Program#/Poster#: 573.3/I8

Title: Functional alpha7 nicotinic acetylcholine receptors are present in CA1 stratum radiatum interneurons in the hippocampus of guinea pigs

Location: San Diego Convention Center: Halls B-H

Presentation Start/End Time: Tuesday, Nov 06, 2007, 10:00 AM -11:00 AM

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Nicotinic acetylcholine receptors (nAChRs) play important roles in attentional processing, learning and memory in humans. The functional and pharmacological properties of nAChRs have been studied largely in the brains of mice and rats. However, these rodents are short-gestation animals. In short-gestation species, the brain is very immature at birth and the perinatal period represents a critical time window during which the cholinergic system develops (Neuroscience 74:119, 1996). In long-gestation species, including humans, non-human primates, and guinea pigs, the brain has a high degree of neurological maturity at birth (Cell Mol Neurobiol 17:627, 1997). Hence, it may not be valid to extrapolate data from the cholinergic system in rats and mice to all mammals. Therefore, the present study was designed to investigate the presence of functional nAChRs in the neurons of guinea pig hippocampus. Hippocampal slices at 300 µm-thickness were obtained from brains of male and female guinea pigs at postnatal days 7 to 11. Whole-cell patch-clamp recordings were performed on visually-identified CA1 stratum radiatum (SR) interneurons. Short pulses of agonists were delivered via a U-tube. Interneurons voltage clamped at -60 mV responded to choline (10 mM) with nicotinic inward currents that decayed to the baseline within the agonist pulse. The currents had larger amplitudes and faster decay phases as the concentrations of choline increased from 0.3 mM to 10 mM. Choline-evoked currents were sensitive to blockade by nanomolar concentrations of the α7 nAChR antagonists methyllycaconitine (1-10 nM) and α-bungarotoxin (50 nM). The pharmacological and kinetic properties of these choline-evoked responses resembled those of α7 nAChR-mediated type IA currents recorded from CA1 SR interneurons in the hippocampus of rats (J Neurosci 19:2693, 1999). The peak amplitudes of type IA currents recorded from CA1 SR interneurons of guinea pigs ranged between 21 pA and 260 pA (n = 13 neurons), and were generally larger than those recorded from CA1 SR interneurons in the hippocampus of age-matched rats. The magnitude of type IA currrents recorded from the interneurons of 7-11-day-old guinea pigs was more comparable to that recorded from interneurons of young adult rats. The present results suggest that at the end of the first postnatal week the nicotinic cholinergic system is more developed in long- than in short-gestation species.

Disclosures: **M. Alkondon**, None; **E.F.R. Pereira**, None; **E.X. Albuquerque**, None.

Support: NIH Grant U01NS059344
NIH Grant NS25296

[Authors]. [Abstract Title]. Program No. XXX.XX. 2007 Neuroscience Meeting Planner. San Diego, CA: Society for Neuroscience, 2007. Online.