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Research report

Auditory inhibitory gating in the amygdala: Single-unit analysis in the behaving rat

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Abstract

Inhibitory sensory gating has been proposed to be a fundamental physiological process that filters neural input. Its temporal properties could allow for a rapid influence on vigilance and attention processes. Inhibitory mechanisms are reflected by reductions in neural responsiveness to repeated and well-predicted stimuli; for auditory gating, this translates into an inhibition of the neural activation to subsequent tone stimuli embedded within sequential and identical tone presentations. Here we expand previous neurophysiological data on inhibitory gating by examining gating in the amygdala using single-unit recording in freely moving animals. Previous data have shown the amygdala to be important in mediating rapid auditory sensory processing involved in emotional conditioning. We measured inhibitory gating with two matching auditory tones presented in a repetitive fashion (10 ms tones, ISI = 500 ms and 10 s between pairs) for 1 h (360 pairs). The majority of the tone responsive units showed inhibitory gating (78/95 units) located in both the medial and lateral subnuclei of the amygdala. Different types of tone responses were gated, including both shorter- and longer-duration excitatory tone responses as well as inhibitory tone responses. Different degrees of gating were found ranging from 100% inhibition (complete gating category) to 25% inhibition (graded gating category). The degree of gating varied over short-term and long-term time intervals. These findings demonstrate the existence of inhibitory gating in the amygdala and provide a detailed description of the basic properties of this rapid neural inhibition that could play an important role in filtering stimulus input.

Theme: Other systems of the CNS
Topic: Limbic system and hypothalamus

Keywords: Auditory processing; Gamma amino butyric acid; Neural inhibition; Aversion; In vivo electrophysiology; Schizophrenia; Autism

1. Introduction

Inhibitory sensory gating has been a useful term for the primary neural filter thought to play a critical role in the selection of incoming sensory information. Traditional definitions for inhibitory gating have emphasized 'gating out' or the blockage of sensory information [21]. More recent definitions have extended the functional role of gating to involve both 'gating out' and 'gating in' as distinct processes. These opponent processes could function interactively to both disable and enable central access for incoming information [10,33,44,73]. A neurophysiological assay to explore gating involves repeated presentations of identical stimuli to gauge the strength of intrinsic inhibitory processes. Physiologists have used this well-established paradigm to examine the role of inhibition in basic neural communication [14,15,21,63,75]. Over the last several decades, clinical neurophysiologists and psychologists have adopted the paradigm and have offered it as a potential neurophysiological indicator of attentional and arousal deficits in patients with cognitive disorders [3,11,23,24]. In the clinical paradigm, the experimenter places the subject in a relaxed setting and presents

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identical auditory stimuli at very short intervals (0.5 s) for an extended session (1-h session). The tones are well predicted and presented at a constant interval (10 s interpair interval) [18,24,50,60]. In the control subject with no attentional deficits, the second auditory evoked potential is dramatically reduced, while in certain patients with cognitive impairment, this inhibition is compromised [2,18,23,39].

Little is known about the basic underlying neurophysiological mechanisms of this clinical observation. Several recent studies have focused on the role of the hippocampus in inhibitory gating [9,20,35,56]. Freedman and colleagues have suggested that inhibitory networks within the hippocampus play a central role in filtering information and that inhibitory gating in this structure influences sensory processing as a dynamic event in several other brain regions [2,23,25,26]. In a recent study recording brain activity from freely moving rats, inhibitory gating was found to be robust in hippocampus, medial septal area, and brain stem regions [57]. Inhibitory gating of the hippocampal response was well correlated with gating in the medial septal nucleus and brainstem reticular nucleus [57]. In contrast, sensory gating in hippocampus was not well correlated with reductions in tone responses seen in auditory cortex, suggesting that the inhibitory gating of an auditory-evoked response depends upon multiple brain circuits including subcortical non-lemniscal pathways which include structures outside of the typical, primary auditory receiving pathway [31].

The amygdala has strong connections with the hippocampus [4,5,64] and has been suggested to be a critical brain structure in the rapid processing of meaningful auditory information [28,48]. Interestingly, the amygdala has been thought to receive auditory information through both a cortical route and a non-cortical, thalamic pathway [37,48]. A growing amount of data has supported the idea that the amygdala plays a key role in basic mechanisms of vigilance related to adaptive responses [27,59,80]. Lesions to the amygdala reduce the rapid, reflexive responses of startle or freezing that are observed to conditioned stimuli following fear conditioning [48]. Recordings of amygdala single units before and after conditioning have shown that neuronal activity can selectively be recruited to auditory stimuli paired with an aversive stimulus [66].

Our aim was to initially characterize the inhibitory gating at the single-unit level in the amygdala and begin to describe the basic temporal and functional properties of the neural inhibition. The functional role of rapid inhibitory gating could substantially vary in different brain regions and depend upon a host of specific properties inherent to the individual brain region. In order to pinpoint these potential unique structure-dependent contributions of inhibitory gating, it is imperative that a detailed characterization of the mechanism be completed at a reduced level of physiological analysis within these different yet interconnected brain regions. If inhibitory gating is important for attentional and motivational processing, then it should play a significant role in amygdala physiology and the processing of sensory input. The results of this work have been presented previously in abstract form [81].

2. Materials and methods

2.1. Animals and surgery

Eighteen male Sprague–Dawley rats weighing 250–350 g were used in these experiments. Animals were singly housed under a reverse light–dark cycle (lights off from 7:00 to 19:00 h). Animals were housed at least 7 days in the reverse light–dark cycle prior to neurosurgery. Recording microwires were implanted following administration of ketamine (100 mg/kg, im) and xylazine (10 mg/kg, im). Two splayed bundles of eight stainless steel Teflon-insulated microwires (50 μm diameter, NB Labs, Denison Texas), soldered onto connecting pins on a headstage, were stereotaxically lowered bilaterally into the amygdala (8 wires per hemisphere). Coordinates for the amygdala from the atlas of Paxinos and Watson [61] were −2.8 mm posterior to bregma, ±4.7 mm lateral to longitudinal suture, and −8.2 mm ventral to the brain surface. Four screws were embedded in the skull for anchoring the implant and for acting as reference grounds. Electrode connectors were secured onto the cranium using dental cement. Rats were allowed 7 days post-surgery to recover before recording was initiated. All procedures were approved by the Wake Forest University School of Medicine Animal Care Committee and all animals were treated in accordance with the U.S. Public Health Service *Guide for the Care and Use of Laboratory Animals*.

2.2. Two-tone paradigm

During the final 4 days of post-surgical recovery, the animals were handled daily to acclimate them to the experimental procedure. Following the 1-week recovery period, animals were taken to the recording chamber and connected to a FET headstage plug with lightweight cabling between a commutator and the implanted microwire assembly. The commutator was free to rotate as needed and this permits unrestrained ambulation of the subject during the recording session. Neuroelectric signals were sent from the headset assembly to programmable amplifiers, filters (0.5 and 5 kHz cutoffs) and a multichannel spike-sorting device (Biographics Inc., Winston-Salem, N.C.). Spike activity and tone presentations were monitored and controlled with custom data acquisition software operating at a time resolution of 1 ms (Magnet Software, Biographics Inc., Winston-Salem, N.C.).