# Unraveling how locus coeruleus activity mechanistically shapes brain network activity to govern context-dependent cognitive behavior

**Koesling J (1,2), van den Berg M (1,2), Adhikari MH (1,2), Bertoglio D (1,2), Verhoye M (1,2)**

1) Bio-Imaging Lab, University of Antwerp, Belgium
2) µNeuro Research Center of Excellence, University of Antwerp, Belgium

The locus coeruleus (LC), a brain region in the brain stem, is a key regulator of exploration, attention and memory. Neuroimaging techniques have revealed that the LC can affect several brain networks to shift between different cognitive states such as exploration or attention. However, the specific connections between the LC and other brain regions enabling this cognitive flexibility remain elusive.

In this project, we aim to uncover i) how the LC directly influences other brain regions to shape specific cognitive processes and ii) how enhancement of LC activity causally influences other brain regions and thereby cognitive states in health and disease.

To this end, we will measure whole-brain activity in awake rats using non-invasive functional MRI on a 9.4 T MRI system. Structural connectivity between brain regions will be derived from diffusion-weighted MRI and used to infer model-based effective connectivity (EC) from functional MRI data. EC can discern causal influences brain regions yield over one another. These neuronal measures will be linked to behavioral paradigms assessing explorative behavior and novelty identification to uncover neural correlates of different cognitive states. First, we will assess which directed connections originating from the LC to other brain regions shape different cognitive states. Next, we will chemogenetically activate LC neurons to investigate how this affects EC and cognition in healthy rats. Lastly, we will enhance LC activity in a rat model for Alzheimer's disease, where the LC activity is known to be impaired through the disease, and assess if it can improve cognitive impairments.

By uniquely bridging the gap between cognitive behavior and how the LC causally reshapes brain activity, we will generate novel insights into the specific regulatory role of the LC in both health and disease which may eventually guide novel therapies to enhance cognition.