Somatosensory Input to Auditory Association Cortex in the Macaque Monkey

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1Cognitive Neuroscience and Schizophrenia Program, Nathan Kline Institute for Psychiatric Research, Orangeburg 10962; 2Department of Neuroscience, 3Department of Psychology, and 4Department of Neurosurgery, Albert Einstein College of Medicine, Bronx 10461; and 5Department of Psychiatry, New York University Medical Center, New York, New York 10003

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Schroeder, Charles E., Robert W. Lindsley, Colleen Specht, Alvin Marcovici, John F. Smiley, and Daniel C. Javitt. Somatosensory input to auditory association cortex in the macaque monkey. J Neurophysiol 85: 1322–1327, 2001. We investigated the convergence of somatosensory and auditory inputs in within subregions of macaque auditory cortex. Laminar current source density and multiunit activity profiles were sampled with linear array multielectrodes during penetrations of the posterior superior temporal plane in three macaque monkeys. At each recording site, auditory responses to binaural clicks, pure tones, and band-passed noise, all presented by earphones, were compared with somatosensory responses evoked by contralateral median nerve stimulation. Subjects were awake but were not required to discriminate the stimuli. Borders between A1 and surrounding belt regions were identified by mapping best frequency and stimulus preferences and by subsequent histological analysis. Regions immediately caudomedial to A1 had robust somatosensory responses co-represented with auditory responses. In these regions, both somatosensory and auditory response profiles had “feedforward” patterns; initial excitation beginning in Lamina 4 and spreading to extragranular laminae. Auditory and somatosensory responses displayed a high degree of temporal overlap. Anatomical reconstruction indicated that the somatosensory input region includes, but may not be restricted to, the caudomedial auditory association cortex. As was earlier reported for this region, auditory frequency tuning curves were broad and band-passed noise responses were larger than pure tone responses. No somatosensory responses were observed in A1. These findings suggest a potential neural substrate for multisensory integration at an early stage of auditory cortical processing.

INTRODUCTION

The brain’s ability to combine inputs from different sensory modalities yields an enriched description of objects as well as converging evidence concerning their position, movement, and identity. For such “multisensory integration” to occur, requires that at some point in sensory processing, excitatory signals arising from different sense modalities converge onto either single neurons or interconnected ensembles of neurons. In the first case, single neurons would be directly excitable through each modality. In the second case, single neurons would be excitable through one modality and might also be subject to more subtle modulatory influences (excitatory and/or inhibitory) from the other. Although neither type of convergence guarantees occurrence of multisensory interactions (Stein and Meredith 1993), they collectively provide the necessary anatomical substrates for such interactions. Definition of the brain areas in which convergence occurs is therefore fundamental to our understanding of the brain mechanisms of multisensory processing and integration.

Prior studies in primates have demonstrated multisensory convergence in parietal (e.g., Duhamel et al. 1998; Hyvarinen and Shelepin 1979), temporal (e.g., Benevento et al. 1977; Bruce et al. 1981; Leinonen et al. 1980), and frontal regions of neocortex (e.g., Graziano et al. 1994; Rizzolatti et al. 1981). It is noteworthy that these studies typically find both “multisensory” neurons with clear excitatory inputs from two or more modalities (i.e., convergence at the neuronal level) and, in the same cortical area, intermingled populations of apparently “unimodal” neurons with different input sources (i.e., convergence at the areal/ensemble level).

The present study expands on a preliminary finding of a somatosensory input to auditory association cortex. Our methods entail analysis of current source density (CSD) and multiunit action potential profiles sampled with linear array multielectrodes in awake macaques. CSD analysis provides an estimate of transmembrane current flow, which is the first-order response to synaptic input. Analysis of concomitant multiunit activity reveals the degree to which synaptic activity generates a net change in local action potentials. Collection of these measures with a linear array electrode enables us to gauge the laminar activation sequence, which helps to differentiate feedforward from feedback and lateral input patterns (Schroeder et al. 1995, 1998). While these methods do not address convergence at the single neuron level, they provide for an efficient, well-controlled evaluation of multisensory convergence at the neuronal ensemble level.

METHODS

One rhesus and two cynomologus macaques (Macaca mulatta and M. fascicularis), weighing 5–8 kg, were prepared for chronic awake...
recording used aseptic techniques, under general anesthesia (pentobarbital sodium, 25–35 mg/kg iv) (Schroeder et al. 1998). During recording, animals were monitored continuously using electroencephalography (EEG) and video displays and were maintained in an alert state but were not required to attend or discriminate stimuli in any sensory modality. Laminar CSD and multiunit activity (MUA) profiles were collected bilaterally from sites in A1 and the adjacent regions posterior to A1, concentrating on caudomedial (CM) auditory cortex. CSD profiles were calculated from field potential profiles using a three-point formula for estimation of the second spatial derivative of voltage (Freeman and Nicholson 1975; Nicholson and Freeman 1975). MUA was obtained from the signal at each contact by high-pass filtering the amplifier output at 500 Hz to isolate action potential-frequency activity, full-wave rectifying the high-frequency activity, and averaging the single sweep responses together. With the rectification step, each averaged MUA tracing (see e.g., Fig. 1) is in effect an action potential histogram; upward deflection represents activity increase and downward deflection represents activity decrease relative to the prestimulus baseline. See Schroeder et al. (1998) for further details and illustration of these methods.

Figure 1 illustrates the positioning of the electrode array for laminar profile analyses. For quantification, CSD profiles were full-wave rectified, then averaged into a single waveform (AVREC; see Fig. 1), and grand mean responses were computed across subjects.

Auditory stimuli were delivered at 65 dB (SPL) binaurally through Sennheiser HD565 headphones coupled with 50-ml tubes placed against the external auditory canal (Javitt et al. 1996). A combination of 100-μs clicks and 100-ms pure tones and band-passed noise (5 ms on/off ramps) was used to characterize best frequency and to optimize stimulation at each recording site. For routine assessment of the best frequency at each site, we analyzed responses to pure tones presented at 2/α (Steinschneider et al. 1998). Specifically we measured the peak of the MUA onset, in a window of 0–50 ms poststimulus, at the Lamina 3–4 border. At each site, a first approximation of the tuning curve was derived by taking this measurement from responses to 0.5, 1, 2, 4, 8, 16, 20, and 30 kHz. In some cases, the tuning estimate was further refined as indicated by the first approximation, but the first approximation was the only measure available for all recording sites.

Averaged responses to optimized stimuli were obtained at each recording site. Co-located somatosensory responses were quantified using electrical stimulation of peripheral nerves from the hand; 100-μs square-wave (constant current) electrical pulses were delivered with gold cup EEG electrodes to the skin over the median nerve in the forearm contralateral to the recording site (Peterson et al. 1995; Schroeder et al. 1995, 1997) and constant 80-dB white noise masked any co-incident auditory stimulation. It was established earlier that repetitive electrical stimulation of the median nerve at the wrist produces an averaged response in somatosensory cortex, extremely similar to that produced by repetitive cutaneous stimulation of the appropriate (radial) half of the glabrous hand surface. Specifically, Schroeder et al. (1995) showed that in “median nerve territory in primate Area 3b, the timing and distribution of action potentials and

FIG. 1. Laminar current source density (CSD) and concomitant multiunit activity (MUA) profiles (each an average of 100 trials) sampled using a multielectrode with a linear array of recording contacts (150-μm spacing) straddling auditory Area CM. Auditory (left) and somatosensory (right) responses were elicited in this site by binaural 65 dB clicks and contralateral median nerve stimuli, respectively. Downward CSD deflections (dark) signify net extracellular current sinks (inward transmembrane current); upward deflections (stippled) indicate net extracellular current sources (outward current). MUA histograms are obtained by full-wave rectification and averaging of the high-frequency activity at each electrode contact. The boxes circumscribe CSD configurations that reflect the initial excitatory response at the depth of Lamina 4, and the subsequent excitation of the pyramidal cell ensembles in Laminae 2/3. Scale bar (bottom right) = 1.4 mv/mm² for CSD, 0.1 mv/mm² for AVREC, and 1.6 μV for MUA.
CSD components evoked by electrical stimulation of median nerve and by stimulation of the volar surface of digit 1, were equivalent (see Schroeder et al. 1995, Fig. 1 vs. 3A). In the same recording site, neither electrical stimulation of the ulnar nerve nor cutaneous stimulation of the volar surface of digit 5 produced a measurable response (Schroeder et al. 1995, Figs. 2B and 3C). Thus median nerve electrical stimulation clearly produces a specific “somatosensory” response. In the present study, the definition of the median nerve-evoked response as a somatosensory response is supported by the specificity of its cortical distribution (see following text).

Recording sites were confirmed by histological analyses. Serial sections were made and every third one was stained for Nissl substance, acetylcholine esterase (AchE) or parvalbumin (PV) to help determine the borders between A1 and surrounding regions (Hackett et al. 1998; Kosaki et al. 1997; Morel et al. 1993).

RESULTS

Areal convergence of somatosensory and auditory inputs, as illustrated in Fig. 1, was found in 10/18 sites we examined that were in auditory cortex, immediately posterior to A1. As detailed in the following text, somato-auditory convergence sites were concentrated in the caudomedial (CM) belt region of auditory association cortex. The laminar profiles of co-represented auditory and somatosensory responses describe a characteristic activation sequence triggered by ascending synaptic inputs in sensory cortex (Schroeder et al. 1995, 1998; Stein-schneider et al. 1998): initial depolarization of input terminals in and near Lamina 4, along with discharge of stellate cells, producing a current sink over source configuration (lower boxes) and associated action potentials, followed by excitation of supra- and infragranular pyramidal cells. To allow better visualization of the temporal pattern of synaptic activation in Lamina 4 and lower Lamina 3, data from an additional somatosensory input site in auditory cortex are presented on an expanded scale in Fig. 2. The excitatory CSD configuration in supragranular pyramidal cells is typically source/sink (upper boxes, Fig. 1), with associated action potentials displaced below this to the base of Lamina 3. With the stimuli used here, only the initial phase of excitation in the pyramidal cell ensemble is reflected in action potentials.

Under the present conditions, somatosensory and auditory responses in CM begin at nearly the same time and have similar amplitude at the first response peak; however, the former tend to have larger amplitude during the later time course of the response. This is shown by representative patterns of auditory and somatosensory response from single penetration sites in each of the three monkeys (Fig. 3A) and the grand mean data for the same conditions, across subjects, in CM (Fig. 3B).

A1 penetrations, as distinguished by anatomical location (see penetration 1, Fig. 4A), demonstrated no somatosensory responsiveness (Fig. 3C). This fact supports the sensory specificity of the median nerve-evoked response (Schroeder et al. 1995). Sites displaying somato-auditory co-representation were located in the caudal belt/parabelt regions. Reconstruction of three penetrations through this region is illustrated in Fig. 4B. Two of these were in medial sites (3 and 4) and showed clear somatosensory responsiveness, while the penetration through a more lateral site (2) showed none. All sites...
discussed in this report had robust auditory responses. The overall distribution of auditory alone and somato-auditory convergence sites is represented in Fig. 4C. As illustrated there, somato-auditory convergence sites appeared concentrated in the CM but may extend posterior to CM into the adjacent parabelt.

As reported earlier (Merzenich and Brugge 1973; Rauschecker et al. 1995, 1997; Recanzone et al. 2000a), frequency tuning in posterior sites (Fig. 5, B and C) was broad relative to that in A1 (Fig. 5A). This is apparent even with the approximation methods used in this study. With the same methods, the sharpness of best frequency tuning in sites showing somatosensory input in the regions posterior to A1 (Fig. 5B) cannot be distinguished from that in sites unresponsive to median nerve stimulation (Fig. 5C). We would not rule out the possibility that more precise testing in a larger sample would show such a distinction.

**DISCUSSION**

The present study demonstrates areal convergence of somatosensory and auditory inputs within posterior auditory as-

**FIG. 4.** A: a parvalbumin (PV) immunolabeled section showing an electrode penetration (1) in the PV-rich zone that corresponds to A1. B: a section through auditory association cortex posterior to A1 in the same hemisphere, lacking the PV-rich zone corresponding to A1. Arrows mark the point at which each of the 3 visible electrode tracks (2–4) sampled from auditory cortex. LS, lateral sulcus. C: a depiction of the recording sites examined in this study. To make this figure, the pattern of penetrations in each of the 6 brain hemispheres we sampled was reconstructed with respect to the caudal border of A1, and these were collapsed across hemispheres and subjects and registered onto the histological reconstruction of caudal superior temporal plane in one subject. The sections were separated by 800 μm.

**FIG. 5.** Auditory frequency tuning curves for recording sites in A1 (A) and for sites posterior to A1, including those exhibiting convergent somatosensory input (B) as well as those posterior sites without convergent somatosensory input (C). Values represent the response to each stimulus frequency as a percentage of the peak amplitude for the largest multiunit response measured at the Lamina 3/4 border in each recording site. See text for further details.

somatosensory input to auditory cortex in the macaque monkey. The convergence appeared concentrated in Area CM but may not be confined to this area. Because CM represents an early stage of cortical auditory processing, only one step removed from A1 (Kaas et al. 1999; Rauschecker et al. 1997; Recanzone et al. 2000b; Romanski et al. 1999), the somatosensory input is unexpected. The only functional indications of somato-auditory conver-
gence in this region are indirect and come from human experiments. Magnetoencephalographic recordings (Levanen et al. 1998) have localized vibration-induced activation within auditory cortex in congenitally deaf humans. Although it should be emphasized that this result has not been shown in subjects with normal hearing, event-related potential (ERP) studies in normal humans have observed short-latency somato-auditory integration effects having a time course and voltage topography consistent with an ERP generator source in the superior temporal plane (Foxe et al. 2000).

Both the auditory and somatosensory activation profiles in CM have a characteristic “feedforward” pattern, predicted by the anatomy of feedforward projections (Rockland and Pandya 1979); excitation begins in Lamina 4 and spreads to the extragranular layers (Fig. 2). Although spatially overlapping neuronal populations in CM are clearly activated by each modality (areal convergence), the proportion of local neurons that exhibit excitatory somato-auditory convergence relative to those with unisensory excitatory input remains to be determined.

Even assuming that there is excitatory convergence in a high proportion of single neurons, the strength and nature of any resulting multisensory interactions is an open question, which we are presently unable to resolve. We regard the actual integration of somatosensory and auditory input within CM neurons as a likely possibility, although alternatives are equally interesting. Independent use of single neurons (or intermingled populations of neurons) by separate sensory modalities, for example, would represent a novel and intriguing use of cortical architecture.

An earlier study observed somato-auditory convergence within single units in area Tpt (Leinonen et al. 1980), but Tpt is within the “parabelt” region of auditory cortex (Hackett et al. 1998), whereas our recordings were mainly in CM, which corresponds to a part of the “belt” region of auditory cortex (Hackett et al. 1998). Several studies have suggested that body maps exist in the region caudolateral to the insula and SII/PV cortices (Burton and Robinson 1981; Krubitzer et al. 1995; Leinonen 1980; Robinson and Burton 1980). However, because none of these investigated somato-auditory convergence, the degree of correspondence, if any, between the somatosensory inputs we describe and those defined earlier is not yet clear.

In the present study, somatosensory stimulation was confined to the afferents from the hand, and thus we cannot comment on the nature of the body map in CM. Krubitzer et al. (1995) reported one or more partial body maps that abut the SII/PV body maps in the fundus of the lateral sulcus and extend out onto the superior temporal plane; that is, into a region that very likely includes CM. This finding clearly predicts the somato-auditory convergence we report here but does not tell us whether CM contains a full body map or a representation that is biased toward a particular surface(s), similar to the “hand” and “face-biases” found for somatic input to visual areas MIP and VIP (Duhamel et al. 1998). This question is a specific target of our ongoing studies.

The functional significance of somato-auditory convergence in CM may be related to spatial localization in keeping with the hypothesis that the caudal auditory cortices in general are specialized for this function (Kaas 1999; Rauschecker et al. 1995; Romanski 2000). There does appear to be spatial correspondence between the auditory and somatosensory receptive fields of Tpt neurons (Leinonen et al. 1980), but this has not been investigated in CM. While there are only a few studies of spatial receptive fields in auditory cortical neurons (Ahissar et al. 1992; Benson et al. 1981; Recanzone et al. 2000), one of these does suggest a special role for CM in sound localization (Recanzone et al. 2000). A related possibility is that caudal auditory regions are part of a network that combines vestibular with other sensory inputs to compute the position of the head in space and/or in relation to the other parts of the body (Gulden and Grusser 1998). Somato-auditory convergence would be extremely useful in such computations.

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