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UnscrAMBLY

Project Title: Understanding brain circuit dysfunction in amblyopia using large-scale multimodal recordings in a new visuomotor task applied to animal models and patients

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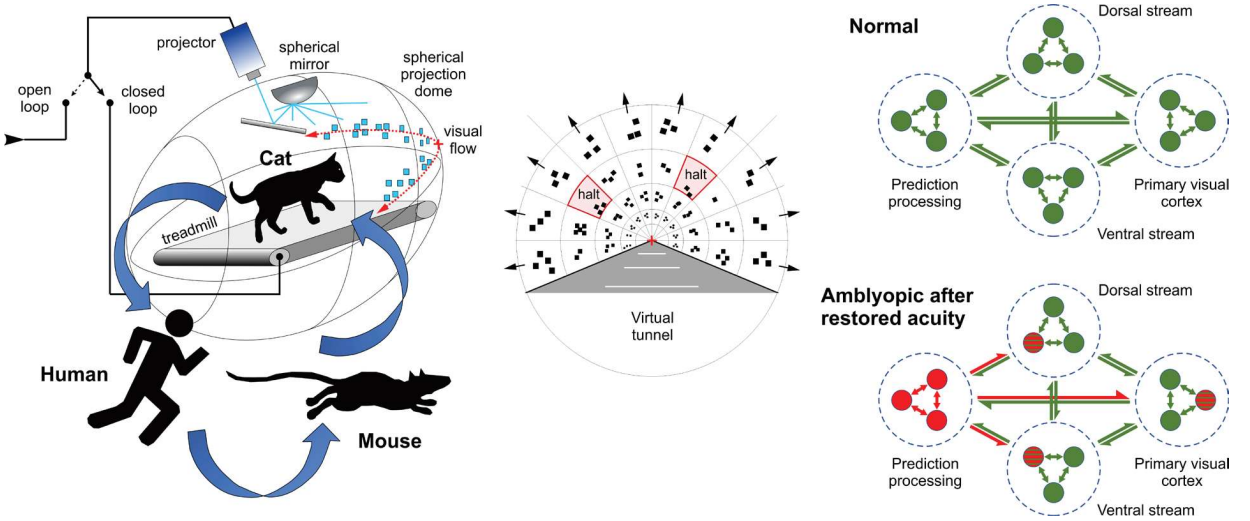
Amblyopia (also known as "lazy eye") is one of the most studied neurodevelopmental vision disorders. Amblyopia must be diagnosed early and treated promptly because current treatments cannot efficiently recover lost vision beyond the age of 8 years. Only a small fraction of about 200 million affected patients, mostly those living in locations with high-quality healthcare and education structures in place, have access to timely and precise diagnosis and long-term support. The lack of proper treatment can lead to permanently decreased performance in everyday tasks including reading, driving or walking, motivating us to develop a new, efficient and widely accessible test for diagnosis and treatment monitoring. Our study aims to exploit the capacity of the brain to predict expected changes in the visual scene, especially those caused by our own motion. Subjects will pedal or run forward in a virtual reality corridor while brain activity, eye- and limb motion is recorded. We briefly halt the visual motion at small regions of the scene and analyze brain activity, eye- and limb-motion data. Using machine learning we determine differences between healthy and amblyopic subjects. In humans we use noninvasive recording that captures brain surface activity. Magnetic resonance imaging could also record deep brain activity but requires a fixed body and head for prolonged times thus is not applicable to our study. To collect high-resolution data also from deep regions of the brain we use cats and mice as amblyopia models. Visual function of the cat is very similar to humans. We use functional ultrasound imaging in behaving cats to link activity of deep brain areas

to amblyopia. Genetic tools available in mice allow us to test the functional role of brain regions involved in amblyopia in even more detail. This combined method will help us to provide a very robust network view of the origins of amblyopia and serve as a first step to set new and better directions for therapy. Our new method may be applicable to other neurodevelopmental disorders, providing a widely useful tool for clinical diagnosis and basic research.



Legend: A) Human, cat or mouse subject is moving forward in a virtual reality corridor. B) Brief perturbations (halts) of the coupling between self-generated visual flow and locomotion activate prediction error computations while large-scale activity is recorded in each species. This task may reveal the role of prediction computations in amblyopia. C) Functional networks of brain areas will be inferred from species-specific functional ultrasound imaging, 2P imaging, and hd-EEG.