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Research Report

Cholinergic modulation of sensory interference in rat primary somatosensory cortical neurons

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ABSTRACT

Sensory interaction was studied using extracellular recordings from 275 neurons in the primary somatosensory (SI) cortex of pentobarbital-anesthetized rats. Tactile stimulation was applied to the receptive field using a 1 mm diameter probe that indented the skin for 20 ms, at 0.5 Hz, (test stimulus). Tactile test responses of SI neurons decreased during simultaneous application of a gentle tickling (distracter stimuli) continuously for 60 s on a separate receptive field located in the same or the contralateral hindlimb (ipsi- or contralateral distraction). This decrease in neural response produced by distracter stimuli was interpreted as "sensory interference". Sensory interference was observed in 66% and 61% of recorded SI neurons when ipsi- or contralateral distracters were applied, respectively and was blocked by a novel stimulus obtained by increasing the stimulation frequency of the test tactile stimuli from 0.5 to 2 Hz. The number of neurons showing sensory interference in response to a contralateral distracter was not modified after corpus callosum transection, suggesting that interhemispheric connections are not crucial for sensory interference. In contrast, the number of neurons showing sensory interference decreased in animals with 192 IgG-saporin basal forebrain lesions that decreased the number of cortical cholinergic fibers. This finding indicates that cholinergic afferents from the basal forebrain are fundamental to sensory interference and suggests that the associative cortices – basal forebrain – sensory cortices network may be implicated in sensory interference.

1. Introduction

When animals explore their environment, somatosensory stimuli are not experienced as isolated stimuli but instead they are sampled along with multiple contextual factors including other stimuli. The ability to focus on selected sensory inputs while ignoring irrelevant inputs is a critical feature of cognition. It must be remembered that sensory response properties are dynamic and depend on interaction between different stimuli (Fanselow and Nicolelis, 1999). Moreover, processing of multisensory stimuli is strongly modulated by attention and by sensory environment (Reynolds and Desimone, 2003; Petkov et al., 2004; Sussman and Steinschneider, 2006).

Recently we reported that the response to tactile stimulation in the primary somatosensory (SI) cortical neurons of

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Abbreviations: ACh, acetylcholine; BF, basal forebrain; ChAT, choline acetyltransferase; GABA, γ-aminobutyric acid; PSTH, summed peristimulus time histogram; RF, receptive field; SI, primary somatosensory cortex

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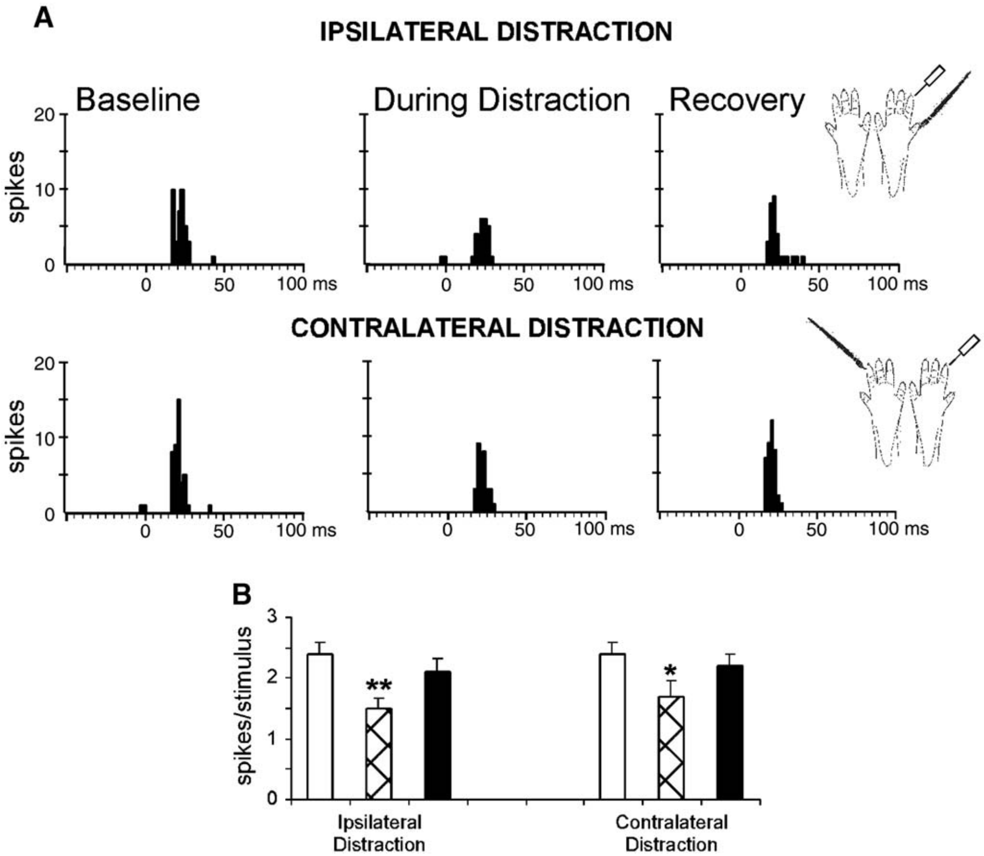

Fig. 1 – SI cortical neurons decreased tactile responses when sensory interference stimuli were applied. A, PSTHs of neuronal responses elicited by test tactile stimulation (left histograms; baseline), during simultaneous application of test tactile stimulation plus a distracter stimulus (paintbrush tickling; middle histograms; during distraction) and by test tactile stimuli again 1 min after the presentation of the distracter stimulus (right histograms; recovery). Zero reference indicates the onset of tactile stimuli ($n=30$). Application of an ipsi- or contralateral distracter decreased test tactile responses. Insets show diagrams of experimental protocols during sensory interference. B, plot of responses elicited by test tactile stimulation before (control) and after distracter stimuli application (open and closed bars, respectively) and during application of ipsi- or contralateral distraction (hatched bars) in SI neurons ($n=71$). Tactile responses decreased during simultaneous application of distracter stimuli in comparison with control values. In this and in the following figures, the asterisk indicates significant statistical differences ($^*p<0.05$, $^{**}p<0.01$).

anesthetized rats decreased when other somatosensory stimuli were simultaneously applied outside of the receptive field (RF; Alenda and Nuñez, 2004). This decrease in the somatosensory response was interpreted as "sensory interference" and the stimulus that elicited sensory interference was considered to be a "distractor". Those data support the idea that cortical sensory responses are not immutable. On the contrary, responses are modulated by many factors, such as the simultaneous presence of other sensory stimuli.

It has also been suggested that the basal forebrain (BF) could participate in sensory interference effects since the muscarinic receptor antagonist atropine blocked sensory interference between tactile stimuli (Alenda and Nuñez, 2004). The BF is the major source of cholinergic afferents to the neocortex (Mesulam et al., 1983; Semba and Fibiger, 1989; Semba, 2000) and cortical responses to sensory stimuli are facilitated by increase in cholinergic transmission (Sillito and Kemp, 1983; Metherate et al., 1987; Tremblay et al., 1990; Himmelheber et al., 2001). Thus, enhanced acetylcholine (ACh) release in these structures may be a neurochemical substrate for cortical arousal or selective attention (Everitt and Robbins, 1997; Sarter and Bruno, 1997; Rasmusson, 2000). There is compelling evidence for a significant role by the BF cholinergic system in attention (Pang et al., 1993; Muir et al., 1994; Voytko et al., 1994). *In vivo* microdialysis studies have shown large and sustained elevations in cortical ACh release during established attentional performance (Himmelheber et al., 2000; Dalley et al., 2001). Recent *in vitro* studies have demonstrated that ACh reduces the efficacy of feedback and intracortical connections via the activation of muscarinic receptors, and increases the efficacy of feed-forward connections via the activation of nicotinic receptors (Gil et al., 1997; Kimura et al., 1999; Hsieh et al., 2000; Metherate and Hsieh, 2004). Thus, ACh may have multiple effects on cortical activity through activation of pre- and postsynaptic cholinergic receptors.

The current study was designed to investigate sensory interference from tactile stimuli in SI neurons of rat and to