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Aggression and freezing strategies in mice are positively associated with different genetic mechanism defining tryptophan hydroxylase-2 activity.

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Brain neurotransmitter, serotonin, is involved in the regulation of two opposite strategies in social conflict - aggression and freezing. Serotonin synthesis in brain is catalyzed by the second isoform of tryptophan hydroxylase (TPH-2) encoded by the tph2 gene. Here an evidence of TPH-2 involvement in the molecular mechanism of interaction between aggression and freezing in mice is presented. Hereditary variability in TPH-2 activity in mouse brain was divided into constitutive and regulatory. The constitutive variability links to the C1473G polymorphism in tph2 gene. The replacement C by G decreases TPH-2 activity. The regulatory variability is associated with reversible phosphorylation of the enzyme molecules. An interstrain association between the C1473G polymorphism and the intensity of intermale aggression was found: the number of attacks in mice of C/C genotype is increased compared to G/G mice. Although, no association between freezing and the C1473G polymorphism was demonstrated, mice of CBA strain highly predisposed to freezing had increased TPH-2 activity. The increase of TPH-2 activity in CBA mice is regulatory, since training mice for aggression significantly decreases TPH-2 activity in their brains and completely prevented their freezing. The interaction between aggression and freezing was confirmed by attenuation of aggression during selective breeding for high predisposition to freezing. Thus, two opposite strategies in mouse social conflict, aggression and freezing, are positively associated with different genetic and molecular mechanisms determining TPH-2 activity.

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