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MEETING ABSTRACT

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Mapping presynaptic inputs to medial accumbens D1-medium spiny neurons using rabies monosynaptic tracing: focusing on insular cortex input

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Background: The nucleus accumbens (Acb) is a major target for studies on the rewarding effects of drugs of abuse or physiologic reinforcers since it mediates earlier-stage non-automatic drug-seeking behaviour [1]. Our group found that a history of dyadic social interaction conditioned place preference (CPP) profoundly inhibited cocaine CPP-associated activation of the medial Acb shell and core [2]. Since our group found that dopamine D₁ receptor-expressing medium spiny neurons (D1-MSNs) seem to be more involved than D2-MSNs [2] our aim is to map the direct inputs to a genetically defined neural population, the D1-MSNs in the medial Acb. Furthermore we focus on agranular insular area (AI) projection to Acb since it is known to be involved in drug seeking and social behaviour (reviewed in [3]), important features of our work.

Methods: To define the direct inputs to the D1-MSNs in the medial Acb, we have combined the rabies virus mono-trans-synaptic tracing method [4] with a specific Cre-expressing mouse line (Drd1a-Cre::TVA-lacZ).

Results: Several brain regions were identified with direct inputs to medial Acb D1-MSNs: infralimbic, prelimbic, piriform and insular cortex (mainly the ventral region), the paraventricular nucleus of the thalamus and basolateral amygdala. To support our results we also injected fluorescent cholera toxin B (CTB), a non-cell-type-specific retrograde tracer, in the same injection site. Robust retrograde labelling was found in many brain areas similar to the rabies virus tracing, an example being our area of focus, the AI. Thus, to further investigate the insular cortex projection to the medial Acb, we have injected the anterograde tracer *Phaseolus vulgaris* leucoagglutinin (PHA-L) in the AI. However, we only found labelled PHA-L fibers in the medial Acb in a more anterior bregma compared to injection site for the rabies technique. Moreover, this result was only observed when the PHA-L injection site was also at a specific bregma in the AI.

Discussion: These findings give an important insight of the precise region/location of neurons in AI that innervate a specific region of the medial Acb. The increasing knowledge about the regional variations in the connection between AI and medial Acb should be an essential criterion to be taken into account in the design of an experiment and in data interpretation. Therefore, the comprehensive maps of direct inputs to Acb D1-MSNs, particularly the insula–accumbens pathway, will assist future functional dissection of the neuronetworks mediating motivated behaviour.

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Keywords: medium spiny neurons – D1-MSNs – nucleus accumbens – insular cortex – rabies monosynaptic tracing – classical tracers

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