthy individuals the relationship between serotonin and aggression has been studied by raising or lowering serotonin function and studying aggressive or pro-social behavior in the laboratory. One experimental approach is the acute tryptophan depletion (ATD) technique. Participants ingest a mixture of amino acids that is devoid of tryptophan. This induces protein synthesis and as tryptophan is incorporated into protein there is a marked decline in plasma tryptophan [27] and brain serotonin synthesis [28]. ATD increases aggressive responding or irritability in a variety of laboratory situations [29–36]. Another approach is to study the effect of giving SSRIs to healthy individuals. In