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Research Report

Temporal correlation between auditory neurons and the hippocampal theta rhythm induced by novel stimulations in awake guinea pigs

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ABSTRACT

The hippocampal theta rhythm is associated with the processing of sensory systems such as touch, smell, vision and hearing, as well as with motor activity, the modulation of autonomic processes such as cardiac rhythm, and learning and memory processes. The discovery of temporal correlation (phase locking) between the theta rhythm and both visual and auditory neuronal activity has led us to postulate the participation of such rhythm in the temporal processing of sensory information. In addition, changes in attention can modify both the theta rhythm and the auditory and visual sensory activity. The present report tested the hypothesis that the temporal correlation between auditory neuronal discharges in the inferior colliculus central nucleus (ICc) and the hippocampal theta rhythm could be enhanced by changes in sensory stimulation. We presented chronically implanted guinea pigs with auditory stimuli that varied over time, and recorded the auditory response during wakefulness. It was observed that the stimulation shifts were capable of producing the temporal phase correlations between the theta rhythm and the ICc unit firing, and they differed depending on the stimulus change performed. Such correlations disappeared approximately 6 s after the change presentation. Furthermore, the power of the hippocampal theta rhythm increased in half of the cases presented with a stimulation change. Based on these data, we propose that the degree of correlation between the unitary activity and the hippocampal theta rhythm varies with – and therefore may signal – stimulus novelty.

1. Introduction

The processing of auditory sensory information requires temporal coding and we propose that the hippocampal theta rhythm is involved in this process. The phase and power of the theta rhythm (4–10 Hz) have been shown to vary in response to attention changes (Grastyan et al., 1959; Kemp and Kaada, 1975; Vinogradova, 2001; Pedemonte and Velluti, 2005). Several studies have explored the relationship of the theta rhythm with motor activity itself (Buño and Velluti, 1977; García-Austt, 1984) as well as with the sensory processing of motor activity (Grastyan et al., 1959). This rhythm has even been shown to affect diverse sensory systems such as touch (Nuñez et al., 1991), pain (Vertes and Kocsis, 1997), vision (Gambini et al.,

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Abbreviations: EMG, electromyogram; Hipp, hippocampal field activity; ICc, inferior colliculus central nucleus; PSTH, post-stimulus time histogram; W, wakefulness

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2002) and olfaction (Margrie and Schaefer, 2003). Furthermore, its participation in the modulation of autonomic processes such as the cardiac rhythm was also ascertained (Pedemonte et al., 1999, 2003).

A number of studies have illustrated the functional relationship between the hippocampus and the auditory system (Cazard and Buser, 1963; Redding, 1967; Parmeggiani and Rapisarda, 1969; Parmeggianni et al., 1982), leading to the theory that this rhythm may affect the excitability of distant neurons by inducing membrane potential oscillations (García-Austt, 1984; Kocsis and Vertes, 1992).

The neural activity of the auditory system depends on the information arriving from the external world, the body, and the efferent action of the central nervous system. The brain exerts continuous modulation over sensory processing. This has been observed particularly in the auditory system, a system that never ceases its processing, even during sleep (Velluti, 1997, 2008). Neurons in the central nucleus of the inferior colliculus (ICc) have been shown to exhibit changes in their firing frequency and pattern distribution in correlation with an animal's behavioral state (Morales-Cobas et al., 1995).

The hippocampal theta rhythm has been shown to correlate with the activity of sensory neurons. Auditory cortical spikes exhibit phase locking with the theta rhythm both for spontaneous and evoked firing during wakefulness (W), slow wave sleep and paradoxical sleep, although in different proportions in each case (Velluti, 2008). The theta power also showed changes across different behavioral states (Pedemonte et al., 1996, 2001; Gaztelu et al., 1994). Karashima et al. (2007) observed phase locking between the hippocampus theta and paradoxical sleep pontine waves in response to sound. Visual units of the lateral geniculate nucleus were also studied in relation to the hippocampal theta rhythm and were found to exhibit phase locking during W and sleep (Gambini et al., 2002). Pedemonte et al. (2005) found that frequency-modulated light stimulation produced a correlation during W, which was accompanied by an increase in the theta power.

The abovementioned observations led us to propose the hypothesis that a temporal correlation between ICc neuronal firing and hippocampal theta rhythm can occur by changing the characteristics of the sensory stimulus, thus supporting the theory that this rhythm plays an important role in sensory information processing, i.e. providing the role of temporally organizing and participating in the interpretation of both the auditory signals and any lower rhythms that may be providing relevant information leading to the comprehension of the message that enters the brain. The ICc has been selected for this study since it represents critical crossroads of afferent and efferent information.

2. Results

The unitary activity of 27 ICc neurons was extracellularly recorded in response to changes in auditory stimulation during quiet W, that is those periods of W which exhibit no movements neither by direct visualization nor in the EMG. The changes consisted of increase or decrease of the stimulation rate within a range of 1 to 10 Hz. Auditory stimuli were 50 ms tones at the neuron's best frequency.

Of 149 changes processed, 55 corresponded to pure-tone rate increases, 48 to decreases (both ranging between 1 and 10/s), 26 to stimulation onsets (rhythmical and random stimulation) and 20 to interruptions.

The stimulation shift resulted in temporal correlation (phase locking) between ICc neuronal firing and theta rhythm in 36% cases (54 out of 149), and it lasted ~6 s in most cases. Only one fifth of the cases lasted longer, although never beyond 14 s.

Phase locking occurred in different percentages depending on the stimulation shift. Seventy percent of the correlations were the result of an increase in stimulation (pure-tone rate increase and/or onset of stimulation), while 30% of them corresponded to a decrease in stimulation (pure-tone rate decrease and interruption of stimulation, see Table 1).

In order to verify the statistical significance of the phase locking obtained, the number of temporal correlations before the shifts, considered as control ones, was ascertained and contrasted to the number of temporal correlations immediately after shifts, i.e. provoked by the change in stimulus. The Student's *t* test showed that the number of provoked temporal correlations was significant ($p<0.05$). Moreover, it was observed that stimulation increases produced a statistically higher significant number of correlations ($p< 0.01$).

Fig. 1 is an example of a change in the stimuli presentation from 9 stimuli/s to 1 stimulus/s. In this particular case, a temporal correlation was evident immediately after the change (Fig. 1B) but disappeared after a few seconds (Fig. 1C). The spike shuffling was performed to corroborate that the phase locking in B was real. This temporal correlation was accompanied by an increase in the hippocampal power spectrum within the theta range and the theta waves synchronization, as shown in the autocorrelation.

Among the correlations that responded to stimulation increases (70%), 44% corresponded to stimuli rate increases and 26% to stimulation onsets, changing the stimulus rate from 0 to 3/s or initiating a random stimulus from silence.

Of the 30% that responded to stimulation decreases, 24% corresponded to rate decreases and 6% to stimulation interruptions (passing from stimulus-evoked to spontaneous firing).

The temporal correlation was more frequently observed when stimulating within the theta range, for example when changing from 1 to 6 stimuli/s (64% of cases). Conversely,

Table 1 – Temporal correlations between theta rhythm and ICc spikes, and theta power increases for the different changes performed.

	Temporal correlation %	Theta power increase %
Increase in sound stimulation rate	44	41
Sound Stimulation onset	26	15
Decrease in sound stimulation rate	24	33
Sound stimulation interruption (spontaneous activity)	6	11