# Role of NT3/TrkC in the regulation of fear

## ABSTRACT:

**Background**
Anxiety disorders are among the most prevalent psychiatric conditions, sharing exaggerated fear and resistance to extinction. A role for NT3-TrkC pathway in the regulation of pathological fear has been described, though its role in physiological conditions has never been investigated.

**Aims**
The aim of this project was to investigate the contribution of the NT3-TrkC pathway to the formation and extinction of physiological fear memories.

**Method**
Young adult male mice were trained in the contextual fear conditioning and extinction paradigm, a flagship model to study learned fear and extinction. We used a multidisciplinary approach that combined rodent behavior with pharmacological and molecular tools, and ex vivo electrophysiological recordings, to investigate the cellular and molecular mechanisms underlying the role of NT3-TrkC in fear memories.

**Results**
We found that a strict spatio-temporal regulation of TrkC activation is necessary for the proper formation and extinction of fear memories. Moreover, we identified a role for the amygdalar NT3-TrkC pathway in the naturally existing inter-individual variation in fear extinction in mice. Amygdalar TrkC activation is sufficient to rescue fear extinction deficits through modulation of synaptic plasticity. In particular, activation of TrkC induces LTD, weakens LTP and results in the synaptic accumulation of GluN2B-containing NMDA receptors.

**Conclusions**
Data obtained proves a role for the NT3-TrkC pathway in the formation and extinction of fear memories. This study puts forward TrkC as a molecule of interest in the research of mechanism-based drugs towards patients with fear-related disorders.

**Keywords**
Neurotrophins, Fear extinction, Anxiety disorders, Synaptic plasticity

## Published Work:

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