THE ADAPTOR PROTEIN Nck1 IS AN IMPORTANT REGULATOR OF ANXIETY

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BACKGROUND: Advances in genomics and proteomics have implicated a number of genes involved in actin polymerization in central nervous system disorders linked to irregular synaptic function. Here we examine the function of Nck1, an intracellular scaffolding protein known to play a role in actin dynamics, in the mouse brain and behavior.

METHODS: Immunohistochemistry and immunocytochemistry were used to identify which cell types and brain regions expressed Nck1. A series of behavioural tests for sensorimotor tasks and anxiety-like behaviours were also conducted. Golgi silver impregnation method was used to visualize dendritic spines in the amygdala. An anxiolytic drug was used to determine if anxiety-like behaviours could be rescued in mice lacking Nck1.

RESULTS: We show that Nck1 is distributed in neurons of brain regions associated with learning, memory, and anxiety. Mice lacking Nck1 displayed increased levels of anxiety-like behaviors, but other behaviours, including vision, olfactory responses and locomotion were indistinguishable from controls. Given the amygdala is associate with anxiety-like behaviours, we focused our further analysis on this region and found fewer synapses and changes in synaptic morphologies. The anxiety behaviours were rescued by treatment with diazepam, a positive allosteric modulator of the $GABA_A$ receptor.

CONCLUSION: Taken together our data suggests that Nck1 is necessary for normal synapse development and the loss of Nck1 leads to the development of behaviors linked to anxiety. Finally, our study proposes that Nck1 is important in controlling neuronal excitability since mice lacking Nck1 remain sensitive to anxiolytic drugs.