TRPM2 confers susceptibility to social stress but is essential for behavioral flexibility

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Transient receptor potential melastatin 2 (TRPM2) is a Ca²⁺-permeable, nonselective cation channel and a member of the TRP channel superfamily that acts as a sensor of intracellular redox states. TRPM2 is highly expressed in the brain, but the physiological roles of TRPM2 in the central nervous system remain unclear. In this study, TRPM2-deficient mice were examined in a series of behavioral tests. In the Barnes circular maze, TRPM2-deficient mice learned the fixed escape box position at similar extent to wild-type littermates, suggesting normal reference memory. However, performance of the first reversal trial and probe test were significantly impaired in TRPM2-deficient mice. In the T-maze delayed alternation task, TRPM2 deficiency significantly reduced choice accuracy. These results indicate that TRPM2-deficient mice shows behavioral inflexibility. Meanwhile, social avoidance induced by repeated social defeat stress was significantly attenuated in TRPM2-deficient mice, suggesting that TRPM2 deficiency confers stress resiliency. Our findings indicate that TRPM2 plays an essential role in maintaining behavioral flexibility but it increases susceptibility to stress. (Andoh *et al.*, *Brain Research*, 2018)