Introduction

In Pavlovian auditory Threat Conditioning (PTC), an initially neutral conditioned acoustic stimulus (CS), after being associated with an aversive unconditioned stimulus (US), typically an electric shock, acquires the ability to induce conditioned responses (CR) such as freezing.

The Amygdala is essential for this form of associative learning and memory. The CS and the US information converge in the Lateral Nucleus of the Amygdala (LA) cells. On its part, the Central Nucleus of the Amygdala (CeA) regulates conditioned threat responses.

Most of what is known about PTC and its underlying brain circuitry is based on experiments in which the data is analyzed by averaging measures of different individuals. However, there is great variability on individual conditioned responses.

The use of central tendency measures assumes population homogeneity, and therefore is potentially overlooking the neurobiological basis that might explain exaggerated behaviors.

Results

Figure 1. As expected the individual values of freezing follows a normal Gaussian distribution (D’Agostino & Pearson Omnibus K2=3.458)

Figure 2. Three distinct behavioral phenotypes are found after performing an Unsupervised hierarchical cluster analysis based on Euclidean distances between the average amount of freezing during LTM test of each individual. A) Dendogram constructed from the Euclidean distance matrix. Height Ratio: 71.9% B) Scatter Plot with depicting the 3 clusters in the space.

Figure 3. When memory is tested 48 hours after conditioning, the 3 groups show significantly different level of freezing to each CS presentation (A). The extinction rate and the final level of extinction is significantly different depending on the groups (B). A: Two-way ANOVA F(18,590)=2.423 p<0.0009; B: Two-way ANOVA F(2,118)=11.69 p<0.0001

Conclusions

• Unsupervised data clustering results in 3 clearly different group of animals based on their individual freezing response. Animals showing regular freezing are approximately 70%, 20% exhibit exaggerated freezing while 10% observe any extinction in the high-freezers.

• Low-freezers extinguished faster than do regular-freezers. The repeated presentation of 10 CSs is not enough to treat psychiatric conditions characterized by over-responsivity to auditory stimuli.

• There is a differential neural activity in the Lateral Nucleus of the amygdala matching the level of freezing of the high and the low freezers.

• Finding group-related differential neuropsychological characteristics might be key to understand and potentially treat psychiatric conditions characterized by over-responsivity to auditory stimuli.

The authors like to thank Jennifer Jo Brout, Psy.D. for her intellectual contributions.