

MEETING ABSTRACT

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# 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<sub>A</sub> 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<sub>A</sub> 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<sub>A</sub>  $\gamma 2$  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<sub>A</sub>  $\gamma 2$  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<sub>A</sub>  $\gamma 2$  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  $0.034 \pm 0.001 \mu\text{m}^2$  ( $n = 227$  full synapses from 3 animals; CV = 0.62). Fear-conditioned animals showed a significantly ( $p < 0.01$ ) larger average synaptic size ( $0.040 \pm 0.001 \mu\text{m}^2$ ;  $n = 249$ ; CV = 0.59), whereas in fear extinction mice it was similar to controls ( $0.031 \pm 0.001 \mu\text{m}^2$ ;  $n = 290$ ; 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<sub>A</sub>  $\gamma 2$  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<sub>A</sub> receptors.

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