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Title: Effects of antidotal galantamine dose on synaptic transmission in hippocampus and basolateral amygdala

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In a recent study carried out in guinea pigs, galantamine, a drug currently used to treat Alzheimer's disease, emerged as an effective medical countermeasure against organophosphorus (OP) toxicity (PNAS 103:13220, 2006). Galantamine (5-8 mg/kg, i.m.) prevents the acute toxicity of 1.5-2.0xLD50s of even the most deadly OPs. However, the effects of galantamine on synaptic transmission and plasticity in the brain of guinea pigs remain unknown. Here, evidence is provided that a single antidotal dose of galantamine (8 mg/kg, i.m.) has acute and delayed effects on synaptic transmission and plasticity in the hippocampus and in the basolateral amygdala (BLA) of prepubertal guinea pigs. Slices were obtained from the hippocampus and the BLA at 1 h, 24 h or 7 days after the treatment of animals with galantamine or saline. Evoked field potentials (eFP) were recorded from the CA1 stratum radiatum of the hippocampus or from the BLA. In BLA slices from saline-treated guinea pigs, partial disinhibition with bicuculline (1 μM) caused substantial facilitation (200-300%) of eFP. At 1 h after galantamine, the threshold to elicit polysynaptic population spikes in the BLA was significantly increased compared to that observed in saline-treated animals. Only 50% of the bicuculline-perfused BLA slices after 1 h showed weak facilitation of eFPs. At 24 h or 7 days after galantamine, bicuculline caused variable degree of eFP facilitation . In BLA slices from saline-treated animals, tetanization resulted in induction of long-term potentiation (LTP). At 1 h after galantamine treatment, only long-term depression could be induced in response to the same tetanic stimuli. At 24 h or 7 days after treatment with galantamine, LTP of various degree could be induced in BLA slices. At 1 h after the galantamine treatment, tetanization resulted in weak or moderate LTP (5-10%) in hippocampal slices. At 24 h or 7 days after galantamine, however, the magnitude of LTP in the hippocampus was comparable to that recorded from saline-treated animals. The reduced excitability and synaptic plasticity observed in the BLA and in the hippocampus of guinea pigs acutely after their treatment with galantamine may result from galantamine-induced modulation of GABAergic inhibition in these areas of the brain.

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