## Title: Integration of appetitive and aversive reinforcers and the neuromodulation of reward seeking and pain avoidance

## Abstract

New behaviours in animal and man can be acquired, in principle, by either reward- or punishment-reinforced learning. But as popular wisdom maintains, learning may be most efficient if "carrot and stick" reinforcements are combined. In spite of its high theoretical, clinical and educational relevance, neither the general nature nor the detailed dynamics of the direct interaction of reward and punishment nor its dynamics during learning are understood.

Midbrain dopamine system, especially the ventral tegmental area (VTA) plays a vital role in motivated behaviour. Electrical stimulation of this system has a positively reinforcing effect on behaviour. Using this feature of this widely projecting reward system, we first studied the acquisition and extinction of the tone conditioned hurdle crossing in shuttle-box. In a similar way, we studied the same learning motivated by avoidance of aversive footshock. After studying the learning driven by either positively reinforcing stimulation of the ventral tegmental area or by negatively reinforcing footshock, we integrated both reinforcers. The boosted learning observed for the combination of reward and punishment in the same session demonstrated a putatively dopamine-dependent convergent effect. Subsequently, omission procedures were employed to clarify the respective roles of appetitive and aversive reinforcers previously observed in the interaction scenario. Further clarification was achieved by comparing results from continuous reinforcement and partial reinforcement protocols. Taken together the results demonstrate that, reward and punishment operate differently during fully predicted continuous and partially predicted reinforcement conditions. The results further imply that suggests that instrumental learning mechanisms vigorously rely on dopamine signal that is associated with response. Consequently, dopamine plays discernible but important roles in both reward seeking and pain avoidance.

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