Structural and functional abnormalities in the olfactory system of fragile x syndrome models

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Fragile X Syndrome (FXS) is the most common inherited form of intellectual disability. It is produced by mutation of the Fmr1 gene that encodes for the Fragile Mental Retardation Protein (FMRP), an important RNA-binding protein that regulates the expression of multiple proteins located in neuronal synapses. Individuals with FXS exhibit abnormal sensory information processing frequently leading to hypersensitivity across sensory modalities and consequently a wide array of behavioral symptoms. Insects and mammals engage primarily their sense of smell to create proper representations of the external world and guide adequate decision-making processes. This feature in combination with the exquisitely organized neuronal circuits found throughout the olfactory system (OS) and the wide expression of FMRP in brain regions that process olfactory information makes it an ideal model to study sensory alterations in FXS models. In the last decade several groups have taken advantage of these features and have used the OS of fruit fly and rodents to understand neuronal alteration giving rise to sensory perception issues. In this review article, we will discuss molecular, morphological and physiological aspects of the olfactory information processing in FXS models. We will highlight the decreased inhibitory/excitatory synaptic balance and the diminished synaptic plasticity found in this system resulting in behavioral alteration of individuals in the presence of odorant stimuli.

Dfmr1

Excitation/inhibition balance

Fmr1-KO

FMRP

Olfactory behavior

Olfactory coding

Structural plasticity

ataxin 2

calcium calmodulin dependent protein kinase II

Dff related protein 2

disks large homolog 4

fragile X mental retardation protein

Futsch protein

MAP1B protein

metabotropic receptor

microtubule associated protein 5

protein ZC3H14

RNA binding protein

Shrub protein

unclassified drug

Drosophila

fragile X syndrome

gene mutation

hippocampus

human

information processing

intellectual impairment

memory disorder

nerve cell plasticity

neuromuscular junction

nonhuman

olfactory associative learning test

olfactory cortex

olfactory discrimination

olfactory epithelium

olfactory memory

olfactory nerve disease

olfactory receptor neuron

olfactory system

protein expression

protein phosphorylation

Review

short term memory

smelling

translation regulation