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IMAGE

Conditional CRH overexpressing mice: an animal model for stress-elicited pathologies and treatments that target the central CRH system

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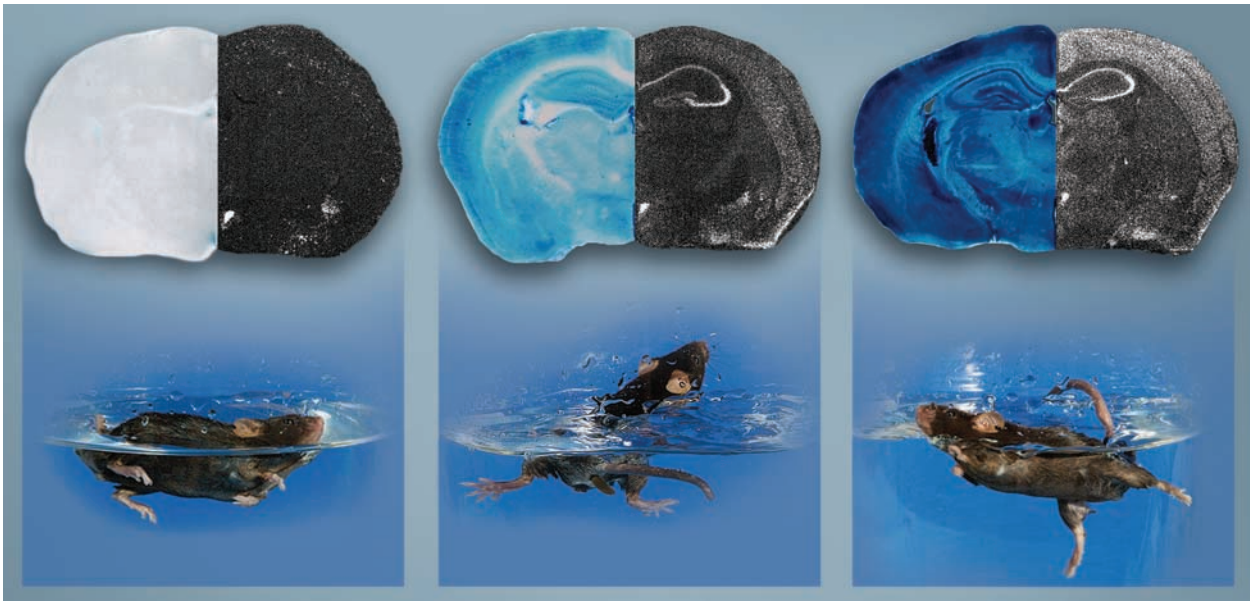

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Conditional mouse mutants overexpressing corticototropin-releasing hormone (CRH) restricted to the central nervous system exhibit enhanced active stress-coping behavior. A highly flexible gain-of-function mouse model was created by combining the properties of the ubiquitously expressed *ROSA26* locus with those of the *Cre/loxP* system. The knock-in of a *Crh-LacZ* expression unit, which is sensitive to activation by Cre recombinase, allows the spatio-temporally controlled overexpression of CRH at different dosages. In control mice (left), only endogenous CRH expression was detectable in the brain, whereas heterozygous (middle) and homozygous (right) CRH-COE-Nes mice expressed increasing levels of exogenous CRH throughout the brain. The pattern of CRH induction paralleled the activation of the simultaneously introduced *LacZ* reporter gene (left brain half). CRH-COE-Nes mice exhibited a marked gene-dosage-dependent increase in active stress-coping behavior as reflected by reduced immobility in the forced swim test (bottom), which depends on catecholaminergic transmission and enhanced activation of the *locus coeruleus*. For more information on this topic, please refer to article by Deussing *et al.* on pages 1028–1042.

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