Blue light effect on intrinsically photosensitive ganglion cells of the retina and aggression connectome

Light is considered the most important “zeitgeber” of living organisms (day/night cycle, seasonal variations, reproduction…) playing an essential role as synchronizer between the environment, internal physiology and behaviour. The question of how artificial blue light acts on human brain has become a dominant health issue (ANSES report 2019). Inappropriate chronic use of blue light-emitting devices disrupt sleep and circadian rhythms, both of which can influence alertness, mood, cognition and behaviour and potentially lead to enhanced impulsivity and impaired recognition of social cues, components of uncontrolled aggression.
The non-visual information is mediated by a melanopsinergic pathway (intrinsically photosensitive ganglion cells (ipRGC) sensitive to short wavelength blue light, 460-480 nm), projecting from the retina to the central circadian clock in the hypothalamic suprachiasmatic nuclei (SCN). Besides the regulation of circadian rhythms recent data highlights the direct effects of light on cognition, mood and alertness (Vandewalle et al, Science Report, 2018 ; Fernandez et al, Cell 2018) explained by widespread projections of ipRGCs (Hattar et al. 2006). These projections include nuclei involved in the emotional regulation and aggression system (i.e. medial amygdala (MA), lateral septum, orbital frontal cortex (OFC), hypothalamus and periaqueducal gray (PAG) (Delwig et al, PLOS ONE, 2016, Todd et al, Nature Neuroscience 2018), a neural circuitry which is common interspecies including humans (Nelson and Trainor, Nat Rev Neurosc. 2007). We have demonstrated that monoaminooxydase A KO mice (catecholamines catabolism) chronically exposed to blue light at an inappropriate timing (during the day for a nocturnal animal) are more aggressive than their counterparts exposed to white light without blue.

The aim of this PhD project is to understand how light modulates anatomo-functional links between ipRGCs and aggression connectome in the brain. The **objectives** are 1) to confirm ipRGCs projections towards MA and ventromedial hypothalamus (VMH) as well as the nature of target cells. 2) Characterize the light effect on amygdala connectome by ex-vivo analysis. 3) Study the blue light impact on aggressive behavior of different murine strains.

We will provide training in intra-ocular injections, retina dissection, in vivo experimentation with rodents (habituation, light exposure, behaviour), electroretinograms, multi-electrode arrays, patch-clamp, immunohistochemistry, qPCR, collaboration for fMRI.

The candidate will apply for a PhD Fellowship of the French Ministry of National Education, Higher Education and Scientific Research in June 2020. Training for the selection process will be provided by the host research laboratory.The candidate should have a good working knowledge in neuroscience and physiology. An interest for functional neuroanatomy and electrophysiology is a plus. Send your application (cover letter with motivations, CV with academic grades) to Virginie Laurent-Gydé gydelaurent@inci-cnrs.unistra.fr

Selected publications from the host laboratory :

Goyal V, DeVera C, **Laurent V**, Sellers J, Chrenek MA, **Hicks D**, Baba K, P. Michael Iuvone PM, Tosini G. Dopamine 2 receptor signaling controls the daily burst in phagocytic activity in the mouse retinal pigment epithelium. *Invest Ophthalmol Vis Sci.* Accepté le 25 Mars 2020.

Laurent V, Sengupta A., Sánchez-Bretaño A., Hicks D., Tosini G (2017) Melatonin Signaling Affects the Timing in the Daily Rhythm of Phagocytic Activity by the Retinal Pigment Epithelium. *Exp. Eye Res.*; Dec; 165:90-95.

Gianesini C., Hiragaki S., Contreras-Alcantara S., Laurent V., Hicks D., Tosini G.; Cone viability is affected by interruption of melatonin signaling.Investigative Ophthalmology and Visual Science 2016, Jan 1; 57(1):94-104.3)

Gianesini, C., Clesse, D., Tosini, G., Hicks, D., & Laurent, V. (2015). Unique regulation of the melatonin synthetic pathway in the retina of diurnal female Arvicanthis ansorgei (Rodentia). Endocrinology, EN.2015–1267.