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Evolution of the Subcortical Circuits Controlling Goal-Directed Behaviour

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ABSTRACT

The aim of the work presented in this thesis was to reconstruct the minimal neural hardware that vertebrates use for goal-directed behaviour. By studying lamprey, one of the phylogenetically oldest vertebrates, we were able to identify the neural circuitry that has been conserved since jawed and jawless vertebrates diverged over 560 million years ago. Specifically we examined the conservation of the subcortical circuits involving the optic tectum, basal ganglia and habenula. These structures are responsible for steering, action selection and motivation in mammals.

Optic tectum; this structure is essential for visually guiding purposeful movements to either avoid or approach objects of interest. Using a combination of tract tracing and stereology we demonstrated that the pattern of sensory innervation is conserved as the retinotectal connection in lamprey is arranged in a retinotopic. By analyzing the spatial arrangement between this retinotopic map and the underlying motor map (Saitoh et al., 2007) we revealed that optic tectum can guide lamprey towards or away from the source of visual input. This suggests that tectal circuits controlling both approach and avoidance were present at the dawn of vertebrate evolution and have subsequently been conserved. Furthermore, our result indicate that there are two independent retinal circuits in lamprey; one that may contact the photoreceptors directly and transmit information to the pretectum with a minimal delay for reflexive behaviours and another that contacts the image forming part of the retina (inner plexiform layer) that sends projections to the optic tectum to control goal-directed visual behaviours.

Basal ganglia; these nuclei play a key role in action selection in mammals. We showed, using immunohistochemistry, tract tracing, and whole-cell recordings, that all parts of the mammalian basal ganglia (striatum, globus pallidus interna [GPi] and externa [GPe], and subthalamic nucleus [STN]) are present in the lamprey forebrain. In addition, the circuit features, molecular markers, and physiological activity patterns are conserved. Thus, GABAergic striatal neurons expressing substance P project directly to the pallidal output layer, whereas enkephalin- expressing striatal neurons project indirectly via nuclei homologous to the GPe and STN. These results show for the first time that both the “direct” and “indirect” pathways are present in a lower (anamniote) vertebrate. Our results suggest that this circuitry has been conserved in all vertebrates, most likely as a mechanism for action selection, for over 560 million years.

Extending our analysis we revealed that the phylogenetically oldest basal ganglia include the pedunculopontine nucleus and a separate habenula projecting pallidal nucleus. This later nucleus differs from other pallidal nuclei, as its neurons project to a reward-related structure, are glutamatergic and differ from other pallidal neurons in their molecular expression, connectivity and electrophysiological properties. These results suggest that this nucleus may represent the output of a previously unappreciated pathway through the basal ganglia.

Habenulae; the medial (MHb) and lateral (LHb) habenulae are a small group of nuclei that contribute to a range of cognitive and motor functions by regulating the neuromodulatory systems. Based on connectivity and molecular expression, we show that the MHb and LHb circuitry is conserved in the lamprey. As in mammals, neurons in the LHb homolog project indirectly to dopamine and serotonin neurons through a nucleus homologous to the GABAergic rostromedial mesopontine tegmental nucleus. This suggests that the LHb may exert an inhibitory influence on the neuromodulatory systems to regulate reinforcement learning and motivation as it does in mammals. The efferents of the MHb homolog selectively target the interpeduncular nucleus, which in turn projects to regions involved in innate behavioral responses such as fight or flight. In contrast to mammals, the MHb afferents arise from sensory (medial olfactory bulb, parapyneal, and pretectum) and not limbic areas. This suggests that the “context” in which this circuitry is recruited but not the role of the circuit may have changed during evolution. Our results indicate that the habenular nuclei provide a common vertebrate circuitry to adapt behavior in response to rewards, stress, and other motivating factors.