

THE ROLE OF THE BASOLATERAL AMYGDALA (BLA) – PREFRONTAL CORTEX (PFC) AXIS IN SOCIAL COGNITION, HIERARCHY AND COLLABORATION: A CROSS-SPECIES APPROACH

Social behavior is one of the most important driving forces of human society evolution. This has allowed us to reach major achievements in which a large number of individuals are involved with each fulfilling a specialized task. Going to the Moon and back is one of these quoted examples by excellence, but many other tasks on earth remain to be accomplished to resolve concrete problems at hand, which will and will continue to require collaborative efforts from large social groups. An insight in how and why the brain of our species is able to organize individual efforts at such large scale would therefore represent an important goal for human brain research.

Central to social organization are social interactions that ultimately depend on social learning, social decision making and social hierarchy. Such social cognition is of key importance to our understanding of social phenomena ranging from basic evaluations of other individuals to the internalization of social norms and values, i.e. of social cohesion in a group. Especially in humans, hierarchy may be dynamic, depending on particular knowledge and competence in the context of collaboration of experts from different disciplines. In the human brain a number of regions have been identified to play a role in social behavior mostly through non-invasive techniques such as EEG and imaging. However, these only allow to establish correlative relationships between behavior and brain function, since causal relationships would require interventions that are necessarily bilateral so as to clearly affect function in the human brain. These are very rarely found in nature and ethically not (or very exceptionally) justifiable through surgical intervention.

Recently, we have reported a population of humans with individuals that suffer from bilateral calcification of the basolateral part of the amygdala (BLA) as a result of Urbach Wiethe disease (UWD), caused by a very rare genetic mutation. Our most recent observations have also revealed important changes in social and collaborative behaviors in this patient group, suggesting that the BLA and its connections, in particular to prefrontal cortical areas, may play an important role in social relationships. In the present project we would like to explore this role of the BLA and prefrontal cortical areas through a comparative human-animal translational approach in which we will use rats transgenic for oxytocin receptor as animal models. Transgenic rats allow for recordings and interventions in both BLA and PFC, and specific targeting of the oxytocin signaling system. Furthermore, whereas social hierarchy structure is mostly described between male rats, much less is known whether a stable linear social hierarchy structure can be found in females. Moreover, social hierarchy can rapidly change in males, allowing for further potentially interesting comparative insights in the role of gender in this species.

References

- Huber D, Veinante P, Stoop R. Vasopressin and oxytocin excite distinct neuronal populations in the central amygdala. *Science*. 2005 Apr 8;308(5719):245-8.
- Viviani D, Charlet A, van den Burg E, Robinet C, Hurni N, Abatis M, Magara F, Stoop R. Oxytocin selectively gates fear responses through distinct outputs from the central amygdala. *Science*. 2011 Jul 1;333(6038):104-7.
- Charlet A, Knobloch HS, Hoffmann LC, Eliava M, Khrulev S, Cetin AH, Osten P, Schwarz MK, Seeburg PH, Stoop R*, Grinevich V*. Evoked axonal oxytocin release in the central amygdala attenuates fear response. *Neuron*. 2012 Feb 9;73(3):553-66
- Terburg D, Scheggia D, Triana Del Rio R, Klumpers F, Ciobanu AC, Morgan B, Montoya ER, Bos PA, Giobellina G, van den Burg EH, de Gelder B, Stein DJ, Stoop R*, van Honk J. The Basolateral Amygdala Is Essential for Rapid Escape: A Human and Rodent Study. *Cell*. 2018 Oct 18;175(3):723-735 (*lead contact)