Chronic fluoxetine treatment induces maturation-compatible changes in the dendritic arbor and in synaptic responses in the auditory cortex

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Fluoxetine is a selective serotonin reuptake inhibitor (SSRI) used to treat mood and anxiety disorders. Chronic treatment with this antidepressant drug is thought to favor functional recovery by promoting structural and molecular changes in several forebrain areas. At the synaptic level, chronic fluoxetine induces an increased size and density of dendritic spines and an increased ratio of GluN2A over GluN2B N-methyl-D-aspartate (NMDA) receptor subunits. The ?maturation?-promoting molecular changes observed after chronic fluoxetine should also induce structural remodeling of the neuronal dendritic arbor and changes in the synaptic responses. We treated adult rats with fluoxetine (0.7 mg/kg i.p. for 28 days) and performed a morphometric analysis using Golgi stain in limbic and nonlimbic cortical areas. Then, we focused especially on the auditory cortex, where we evaluated the dendritic morphology of pyramidal neurons using a 3-dimensional reconstruction of neurons expressing mRFP after in utero electroporation. With both methodologies, a shortening and decreased complexity of the dendritic arbors was observed, which is compatible with an increased GluN2A over GluN2B ratio. Recordings of extracellular excitatory postsynaptic potentials in the auditory cortex revealed an increased synaptic response after fluoxetine and were consistent with

an enrichment of GluN2A-containing NMDA receptors. Our results confirm that fluoxetine favors maturation and refinement of extensive cortical networks, including the auditory cortex. The fluoxetine-induced receptor switch may decrease GluN2B-dependent toxicity and thus could be applied in the future to treat neurodegenerative brain disorders characterized by glutamate toxicity and/or by an aberrant network connectivity.

Antidepressant

Auditory cortex

Dendritic architecture

Neuronal segmentation

NMDA receptors

fluoxetine

monomeric red fluorescent protein

n methyl dextro aspartic acid receptor

n methyl dextro aspartic acid receptor 2A

n methyl dextro aspartic acid receptor 2B

red fluorescent protein

unclassified drug

adult

animal cell

animal experiment

animal tissue

Article

auditory cortex

brain maturation

controlled study

dendritic spine

drug effect

embryo

excitatory postsynaptic potential

female

fetus

Golgi stain

limbic cortex

male

nonhuman

protein expression

pyramidal nerve cell

rat

synapse