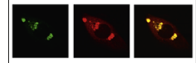


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## Research Report

# Adaptation of the cortical somatosensory evoked potential following pulsed pneumatic stimulation of the lower face in adults

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### ARTICLE INFO

#### Article history:

Accepted 18 June 2015

Available online 26 June 2015

#### Keywords:

Electroencephalography (EEG)

Pneumotactile stimulation

Trigeminal

Neuroplasticity

### ABSTRACT

Cortical adaptation to sustained sensory input is a pervasive form of short-term plasticity in neurological systems. Its role in sensory perception in health and disease, or predicting long-term plastic changes resulting from sensory training offers insight into the mechanisms of somatosensory and sensorimotor processing.

A 4-channel electroencephalography (EEG) recording montage was placed bilaterally (C3-P3, C4-P4, F7-P3, F8-P4) to characterize the short-term effects of pulsed pneumatic orofacial stimulation on the cortical somatosensory evoked potential (cSEP) in twenty neurotypical adults (mean age =  $21 \pm 2.88$  years). A servo-controlled pneumatic amplifier was used to deliver a repetitive series of pneumatic pulse trains (six 50-ms pulses, 5-second intertrain interval) through a linked pair of custom acetal homopolymer probes (*aka* TAC-Cells) adhered to the nonglabrous skin of the lower face proximal to the right oral angle to synchronously activate mechanoreceptive afferents in the trigeminal nerve. Blocks of pulse trains were counterbalanced among participants and delivered at two rates, 2 and 4 Hz.

TAC-Cell stimulation of the lower face consistently evoked a series of cSEPs at P7, N20, P28, N38, P75, N85, and P115. The spatial organization and adaptation of the evoked cSEP was dependent on stimulus pulse index (1–6 within the pulse train,  $p = .012$ ), frequency of stimulus

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<http://dx.doi.org/10.1016/j.brainres.2015.06.025>

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presentation (2 vs 4 Hz,  $p < .001$ ), component (P7-P115,  $p < .001$ ), and recording montage (channels 1–4,  $p < .001$ ). Early component latencies (P7-N20) were highly stable in polarity (sign) and latency, and consistent with putative far-field generators (e.g., trigeminal brainstem, ventroposteromedial thalamus).

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## 1. Introduction

Neural adaptation in response to repetitive stimulation is a fundamental property of sensory systems. In neocortex, this phenomenon represents one of the most ubiquitous forms of short-term plasticity. From a biologic-experiential perspective, adaptive neural mechanisms that facilitate the detection of salient stimuli, or enable the attenuation of sensory responses to redundant stimuli, permit a wide range of response tuning capable of encoding ever-changing environmental conditions. Its potential to characterize the dynamics of sensory perception in both health and disease, or to predict lasting plastic changes that occur as an outcome of sensory training following neural injury remains to be fully explored.

Cortical plasticity and adaptation research over the last several decades has shown that somatosensory representations are not fixed, but remain modifiable throughout the lifespan, with the highest degree of plasticity apparent in the neonatal period of many species. A growing body of literature has identified somatosensory stimulation or combined sensorimotor training as a key beneficial factor in functional recovery of motor output following acute (Lay et al., 2012; Lay and Frostig, 2014) and subacute (Conforto et al., 2010; Dinse et al., 2011) cortical injury, as well as in some instances of incomplete cervical spinal damage (Martinez et al., 2009). The mechanisms underlying the therapeutic effects of sensory stimulation are likely tied to the unique architecture and molecular biology of the somatosensory system, whose design supports dynamic and continuous interaction with the outside environment through motor pathways (Winship and Murphy, 2009; Della-Maggiore et al., 2014; Stehberg et al., 2014).

Synaptic changes associated with short-term somatosensory adaptation are the result of a shift in the balance of excitatory (glutamate-gated NMDA and AMPA, and  $\text{Ca}^{2+}$ -dependent signaling) and inhibitory (GABAergic) neurotransmission (Kim et al., 1995; Kohn and Whitsel, 2002; Rao and Finkbeiner, 2007; Malina et al., 2013). Additionally, global synaptic scaling associated with spike-timing dependent regulation, the recent response history of populations of neurons, and behavioral relevance, also drive and adjust somatosensory cortical plasticity (Abbott and Nelson, 2000; Gambino and Holtmaat, 2012; Li et al., 2014).

From a potentially therapeutic direction, short-term adaptation resulting from exposure to repeated peripheral mechanical stimuli has been shown to enhance intensity and frequency discrimination of supraliminal tactile stimuli (Lundstrom, 1986; Goble and Hollins, 1993, 1994), and improve spatial localization of subsequent stimuli (Tannan et al., 2006). Sustained adaptation can occur following prolonged

stimulation (minutes, hours, days), resulting in changes of extracellular concentrations of ions (Franceschetti et al., 1995; Egelman and Montague, 1998), gene and protein expression (Polleux et al., 2007; Carulli et al., 2011; Vallès et al., 2011), and ultimately axonal sprouting and dendritic arborization which can modify regional connectivity (Lay et al., 2011; Freyer et al., 2012; Nudo and McNeal, 2013). Modifications associated with changing neuronal interaction enable system-wide synaptic signaling flexibility. Stimulation- and activity-dependent changes in cortical neuron receptive fields result from either long-term potentiation (LTP) or long-term depression (LTD) of excitatory post-synaptic potentials (EPSPs) in conjunction with specific activity in presynaptically connected neurons (Buonomano and Merzenich, 1998; Gambino et al., 2014).

This type of neurophysiological restructuring offers enticing prospects for diagnostic and rehabilitative applications. Connections between motor and sensory systems are crucial for developing and maintaining motor skills, particularly in cases of recovery from cortical insult associated with degenerative disease, ischemia, acute vascular accident, or trauma. Apart from overt diminished sensory awareness, damage to sensory systems can result in altered preservation of cortical representations in both sensory and motor cortices. Conversely, plastic changes in somatosensory networks that result from sensory stimulation or relevant behavioral experience can directly affect corticomotoneuronal excitability (Hamdy et al., 1998; Ridding et al., 2001; Kaelin-Lang et al., 2002; Charlton et al., 2003).

As a descriptive tool for neurotypical response, or a diagnostic probe for atypical integrity in disease states, short-term cortical adaptation to sensory stimulation can be assessed with high temporal resolution methods such as EEG and MEG. Historically, much of the neurophysiological information about adaptation to sustained stimuli in humans comes from research using cutaneous electrical stimulation, usually applied to the distal extremities of the upper limb with either biphasic or monophasic current pulses delivered at select frequency and intensity settings (Hamada et al., 2002; Peurala et al., 2002; Wu et al., 2006; Celnik et al., 2007). Comparatively little is known about other body regions, including the trigeminal somatosensory pathway responsible for processing the complex array of cutaneous afferent information associated with facial sensation and proprioception. Additionally, research evaluating non-electrical tactile stimulation as a potential neurotherapeutic application is rare, except in preterm infants in the neonatal intensive care setting learning to orally feed (Barlow et al., 2008, 2014a, 2014b, 2014c; Fucile and Gisel, 2010; Fucile et al., 2012).

Previous research in our laboratory employing non-electrical cutaneous stimulation has shown there are distinctly different response adaptation patterns to repetitive

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