EVIDENCE FOR A DECISIVE ROLE OF TRPV1 IN ANXIETY, CONDITIONED FEAR AND SYNAPTIC PLASTICITY

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The transient receptor potential vanilloid type 1 channel (TRPV1; formerly called vanilloid receptor VR1) is known for its key role of functions in sensory nerves such as perception of inflammatory and thermal pain. Much less is known about the physiological significance of the TRPV1 expression in the brain. We used TRPV1 knockout mice (TRPV1-KO) to demonstrate that the absence of TRPV1 leads to reduced anxiety-related behaviour in the light-dark test and in the elevated plus-maze without affecting locomotion. Furthermore, TRPV1-KO mice show less freezing to a tone following auditory fear conditioning and stress sensitisation. This reduction of conditioned and sensitised fear cannot be explained by alterations in nociception. Also tone perception *per se* is unaffected, as revealed by determination of auditory thresholds through auditory brainstem responses and distortion-product otoacoustic emissions. TRPV1-KO show also less contextual fear if assessed one day or one month after strong conditioning protocols. These impairments in hippocampus-dependent learning are mirrored by a decrease in long-term potentiation in the Schaffer collateral-commissural pathway to CA1 hippocampal neurons. Our data provide first evidence for fear-promoting effects of TRPV1 in respect to both innate and conditioned fear, and for a decisive role of this receptor in synaptic plasticity. If we compare the data obtained in TRPV1-KO with those obtained in mice deficient for the cannabinoid receptor type 1 (CB1) it becomes evident that activation of TRPV1 and CB1 by their endogenous ligands seems to provide antagonistic principles that in concert contribute to well-balanced emotional responses and synaptic plasticity.