Anatomical and functional diversity in amygdala and insula circuits

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Abstract

Anxiety disorders are devastating psychiatric diseases and represent one of the main burden on modern society. However, available treatments remain limited and present debilitating side-effects. The lack of efficient treatment is primarily due to our poor understanding of the underlying neural dysfunctions. Inappropriate assignment of emotional valence and dysfunctions of the circuits that govern valence processing are thought to underlie many psychiatric diseases including anxiety, depression and addiction. The basolateral amygdala (BLA) and the insular cortex (insula) are known to play a critical role in the formation of associative memories of both positive and negative valence and contains multiple populations of projection neurons, including populations targeting the ventral hippocampus (vHPC), the nucleus accumbens (NAc) and the central nucleus of the amygdala (CeA).

To define the critical, yet unknown, role of these neural populations we used a combination of cutting edge technologies in mice models. Using optogenetics to activate or inhibit these populations in vivo, we found that BLA-vHPC projection regulates anxiety-related behaviors, while BLA-NAc population support reward seeking and BLA-CeA population induce avoidance. In addition, insula projection neurons showed an increase calcium signal in anxiogenic spaces and optogenetic activation of insula-CeA populations induces real time place aversion.

By combining large-scale single-unit recordings and optogenetic photo-identification in vivo, we identified that despite the heterogeneity of single-cell coding, BLA-NAc and BLA-CeA populations differentially encode the retrieval of positive and negative associations. Consistently, we provided evidences that experiences of opposite valence differentially regulate the synaptic inputs onto BLA-NAc and BLA-CeA populations. Finally, we identified a topographical organization of the three populations within the amygdala and mapped their local connectivity using ex vivo whole-cell patch-clamp recordings.

Together, our findings reveal that valence encoding in the insula and the amygdala is at least partially accomplished through the divergent activity of anatomically defined neural populations.

Image

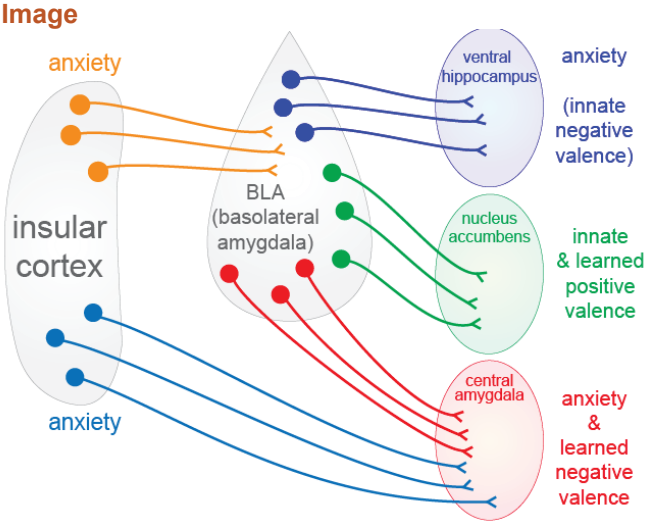


Figure 1: A proposed model for the role of basolateral amygdala and insula projector populations in innate and learned valence. Anxiety is a behavioral state of innate negative valence. *Adapted from Beyeler 2016, Science.*

Recent Publications (*equally contributing / **corresponding authors)

1. Pignatelli M and **Beyeler A. Valence coding in amygdala circuits. **Current Opinion in Behavioral Sciences**, *in press*.
2. **Beyeler A, Chang CJ, Silvestre M, Lévêque C, Namburi P, Wildes CP, **Tye KM. Organization of valence-encoding and projection-defined neurons in the basolateral amygdala. **Cell Reports** 2018 Jan, 22(4), 905–918.
3. **Beyeler A. Parsing reward from aversion, investigating the neural circuits encoding emotional valence. **Science** 2016 Nov 4, 354(6312):558
4. *Beyeler A, *Namburi P, Glober, GF, Simonnet C, Calhoon GG, Conyers GF, Luck R, Wildes CP, Tye KM. Divergent routing of positive and negative information from the amygdala during memory retrieval. **Neuron** 2016 Apr; 90(2), 348–361.
5. *Namburi P, *Beyeler A, …. , Gray JM and Tye KM. A circuit mechanism for differentiating positive and negative associations. **Nature** 2015 Apr; 520(7549):675-8.
6. *Felix-Ortiz A, *Beyeler A, Seo C, Leppla C, Wildes CP, Tye KM. BLA to vHPC inputs modulate anxiety-related behaviors. **Neuron** 2013 Aug; 79(4):658-64.



Biography

Anna Beyeler received her undergraduate degree in Biochemistry from the University of Bordeaux, where she then completed her PhD in Neurosciences. As a postdoctoral fellow at the Massachusetts Institute of Technology, she explored the neural circuit mechanisms underlying rewarding and aversive learning in the amygdala. Dr. Beyeler has now established her independent research program aiming at identifying neural substrates of anxiety disorders in circuits of the insular cortex. The Beyeler Lab is included in the *Neurocampus* of the University of Bordeaux and is part of the Neurocentre Magendie, one of the French national institutes of health (INSERM: instituts national de la santé et de la recherche médicale).

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