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Utilising DREADDs to Elucidate the Role of the Mesolimbic Dopaminergic System in Probabilistic Reversal Learning

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Abstract

Cognitive inflexibility is an important trait that is displayed in a multitude of neuropsychiatric disorders. It is often modelled using reversal learning paradigms which measure the capacity to inhibit a previously learned discrimination and learn a new response following sudden changes in stimulus-response (S-R) contingencies. Previous research has demonstrated the role of dopaminergic neurotransmission in the mesocorticolimbic system in positive and negative reinforcement which are both important in reversal learning. Our study aims to investigate the role of dopaminergic neurons originating from the VTA in reversal learning using a two-choice probabilistic learning task. Selective silencing of these neurons was achieved through the infusion of a viral vector into male Th::Cre+/- Long-Evans rats, leading to the selective expression of hM4Di designer receptors exclusively activated by designer drugs (DREADDs) in the VTA. These were then selectively activated by systemic injection of clozapine-N-oxide (CNO). We found this did not produce significant effects on reversal learning through either positive or negative reinforcement, but we did observe a significant increase in response choice latencies in TH::Cre+ subjects following synaptic silencing. We propose that this effect could be the result of reduced dopaminergic activation of the medial prefrontal cortex (mPFC) by the VTA. This is consistent with the role of dopamine in cognition and invigorating behaviour.

Biography:

Sohail Daniel is a medical students year at the School of Clinical Medicine, University of Cambridge. Graduated completed in 2018 with BA (Hons) degrees in Medical Sciences from the University of Cambridge, specialising in Psychology. Sohail Daniel is currently undergoing research in developmental paediatrics.

Speaker Publications:

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