Journal of Neuroscience Methods 218 (2013) 39–47

Contents lists available at SciVerse ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Basic Neuroscience

A vibrotactile behavioral battery for investigating somatosensory processing in children and adults

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ARTICLE INFO

Article history:
Received 1 February 2013
Received in revised form 15 April 2013
Accepted 17 April 2013

Keywords:
Vibrotactile
Behavioral
GABA
Pediatric
Somatosensory
Stimulator

ABSTRACT

The cortical dynamics of somatosensory processing can be investigated using vibrotactile psychophysics. It has been suggested that different vibrotactile paradigms target different cortical mechanisms, and a number of recent studies have established links between somatosensory cortical function and measurable aspects of behavior. The relationship between cortical mechanisms and sensory function is particularly relevant with respect to developmental disorders in which altered inhibitory processing has been postulated, such as in ASD and ADHD. In this study, a vibrotactile battery consisting of nine tasks (incorporating reaction time, detection threshold, and amplitude- and frequency discrimination) was applied to a cohort of healthy adults and a cohort of typically developing children to assess the feasibility of such a vibrotactile battery in both cohorts, and the performance between children and adults was compared. These results showed that children and adults were both able to perform these tasks with a similar performance, although the children were slightly less sensitive in frequency discrimination. Performance within different task-groups clustered together in adults, providing further evidence that these tasks tap into different cortical mechanisms, which is also discussed. This clustering was not observed in children, which may be potentially indicative of development and a greater variability. In conclusion, in this study, we showed that both children and adults were able to perform an extensive vibrotactile battery, and we showed the feasibility of applying this battery to other (e.g., neurodevelopmental) cohorts to probe different cortical mechanisms.

1. Introduction

The cortical dynamics of somatosensory processing can be investigated using vibrotactile psychophysics. It has been suggested that different vibrotactile paradigms target different cortical mechanisms, and a number of recent studies have established links between somatosensory cortical function and measurable aspects of behavior (Hernandez et al., 2000; Puts et al., 2011; Romo et al., 2003). However, links between GABAergic inhibitory neurotransmission and behavioral measures are less well understood. GABAergic inhibition is important in shaping the neuronal response to sensory stimulation (Alloway and Burton, 1986; Dykes et al., 1984; Juliano et al., 1989), and most vibrotactile tasks rely in part on cortical GABAergic inhibitory mechanisms (Tommerdahl et al., 2010). Recent developments have made it possible to measure neurotransmitter concentration noninvasively in humans and correlate these concentrations with measures of tactile sensitivity (e.g., Puts et al., 2011).

Abbreviations: HA, healthy adults; TDC, typically developing children; LD2/LD3, left digit 2 and left digit 3; sRT, simple reaction time task; cRT, choice reaction time task; sD, static detection threshold task; dD, dynamic detection threshold task; nAD, amplitude discrimination – no adaptation; dAD, amplitude discrimination – dual-site adaptation; sAD, amplitude discrimination – single-site adaptation; sqFD, sequential frequency discrimination; smFD, simultaneous frequency discrimination; ISI, interstimulus interval; ITI, intertrial interval.

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http://dx.doi.org/10.1016/j.jneumeth.2013.04.012

The relationship between GABA and sensory function is particularly relevant with respect to developmental disorders in which altered GABAergic processing has been postulated. For example, in Autism Spectrum Disorder (ASD), abnormal cortical structure (Casanova, 2004) and sensory processing (Blakemore et al., 2006; Tommerdahl et al., 2008b) have been linked to GABAergic processing, and GABA-system genetic variants have been proposed as models for ASD (e.g., (DeLorey, 2005)). In Tourette syndrome, both an altered density of GABAergic neurons (Kalanithi et al., 2005) and sensory impairments have been described (Belluscio et al., 2011; Miguel et al., 2000), and GABA gene markers correlate with tic severity (Tian et al., 2011). Finally, GABA reductions have been shown in attention-deficit hyperactivity disorder (ADHD) (Edden et al., 2012), and impaired inhibition during cortical stimulation suggests reduced abnormal GABA interneuron activity (Gilbert et al., 2011). Thus, understanding the differences in sensory processing between groups may allow for a better understanding of cortical (dys)function in health and disease.

In this study, we present a battery of vibrotactile tasks that targeted different aspects of cortical function. We demonstrate their feasibility in healthy adults (HA) and typically developing children (TDC), a prerequisite for future clinical studies, and present normative results. We present these data in the context of previous work in the field (Puts et al., 2011; Tannan et al., 2007a, 2007b; Tommerdahl et al., 2008b; Zhang et al., 2011) (Lee et al., 2012; Nelson et al., 2012; Nguyen et al., 2013a, 2013b; Rai et al., 2012) to compare the performance of children and adults and to investigate patterns of performance. A priori, we would expect absolute levels of performance to differ between the HA and TDC but the relationships between related tasks to be preserved.

1.1. Overview of task groups

1.1.1. Reaction time

A simple reaction time experiment ('press when you feel the stimulus') is a straightforward task for naïve participantsthat allows them to become familiarized with the vibrotactile stimulation. Reaction time has been closely linked to white matter structure (Kerchner et al., 2012; Tamnes et al., 2012) and GABA concentration (Stagg et al., 2011) in healthy subjects. In addition, reaction time has been shown to be altered in developmental disorders (Debes et al., 2011; Schuerholz et al., 1996; Xiao et al., 2012). Reaction time probes both attentional and sensorimotor components.

1.1.2. Detection threshold

The static detection threshold task is a well-known diagnostic tool. An abnormal detection threshold has been used as an indicator of brain dysfunction (Belluscio et al., 2011; Nudo et al., 2000; Staines et al., 2002) and is dependent on both white matter structure (Mountcastle et al., 1972) and GABAergic mechanisms (DeLorey et al., 2011; Tavassoli et al., 2012). In a static vibrotactile detection threshold experiment, the weakest detectable stimulus is typically determined in either a yes/no or a two-alternative forced-choice (2AFC) manner. In contrast, a dynamic vibrotactile detection threshold experiment consists of a stimulus that is increased until perceived (see Zhang et al., 2011). It is thought that pre-detection sub-threshold stimulation mainly activates local feed-forward inhibitory mechanisms (Blankenburg et al., 2003; Favorov and Kursun, 2011; Middleton et al., 2012; Swadlow, 2003), which thereby raises the detection threshold. Comparing dynamic and static threshold measures probes this feed-forward inhibition.

1.1.3. Amplitude discrimination

Discriminating between two stimuli that are simultaneously applied to adjacent digits engages lateral inhibition to separate the response functions of the cortical areas representing each stimulus. A repetitive or 'adapting' stimulus has been shown to sharpen this response function (Whitsel et al., 1989, 2003), either by improving signal-to-noise or spatial resolution. Behaviorally, Hollins and Goble (1993) have shown that single-digit amplitude discrimination is improved by a 5 s adapting stimulus prior to each trial. In a similar fashion, Tannan et al. (2007b) have shown that in a healthy population, dual-site amplitude discrimination is improved when each trial is preceded by dual-site adaptation but is diminished when each trial is preceded by adaptation on only one of the digits. Interestingly, this effect of adaptation is absent in ASD (Tommerdahl et al., 2007).

1.1.4. Frequency discrimination

Discriminating the frequency of two sequentially applied stimuli relies upon temporal processing. McLaughlin and Juliano (2005) showed that frequencies were, at least in part, encoded by the periodic synchronous firing of neuronal ensembles in the primary somatosensory cortex (S1) and that applying a GABA antagonist destroys this periodicity. We have previously shown that individual differences in frequency discrimination performance were correlated with GABA concentration in the sensorimotor cortex, as measured by edited MRS (Puts et al., 2011). In contrast, when frequencies are applied simultaneously to adjacent digits, temporal synchronization between the cortical areas, mediated by GABAergic lateral inhibition, would be expected to disrupt the temporal and periodic encoding of each stimulus, thereby impairing discrimination (e.g., Tommerdahl et al., 2008b).

2. Materials and methods

2.1. Participants

Two cohorts were tested on a tactile battery consisting of nine tasks. Thirteen healthy adults (aged 30.5 ± 4.9 years old; 3 female) and 22 typically developing children (aged from 8 to 12 years old; 2 female) participated in this study. All of the participants were right-handed, which was confirmed using the Edinburgh Handedness Inventory (Oldfield, 1971) in the TDC cohort and by oral report in the healthy adult cohort. All of the TDC were recruited as controls for ongoing studies of ASD and ADHD. In TDC, the Wechsler Intelligence Scale for Children Third or Fourth Edition (WISC-III/IV) was used to assess intellectual ability. Children with full-scale IQ scores below 80 were excluded from participation (average IQ 114.5 ± 11.6). All of the children in the TDC cohort were free of criteria for psychiatric disorders as tested by the Diagnostic Interview for Children and Adolescents-Fourth Edition (DICA-IV), and none of the children in the TDC cohort were prescribed psychoactive medications. Informed consent was obtained from adult subjects and a parent of each child (who themselves assented to testing), under the approval of the Kennedy Krieger Institute and The Johns Hopkins School of Medicine Institutional Review Boards.

2.2. Stimulus delivery

A CM4 four-digit tactile stimulator (Cortical Metrics) was used for stimulation (Holden et al., 2012). All of the stimuli were delivered to the glabrous skin of the left digit 2 (LD2) and digit 3 (LD3) using a cylindrical probe (5 mm in diameter), and all stimuli were in the flutter range (25–50 Hz). Visual feedback, task responses, and data collection was performed using an Acer Onebook Netbook computer, running CM4 software (Holden et al., 2012).

2.3. Experimental design

The vibrotactile testing battery consisted of nine tasks, as shown in schematic form in Fig. 1. Prior to each task, the participants had