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Opposing Effects of Controllable and Uncontrollable Stress in an Animal Model of Gambling Behaviour

Gambling Disorder (GD) is a behavioral addiction characterized by maladaptive gambling behavior. Major Depression (MD) and GD are comorbid in 30-54% of the cases. Individuals with higher levels of distress (i.e. depressive symptoms) exhibit higher severity of gambling behaviours. The causal link between depression and MD remains unknown. We aimed to investigate this relationship in rodents by evaluating their performances on a rat gambling task (rGT) coupled with a depression-inducing Learned-Helplessness (LH) task. We predicted that stressed rats, exhibiting depressive-like behaviours, will perform significantly worse on the rGT than rats that do not display depressive-like behaviours.

We evaluated the rats' gambling-like behavior using the rGT, which is a task analogous to the Iowa Gambling Task (IGT) used to clinically measure gambling behaviour in humans. Rats chose among 4 options, with varying probabilities of rewards and time penalties, with the objective of maximizing net food gain. The 'advantageous' option (P2) was associated with a higher net food gain than the 'disadvantageous' option (P4). Initially, the rats' (N=45) baseline gambling-like behaviour was obtained; they were then exposed to acute stress (uncontrollable and controllable stress) (LH task) that induced depressive-like behaviours; lastly, their gambling behaviour was reassessed. They were assigned to 3 groups: **1**) Learned-Helplessness (LH); **2**) Learned-Control (LC); and **3**) Cage-Control (CC) rats. The LH rats were initially exposed to inescapable mild foot shocks (uncontrollable stress) and then to escapable shocks (controllable stress), where they were able to escape the shock by pressing a lever. The LC rats were only exposed to the escapable stress session. The CC rats were not exposed to any stress. Every rat was then re-evaluated on the RGT.

Exposure to uncontrollable/inescapable stress significantly impaired the LH rats' gambling performance ($t(26) = -2.38, p < .001$), than both LC ($t(9) = -2.61, p = .028$) and CC ($t(7) = .616, p = .557$) rats. LH rats showed a significantly higher preference for the high-risk option (P4) than the advantageous option (P2). Surprisingly, exposure to controllable/escapable stress seemed to have a 'therapeutic effect' on the LC rats and improved their gambling performance by shifting their choice preference from the risky to optimal option ($t(9) = -2.49, p = .034$).

Therefore, exposure to the uncontrollable stress significantly impaired the gambling-like performance and increased the vulnerability to gambling-like behaviour and risky decision-making. Surprisingly, exposure to controllable stress significantly improved gambling performance and seemed to strengthen resistance to risky decision-making. Exposure to mild/controllable stress is a stable treatment in cognitive therapy for the treatment of OCD, PTSD, depression, etc; where exposure to mild stress may desensitize subjects to further adverse consequences. With controllable stress, subjects have the ability to control the situation and to develop coping strategies and resilience for similar situations in the future. However, due to the unpredictability of uncontrollable stress, it is much more difficult to develop a stable/optimal coping mechanism. So exposure to mild stress seems to be a good way to train subjects to develop coping strategies to deal with future challenges (i.e. decision makings) much better.

Overall, the rGT is a valuable tool to investigate the biological basis of the relationship between gambling and depression and can be utilized to discover therapeutically relevant pharmacological targets for GD.