Neuroscience 159 (2009) 1032–1043

CORTICAL CORRELATES OF AUDITORY SENSORY GATING: A SIMULTANEOUS NEAR-INFRARED SPECTROSCOPY EVENT-RELATED POTENTIAL STUDY

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Abstract—Sensory gating refers to the ability of cerebral networks to inhibit responding to irrelevant environmental stimuli, a mechanism that protects the brain from information overflow. The reduction of the P50 amplitude (an early component of the event-related potential/ERP in electrophysiological recordings) after repeated occurrence of a particular acoustic stimulus is one means to quantitatively assess gating mechanisms. Even though P50 suppression has been extensively investigated, neuroimaging studies on the cortical correlates of auditory sensory gating are so far very sparse. Near-infrared spectroscopy (NIRS) is an optical imaging technique perfectly suitable for the investigation of auditory paradigms, since it involves virtually no noise. We conducted a simultaneous NIRS-ERP measurement to assess cortical correlates of auditory sensory gating in humans. The multi-channel NIRS recording indicated a specific activation of prefrontal and temporo-parietal cortices during conditions of increased sensory gating (dual-click trials). Combining the hemodynamic data with an electrophysiological index of the "gating quality" (gating quotient Q) revealed a positive correlation between the amount of sensory gating and the strength of the hemodynamic response during dual-clicks in the left prefrontal and temporal cortices. The results are in line with previous findings and confirm a possible inhibitory influence of the prefrontal cortex on primary auditory cortices.

Key words: prefrontal cortex, P50, optical topography.

Sensory gating refers to the ability of cerebral networks to transmit only part of the incoming information and filter out irrelevant stimuli (Freedman et al., 1991), a mechanism that protects the human brain from information overflow. If sensory gating is pathologically reduced, disturbances of signal perception and signal processing may result (Freedman et al., 1987), which has been discussed in the context of schizophrenic illnesses, for example. A well-established possible method of detecting gating mechanisms electrophysiologically is the dual-click P50 paradigm (Adler et al., 1982). Briefly, a first conditioning stimulus (S1) activates inhibitory systems that reduce the response to the second (identical) test stimulus (S2), which is presented very shortly after the first one. The magnitude of the brain's response to these acoustic stimuli is quantified by the P50 event-related potential (ERP) that usually peaks about 50 ms after presentation of the stimuli. An insufficient reduction of the P50 amplitude after the second as compared to the first stimulus indicates a deficient sensory gating mechanism. The ratio Q of the mean test/conditioning response amplitudes (Q=A(S2)/A(S1)) has been defined as a measure of sensory gating, with smaller quotients indicating more effective gating mechanisms.

While healthy subjects usually show a highly significant suppression of the P50 response to the second stimulus, some clinical groups, and particularly schizophrenic patients, have been shown to have a significantly increased gating quotient Q (e.g. Adler et al., 1982; Nagamoto et al., 1989; Freedman et al., 1996; Thoma et al., 2003; Ringel et al., 2004) indicating deficient sensory gating mechanisms. The underlying brain mechanisms that account for impairments in sensory gating are largely unknown, mostly because the exact neural substrates of the P50 wave and their modulation have yet to be elucidated. Detailed knowledge of the neuroanatomical correlates of auditory sensory gating would be a precondition for an appropriate understanding of the functional relevance of the dual-click P50 paradigm and of differences in gating mechanisms between different groups of patients and healthy subjects.

Studies that have investigated this issue so far have mainly been conducted with magnetoencephalography (MEG)/electroencephalography (EEG) source localizations and intracranial EEG recordings in epilepsy patients. These studies repeatedly localized the P50 (or the MEG equivalent M50) within the superior temporal gyrus (primary auditory cortex/Heschl's gyrus; Godey et al., 2001; Edgar et al., 2003; Thoma et al., 2003) with an additional modulation of the P50 response after repeated stimulation in the temporo-parietal and prefrontal brain areas (Grunwald et al., 2003). Weisser et al. (2001) similarly localized the P50 within the auditory cortex and found an additional mid-frontal source. Though informative, these studies provide information about the neuroanatomical generator(s) of the P50 ERP, but not necessarily about the neural structures involved in the gating mechanism that accounts for the *modulation* of the P50 component. Observations that might allow more direct conclusions to be made about

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Abbreviations: BOLD, blood oxygenation level-dependent; DLPFC, dorsolateral prefrontal cortex; EEG, electroencephalography; ERP, event-related potential; fMRI, functional magnetic resonance imaging; HHb, deoxygenated hemoglobin; MEG, magnetoencephalography; MRI, magnetic resonance imaging; NIRS, near-infrared spectroscopy; O_2Hb, oxygenated hemoglobin.

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doi:10.1016/j.neuroscience.2009.01.015

neuroanatomical structures involved in auditory sensory gating come from lesion studies. Knight et al. (1999) report an impaired sensory gating in patients with unilateral lesions within the prefrontal cortex, suggesting that prefrontal damage might disrupt inhibitory modulation of inputs to primary sensory cortices, possibly via a prefrontal–thalamic gating system.

So far, there has been only one direct assessment of the hemodynamic processes accompanying the gating mechanism with a brain imaging method, i.e. functional magnetic resonance imaging (fMRI; Tregellas et al., 2007). This striking lack of direct neuroanatomical assessments of the gating phenomenon is at least partly due to the fact that fMRI is not well suited for an investigation of the classical P50 dual-click paradigm, among other reasons because of the considerable scanner noise involved in such a measurement. Tregellas et al. (2007) did conduct a study on auditory sensory gating in a magnetic resonance imaging (MRI) scanner, which mainly focused on activation differences between schizophrenic patients and a control sample. The authors reported that, compared to the control group, schizophrenic patients showed significantly higher gating quotients Q, as well as increased gating-related activation within the hippocampus, dorsolateral prefrontal cortex (DLPFC), and thalamus (as assessed by the blood oxygenation level-dependent (BOLD) response to repeated-click relative to single-click trials). In line with these findings, they furthermore observed positive correlations across all subjects (patients and controls) between the gating quotient Q and the BOLD response to repeated clicks in all three aforementioned regions.

However, the study unfortunately lacks any direct assessment of the strength (significance) of single- and repeated-click-induced activation within each of the two groups; similarly, the correlation analyses were solely performed for the sample as a whole, with no differentiation between patients and controls. Therefore, information on areas showing gating-specific activation in healthy controls, or on the usual relationship between the gating quotient Q and hemodynamic responses, cannot easily be deduced from the data presented by the authors. Moreover, for methodological reasons, Tregellas et al. (2007) did not use a classical P50 gating paradigm for the fMRI measurement, and they did not simultaneously assess the ERP gating responses (instead measuring ERPs separately with a classic P50 paradigm that differed from the one employed in the MRI scanner). Near-infrared spectroscopy (NIRS) is an optical imaging technique that might be a promising alternative for further investigations of the neuronal substrates of auditory sensory gating, because it involves virtually no noise, and a simultaneous recording of ERP responses is very easily possible.

First introduced by Jöbsis (1977), NIRS is an optical imaging method that allows the performance of non-invasive *in vivo* measurements of changes in the concentration of oxygenated (O_2Hb) and deoxygenated (HHb) hemoglobin in the brain. It uses light in the near-infrared range (700–1000 nm wavelength), which easily penetrates biological tissue such as the skull. Once injected into the head, near-infrared light is multiply scattered and partly absorbed; the main absorbers of near-infrared light in brain tissue are the chromophores O_2Hb and HHb. The part of the light that is not absorbed along its path from light source to detector and eventually leaves the head again after a number of scattering events has traveled a so-called banana-shaped sampling volume that comprises the brain tissue in between the light emitter and detector (cf. Obrig et al., 2000; Villringer and Chance, 1997; Lee et al., 2005). Thus, a banana-shaped curve best describes the mean photon path of reflected near-infrared light in the tissue. From the amount of reflected near-infrared light, it is then possible to calculate changes in the concentration of O_2Hb and HHb in living brain tissue by employing near-infrared light absorption characteristics and two-wavelength absorption data. As for the depth of penetration of the near-infrared light, there is agreement on the fact that NIRS can detect changes in hemoglobin concentration on the cortical surface at least covering the top 2–3 mm of the cortex (Firbank et al., 1998).

NIRS methods have increasingly and successfully been employed in functional activation studies. The underlying idea is that when brain activity increases within a particular part of the cerebral cortex, blood supply to this area increases as well, as does the level of O_2Hb. The consumption of oxygen during brain activity leads to an increase in HHb that is, however, soon compensated by the increase in blood supply, which eventually results in a decrease in HHb. These changes in the concentration of O_2Hb and HHb can be detected by means of NIRS, and, in summary, activation of a particular brain region is thought to be reflected in an increase in O_2Hb and a corresponding decrease in HHb (Hoshi and Tamura, 1993, 1997; Villringer et al., 1993; Hock et al., 1995; Hirth et al., 1996; Obrig et al., 1996). Recently, two improvements of the NIRS technique have been implemented. First, task designs employed in NIRS studies have been expanded from blocked to event-related designs, where hemodynamic responses to single events are measured (Schroeter et al., 2002; Jasdzewski et al., 2003). Second, multi-channel NIRS systems have been developed that allow non-invasive functional mapping of the cerebral cortex (e.g. Maki et al., 1996; Watanabe et al., 1996, 1998; Matsuo et al., 2003; Horovitz and Gore, 2004; Ehlis et al., 2005). Since NIRS involves low-noise measurements, it is a method perfectly suitable for paradigms involving auditory stimulation (Kennan et al., 2002), and previous studies have indeed shown that NIRS can measure hemodynamic responses within the auditory cortex (e.g. Minagawa-Kawai et al., 2002). From a theoretical point of view, Okamoto et al. (2004) showed that the depth of the cortical surface relative to the scalp differs between brain regions but does not exceed an average of 2.3 cm at its deepest point, with the relevant parts of the temporal cortex lying approximately 1.1–1.6 cm below the scalp. This is a depth easily accessible by a standard NIRS approach.

The aim of the present study is to investigate cortical substrates of auditory sensory gating by means of multi-channel NIRS conducted in an event-related fashion. By