

# The role of serotonin in risky choice and the acquisition of reciprocal cooperative behaviour: 2 investigations using tryptophan depletion

Robert D. Rogers\*

*University Department of Psychiatry, University of Oxford, Oxford, UK*

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**Abstract.** Making decisions between risky actions involves weighing the pros and cons of each, and considering the relative probabilities with which good and bad outcomes will occur. In this paper, I review 2 recent studies suggesting that serotonin modulates the cognitive and emotional processes involved in such decision-making in both non-social and social contexts. First, we have found that tryptophan depletion – leading to diminishes central serotonin activity – alters attention towards the gains associated with risky options. Second, we have found that tryptophan depletion alters the acquisition of socially cooperative behaviour in an iterated Prisoner’s Dilemma game. These findings highlight the significance of serotonin in altered non-social and social risky choice in psychiatric illnesses. © 2007 Published by Elsevier B.V.

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Everyday decision-making is frequently an emotionally powerful experience. Decision-makers (choosing between occupational or financial opportunities, opportunities to meet and interact with social partners etc.) are frequently confronted with options associated with motivationally significant but uncertain outcomes that differ in their pros and their cons. Deciding under such uncertainty requires the capacity to weigh these potential rewards and punishments, and the ability to control the motivational states that they excite, in order to arrive the most effective choice [1]. Psychiatric illnesses, such as substance dependent disorders, that involve dysfunctional reinforcement processes, are associated with impairments in decision-making that may play a role in aetiology of illness, and increase the risk of relapse [2]. Recent

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\* Tel.: +44 1865 226 399; fax: +44 1865 793 101.

*E-mail address:* [robert.rogers@psych.ox.ac.uk](mailto:robert.rogers@psych.ox.ac.uk).

research has begun to delineate the neural circuitries that represent the benefits and penalties that people consider when making risky decisions [3,4] and provides evidence that dopamine plays a significant role in reinforcement learning [5]. In this paper, I describe 2 recent experiments from our laboratory, involving tryptophan depletion, that demonstrate that serotonin also plays a significant role in the cognitive and emotional processes involved in resolving between risky choices in non-social and social contexts.

Previously, we showed that that rapid dietary tryptophan depletion – leading to reduced central serotonin activity [6] – impaired the decision-making of healthy adults [2]. However, little is known about the mechanisms that might mediate such effects. In our first study reported here, we tested a novel decision-making procedure to reveal the impact of tryptophan depletion on the 3 separable factors known to determine human choice and identified above: the magnitude of possible gains (or reward), the magnitude of possible losses (or punishment), and the probabilities with which these outcomes are delivered [1].

Serotonin might modulate decision-making in several ways. According to perspectives that emphasise the role of serotonin in mediating anxiety and the effective processing of aversive signals [7], we might expect lowered serotonin to impair decision-making by altering the processing of possible losses; that is, punishment cues might fail to generate anticipatory anxiety states associated with risky or maladaptive choices. By contrast, other data highlight the role of serotonin in modulating reinforcement and incentive-motivational processes, possibly through complex interactions with the mesolimbic dopamine system. This evidence includes recent demonstrations that tryptophan depletion reduced subjective ratings of the high produced by intra-nasal cocaine [8]. Consequently, we might instead predict that tryptophan depletion in healthy adult volunteers will alter decision-makers' attention towards, and the processing of, possible gains when making risky decisions.

We tested between these possibilities using tryptophan depletion in a sample of healthy adult volunteers (screened for mood disorders) using a between-subject, cross-over, double-blind design. Eighteen healthy adults consumed an amino acid drink containing tryptophan and 18 healthy volunteers consumed an amino acid drink without tryptophan, before repeatedly choosing between two simultaneously presented gambles that differed in the magnitude of their possible gains, the magnitude of their possible losses (i.e. punishment), and the probabilities with which these outcomes were delivered [9,10]. There were no significant differences between the two groups in terms of age, IQ or state affect at the time of testing.

In general, participants chose gambles significantly more often when they were associated with higher probabilities of winning compared with lower probabilities of winning, with no evidence that this pattern of choice was changed following tryptophan depletion compared with the control treatment (see Fig. 1). However, while participants chose gambles more often when they were associated with large possible gains compared with small possible gains, this pattern of decision-making was significantly attenuated following tryptophan depletion (Fig. 1). Finally, all of our participants chose gambles significantly less often when they were associated with larger possible losses compared with when its possible losses were small, and to a similar extent in both groups of participants (see Fig. 1).

These data suggest that, under some conditions at least, tryptophan depletion alters healthy adults' attention towards the benefits or rewards associated with risky actions and

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