Overcoming Fear: The Effect of Anxiolytic Medication Administration on Interval Timing Distracters

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Overcoming fear: the effect of anxiolytic medication administration on interval timing distracters

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Introduction

Time and emotion are linked together, and as such emotions can influence timing abilities. Interval timing, or the ability to measure time in the second and millisecond range is important in the everyday survival of an organism, and also involved in goal achievement activities. Interval timing relies upon the frontal-striatal circuits located within the anterior portion of the brain [1]. The speed of an internal clock depends on the dopaminergic modulation of this circuit [2].

Fear Conditioning

Rats in the FEAR group were presented with an auditory stimulus paired with footshock in a “fear” context (fear chambers). CTRL rats were exposed to the noise, but no footshock was given.

Test sessions: During test sessions, Sminutes after rats were locally infused as described above, rats were placed in the “timing chambers” and presented with “peak” (PI) trials randomly intermixed with “noise” trials, which were similar to PI trials, except for the emotionally-charged noise which was presented unexpectedly during the trial.

Neuropharmacology: Bilateral cannula guides were implanted into the medial prefrontal cortex (mPFC). During test sessions, rats were locally infused with either saline (SAL) or SSRI fluoxetine (FLX) 6ug/0.5ul/side.

Histology: Rats were transcardially perfused with formalin, their brains removed and sectioned for histological analyses. Only rats with correct cannula placement into the mPFC were used in analyses. CTRL, n = 8, FEAR, n = 13.

Methods

Interval Timing: Sprague Dawley rats (300-350g) were trained to lever press for a 40s duration, signaled by a visual signal, in the Peak-Interval (PI) procedure. During testing, the interval timing behavior was tested in “peak” trials. Interval timing behavior was trained and assessed in a “timing context” (timing chambers).

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Conclusions

Interval Timing

• Both CTRL and FLX rats showed accurate timing in the absence of an emotional distracter. As seen, the timing functions peaked near the expected time, indicating that they acquired the interval timing task.

• FLX infusions did not impact timing in the absence of distracters

• Cannula placement did not alter timing behavior

• As shown in previous studies, emotionally paired distractors cause greater delays than novel distracters [6,7].

Effect of Fluoxetine on Timing to Emotional Distracters

• Infusion of FLX at 6ug significantly decreased the shift in responding during distracted trials (PI+N) for FEAR rats

• Infusion of FLX at 6ug significantly increased the shift in responding during distracted trials (PI+N) for the CTRL rats.

• Infusions of FLX 0.6ug were not effective in changing the delay in responding seen under the saline condition

Time Delay vs Fear Extinction

• CTRL group did not show a relationship between freezing fear behavior, indicated by Fear Extinction and time shift, as expected.

• The FEAR showed a statistically significant relationship between freezing behavior and time shift, under both the Saline and FLX 6ug dose.

References