INTRODUCTION

Previous gene targeting studies addressing the role of the transcription factor CREB in mammalian long-term synaptic plasticity and memory were compromised by incomplete deletion of the β-isofrm of CREB. Therefore, we studied conditional knock-out lines with a deletion of all CREB-isoforms in the brain or specifically in the mature forebrain and compared them with earlier data obtained in hypomorphic CREB mutants.

METHODS

**Animals**
- deletion of all CREB-isoforms: \( \text{CREB}^\text{NesCre} \) mice
- only mature forebrain: \( \text{CREB}^\text{CamKIICre7} \) mice

**Apparatus**
- Hippocampus-dependent learning: Water maze
- Contextual fear conditioning (pictured)

Hippocampus-independent learning: Conditioned taste aversion (pictured)

**RESULTS ‘WATER MAZE’**

Mutants showed slightly reduced escape performance in the watermaze, reminiscent of the phenotype displayed earlier in the same paradigm by hypomorphic CREB mutants. However, the deficit in the watermaze was unrelated to spatial memory. Most strikingly, \( \text{CREB}^\text{CamKIICre7} \) mice showed normal spatial preference during probe trials (see above).

**RESULTS ‘TASTE AVERSION’**

Conditioned taste aversion was impaired in male (blue) and even more so in female (red) \( \text{CREB}^\text{NesCre} \) mice (solid columns) when compared to the respective wildtypes (dotted columns). In contrast, all mice displayed the same preference for the saccharin solution when consumption of it was not followed by malaise (gray bar).

**CONCLUSIONS**

These data of \( \text{CREB}^\text{CamKIICre7} \) and \( \text{CREB}^\text{NesCre} \) mutants imply that CREB:

1. is not essential for assumedly hippocampus-dependent learning and memory in the mouse;
2. might be of relevance in extrahippocampal regions, and
3. possibly undergoes partial functional compensation in the adult brain through upregulation of the associated transcription factor CREM or other mechanisms.

Further, both \( \text{CREB}^\text{CamKIICre7} \) and \( \text{CREB}^\text{NesCre} \) mutants also show normal hippocampal late-LTP and late-LTD (see Balschun et al., Soc. Neurosci. Abstr. 26, 2000), and the more severe deficits of the earlier hypomorphic mutants might have been caused by low prenatal levels of CREB.

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