Effects of Opioid Antagonists on Fear Conditioning in Long Evans Rats

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An abundance of research has focused on rats' conditioned responses to cues that predict painful stimuli. The pairing of a cue with shocks for one-two days (limited training) typically leads to high fear in tests 1-2 days after the end of the fear conditioning. However, when a subject is exposed to extended fear conditioning (such as 10 once daily fear conditioning sessions) the level of fear is often low soon after training and then grows over time. It is unclear why longer fear training causes lower conditioned fear. One possible explanation for this is that endogenous opioids are released during extended training, so that the tones are paired with ineffective shocks and the rats learn to inhibit their initial fear response to the tones. The objective of my experiment was to block the activity of opioid receptors during extended fear conditioning using the opioid receptor antagonist naltrexone to determine if this would prevent the decrease in fear and lead to conditioned responses that resemble high conditioned fear observed in rats given limited fear training.

I implemented a fear conditioning procedure in which three groups of rats that were trained to lever press for food, followed by conditioned fear training. The experimental group (Extended-Nal) received 10 days of fear conditioning with naltrexone subcutaneously injected before training on days 2-10. The control group (Extended-Saline) received 10 days of fear conditioning but was administered saline injections before training on days 2-10. The third group (Limited) received a single day of fear conditioning to determine whether the blockade of endogenous opioids would cause fear that was equivalent to that after a single day of fear conditioning. The rats were tested two days and one month after the termination of fear conditioning. My results supported the hypothesis, in that the fear in Extended-Nal and Limited groups were higher than the fear in the Extended-Saline group in the day two and one month tests. The Extended-Nal and Limited group did not differ from each other in either test. Unexpectedly, fear did not decrease from day one to the one month in either group. My results suggest that endogenous opioids decreasing the aversiveness of the shocks may be responsible for low fear seen soon after extended fear training, and may help us to understand the hidden fear and anxiety that can occur in people exposed to chronic trauma. Future studies should investigate the relationship between conditioned fear and opioid signaling by determining whether the opioid receptor antagonists lead to a non-associative sensitization of responses to external stimuli that have never been paired with aversive outcomes. In addition, future studies should also examine how the potential pairing of cues with ineffective shocks affects the activity of brain areas responsible for representing fear memories.

Figure 1. Conditioned fear result comparisons in tests conducted between the Limited, Extended-Saline, and Extended-Nal groups on two days and one month after the final fear conditioning session.