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MEETING ABSTRACT Open Access

Fear learning induces structural and functional plasticity at GABAergic synapses in the basolateral amygdala

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Background

Previous work has suggested that alterations in GABAergic function within the amygdala underlie fear learning. In particular, it has been shown that Pavlovian fear conditioning induces a downregulation of benzodiazepine binding sites as well as transcripts for gephyrin and some $GABA_A$ receptor subunits in the basal nucleus of the amygdala (BA), which were restored to control levels after fear extinction.

Methods

We have undertaken a combined anatomical and physiological approach to examine whether these alterations distinctively involve $GABA_A$ receptors in synaptic or extrasynaptic areas. Specifically, we analyzed – in the BA of mice that underwent fear conditioning as well as extinction – miniature inhibitory postsynaptic currents (mIPSCs), mRNA levels by *in situ* hybridization, and the density for the $GABA_A$ γ2 subunit by means of the freeze-fracture replica immunolabelling technique (SDS-FRL). SDS-FRL also allowed to precisely measure the size of GABAergic synapses.

Results

A significant decrease in labelling density for the $GABA_A$ γ2 subunit could be detected in the synaptic area in fear-conditioned mice as compared to the control group and mice that had undergone extinction ($p < 0.01$; Kruskal-Wallis and Dunn's multiple comparison tests). Conversely, $GABA_A$ γ_2 extrasynaptic density was lower in the extinction group when compared to both the control and fear-conditioned mice ($p < 0.005$). The average size of GABAergic synapses in control mice was $0.034 \pm 0.001\ \mu m^2$ (n = 227 full synapses from 3 animals; CV = 0.62). Fear-conditioned animals showed a significantly ($p < 0.01$) larger average synaptic size ($0.040 \pm 0.001\ \mu m^2$; n = 249; CV = 0.59), whereas in fear extinction mice it was similar to controls ($0.031 \pm 0.001\ \mu m^2$; n = 290; CV = 0.59). Alterations in synapse size upon fear conditioning and extinction were associated with functional changes. In neurons recorded from acute slices obtained from fear-conditioned animals mIPSCs were larger (increased charge transfer/mIPSC) compared to recordings obtained from slices of control mice and animals subjected to extinction training. *In situ* hybridization analysis of the mRNA content for $GABA_A$ γ2 subunits revealed highly similar levels among the 3 groups in the BA ($p = 31$, one-way ANOVA) and central nucleus ($p = 41$).

Conclusions

Our results indicate that, in the BA, fear conditioning produces a reversible enlargement of GABAergic synapses and an increase in mIPSC charge transfer with no change in the overall number of synaptic $GABA_A$ receptors.

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