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Interaction between taurine and $GABA_A$/glycine receptors in neurons of the rat anteroventral cochlear nucleus

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ABSTRACT

Taurine, one of the most abundant endogenous amino acids in the mammalian central nervous system (CNS), is involved in neural development and many physiological functions. In this study, the interaction between taurine and $GABA_A$/glycine receptors was investigated in young rat (P13–P15) anteroventral cochlear nucleus (AVCN) neurons using the whole-cell patch-clamp method. We found that taurine at low (0.1 mM) and high (1 mM) concentrations activated both $GABA_A$ and glycine receptors, but not AMPA and NMDA receptors. The reversal potentials of taurine-, GABA- or glycine-evoked currents were close to the expected chloride equilibrium potential, indicating that receptors activated by these agonists were mediating chloride conductance. Moreover, our results showed that the currents activated by co-application of GABA and glycine were cross-inhibitive. Sequential application of GABA and glycine or vice versa also reduced the glycine or GABA evoked currents. There was no cross-inhibition when taurine and GABA or taurine and glycine were applied simultaneously, but the response was larger than that evoked by GABA or glycine alone. These results suggest that taurine can serve as a neuromodulator to strengthen GABAergic and glycinergic neurotransmission in the rat AVCN.

1. Introduction

Taurine is one of the most abundant free amino acids in mammals, especially within the central nervous system (CNS). Animals fed a diet lacking taurine exhibit pathological conditions, such as central retinal degeneration (Wu et al., 2009). Taurine has also been shown to play an important role in physiological functions, e.g., as a modulator involved in antinociception at the spinal cord level (Wu et al., 2008), as a trophic factor during the development of the CNS, and as an osmoregulatory factor maintaining normal cellular osmolality (Hussy et al., 1997, 2001; Schaffer et al., 2000). Furthermore, taurine can

Abbreviations: AVCN, anteroventral cochlear nucleus; $I_{EX(Tau+GABA)}$, the expected sum of currents evoked separately by taurine and GABA; $I_{Tau+GABA}$, the actual currents evoked by a combination of taurine and GABA; $I_{EX(Tau+Gly)}$, the expected sum of currents evoked separately by taurine and glycine; $I_{Tau+Gly}$, and the actual currents evoked by a combination of taurine and glycine; $I_{EX(GABA+Gly)}$, the expected sum of currents evoked separately by GABA and glycine; $I_{GABA+Gly}$, and the actual currents evoked by a combination of taurine and GABA; APV, DL-2-Amino-5-phosphonopentanoic acid; NBQX, 2,3-dihydroxy-6-nitro-7-sulfamoyl-benzo[f]quinoxaline-2, 3-dione

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protect neurons against glutamate-induced injury. The neuroprotective function of taurine is believed to be due to the maintenance of intracellular calcium homeostasis and prevention of apoptosis (Chen et al., 2001; Wu et al., 2009).

Taurine can have inhibitory effect on neurons and has been shown to play an important role in modulation of synaptic transmission (Belluzzi et al., 2004; Xu et al., 2004). The characteristics of inhibitory responses to taurine include membrane hyperpolarization, decrease in membrane resistance, and suppression of spontaneous firing. Most of these effects are mediated by taurine receptor (Wu et al., 1992). Taurine receptor is not up- or down-regulated by agonists and antagonists of other receptors (Wu et al., 1992). It has been reported that taurine activates taurine receptors by opening chloride channels (Taber et al., 1986). Taurine receptor has two subtypes, which are distinct from $GABA_A$ receptors ($GABA_A$Rs) and glycine receptors (GlyRs), but can be partially blocked by the $GABA_A$R antagonist, bicuculline, and the GlyR antagonist, strychnine (Kudo et al., 1988). In addition to activating taurine receptors, taurine can also activate $GABA_A$Rs and/or GlyRs in various brain regions. For example, taurine activates both $GABA_A$Rs and GlyRs in neurons of the substantia gelatinosa, supraopic nucleus, *Xenopus* oocytes, and the hippocampal CA1 area (Horikoshi et al., 1988; Hussy et al., 1997; Wu et al., 2008; Wu and Xu, 2003). Activation of $GABA_A$Rs and/or GlyRs by taurine in some brain regions is concentration-dependent. For instance, at moderate concentrations (0.3 mM) taurine activates GlyRs, whereas at high concentrations (3 mM), it acts as a weak agonist to $GABA_A$Rs in substantia gelatinosa neurons (Wu et al., 2008).

There are a few studies that have examined the pharmacological specificity of taurine to $GABA_A$Rs and GlyRs in central auditory nuclei. Taurine activates GlyRs in neurons of the auditory midbrain, inferior colliculus, and the auditory cortex (Tang et al., 2008; Xu et al., 2004). The taurine-activated currents in these neurons were almost entirely blocked by strychnine but not affected by bicuculline. Knocking out the taurine-transporter gene in mice leads to loss of inner hair cells and degeneration of auditory nerve fibers (Xu et al., 2006). However, little is known regarding the physiological effects of taurine in the AVCN, which is the first synaptic station along the central auditory pathway and plays an important role in conveying and processing peripheral auditory information (Oertel, 1999; Tzounopoulos and Kraus, 2009). It is known that GABA, glycine, and glutamate are major neurotransmitters in the cochlear nucleus (Godfrey et al., 2000; Hackney et al.,

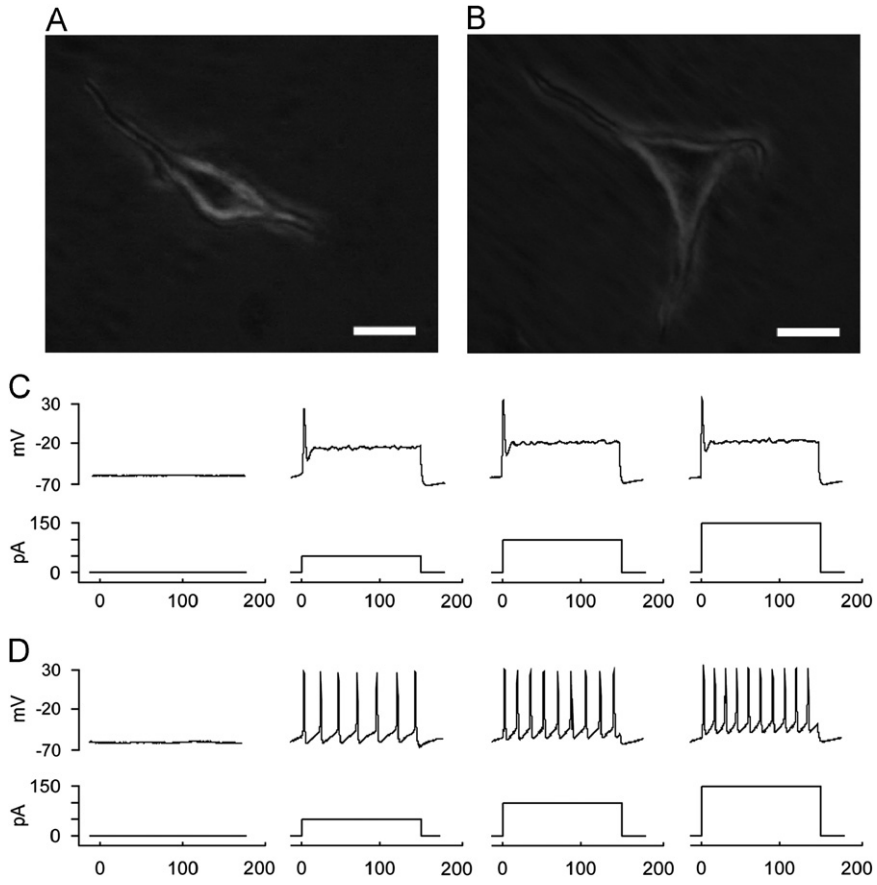

Fig. 1 – Morphology and electrophysiological response properties of isolated AVCN neurons. (A) Morphology of a typical postnatal day (P)14 bushy cell. (B) Morphology of a typical P13 stellate cell. (C) Voltage responses of the same bushy cell shown in (A) to an injection of 0 pA, 50 pA, 100 pA or 150 pA (from left to right traces, current-clamp recordings). (D) Voltage responses of the same stellate cell shown in (B) to an injection of 0 pA, 50 pA, 100 pA or 150 pA (from left to right traces, current-clamp recordings). (Calibration bar: 15 μM in A and B).