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The BNST Mediates the Anxiogenic Effects of Acute SSRI Administration via
Activation of the Central Nucleus of the Amygdala

Selective Serotonin Reuptake Inhibitors (SSRIs), such as fluoxetine, are used to treat depression and a wide range of anxiety disorders. Typically, it takes several weeks of antidepressant treatment, especially those involving SSRIs, for patients to realize their therapeutic benefits.

Paradoxically, numerous clinical studies and studies using animal models suggest that symptoms of anxiety may actually increase during the early stages of SSRI treatment. Little is known about the underlying basis of such anxiogenic effects. Further, there are no comprehensive studies on the cellular/synaptic effects of SSRIs on the amygdala, a structure that is likely to play a pivotal role in such affective side effects. The contrasting effects of acute and chronic SSRI treatment have been previously captured using auditory fear conditioning, an amygdala dependent learning paradigm. Using this framework, our study aims to elucidate cellular mechanisms underlying the acute anxiogenic effects of SSRIs by studying the impact of the SSRI drug, fluoxetine.

To directly address how systemic treatment with an SSRI affects amygdala activity, we examined the expression of the activity-regulated cytoskeletal-associated protein (Arc) in the amygdala of Sprague Dawley rats treated with the SSRI fluoxetine.

Our findings suggested that acute systemic injections of fluoxetine prior to fear conditioning enhance both conditioning and the expression of Arc in the CE. Furthermore, acute injections of fluoxetine into the BNST, but not the CE, enhance acquisition of fear conditioning. Intra-BNST infusions of fluoxetine prior to fear conditioning enhance expression of Arc in the CE. These data suggest that the BNST may be mediating the anxiogenic effects of fluoxetine via interactions with the CE