

No indication of brain reorganization after unilateral ischemic lesions of the auditory cortex

Abstract—We used magnetoencephalography to study contralesional auditory reorganization in three men with chronic unilateral ischemic lesions of the auditory cortex. Although no response was found over the lesioned hemisphere, processing in the unaffected hemisphere was indistinguishable vs healthy controls. In contrast to sensorimotor and language systems, the auditory system seems to lack contralateral reorganization, presumably because patients are typically not aware of hearing deficits and thus do not perform training.

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Functional neuroimaging of patients with stroke revealed that clinical recovery of sensorimotor or language deficits is usually paralleled by the reorganization of neural networks.¹ Such findings corroborate the widely accepted view that neural circuits are dynamic and adapt to changing input and behavior, even in adults. In the human auditory system, plasticity of the auditory cortex has been demonstrated in conjunction with environmental influences, training, or injury of the peripheral auditory system.² Previous studies, however, investigated auditory plasticity after peripheral damage. If and to what extent expanded lesions of the auditory cortex are correlated with reorganizational changes in the contralateral hemisphere have not been sufficiently investigated yet.

We used magnetoencephalography (MEG) to investigate auditory processing in three patients with complete middle cerebral artery (MCA) infarction. MEG allows the recording of cortical magnetic fields with utmost temporal and reasonable spatial resolution. We hypothesized that a large unilateral cerebral lesion, destroying the entire auditory cortex of one hemisphere, alters auditory processing in the intact hemisphere even in the absence of subjective perceptual impairment.

Methods. We studied 3 men, 15 to 21 months after a first-time ischemic infarction of the MCA and a complete lesion of the auditory cortex (age 32, 44, and 65 years). Patients had no subjective auditory deficit, normal audiometric hearing thresholds, and normal language comprehension (token test). The control group con-

sisted of 12 healthy, age-matched male volunteers (mean age 44 years). Patients and controls gave their written informed consent to participate in the study. The study protocol was approved by the Research Ethics Board of the Faculty of Medicine, University of Münster, Germany.

We presented 160 trains, each consisting of four successive stimuli (the vowel *a*), with an interstimulus interval of 450 milliseconds and a randomized interval between trains of 4 to 5 seconds. Stimuli were presented contralateral to the studied hemisphere, through a plastic tube to a silicon earpiece, with an intensity of 60 dB above the individual hearing threshold. Auditory evoked fields were recorded successively from both hemispheres using a 37-channel biomagnetometer system (Magnes, BTi, San Diego, CA; sample frequency = 512.4 Hz). Magnetic waveforms were averaged and bandpass filtered (0.01 to 40 Hz).

The analysis focused on the N1m peak, occurring approximately 100 milliseconds after stimulus onset, and the decrement of the N1m with rapid stimulation, also known as habituation or sensory gating.³ The N1m is assumed to reflect the conscious detection of discrete changes in the auditory environment. The decrement of the N1m is believed to represent cortical filtering of irrelevant input. To obtain a representative dipole of the N1m, we calculated a single equivalent current dipole for each sampling point and averaged the dipole parameters for a 30-millisecond time window around the activity peak (response to first stimulus of series). This N1m dipole was used to calculate the amplitude of the dipole moment over the entire epoch. Dipole moments were measured relative to baseline (–50 to 0 millisecond prestimulus).

The relative amplitudes (RSS) of the second, third, and fourth N1m responses were calculated as $RSS(N1m_i) = 100 \times N1m_i / N1m_1$, where $N1m_i$ ($i = 2, 3, 4$) denotes the amplitude of the i -th N1m response. To assess the variability of these measures in the control group, bootstrapped 95% CIs were calculated (R for Mac OS X).

Results. While robust N1m responses were recorded from the intact hemispheres of the patients, no evidence of time-locked cortical activity was seen in the lesioned hemispheres (figure 1, B and D). In the unaffected hemispheres of the patients, amplitude, latency, and dipole location of the first N1m fell within the range of controls. The relative amplitudes of the second through fourth N1m waves were within or close to the 95% CI of controls (figure 2). All relative amplitudes of the patients were within the range of controls, except the second N1m in Patient 3.

Discussion. We investigated auditory processing in three chronic stroke patients with massive hemispheric ischemia and a complete, unilateral lesion of the auditory cortex. These patients provided the opportunity to study potential contralateral changes of poststroke auditory processing without confounding ipsilateral reorganization. Because of the bilateral representation of each spiral ganglion, unilateral lesions of the auditory cortex rarely provoke manifest

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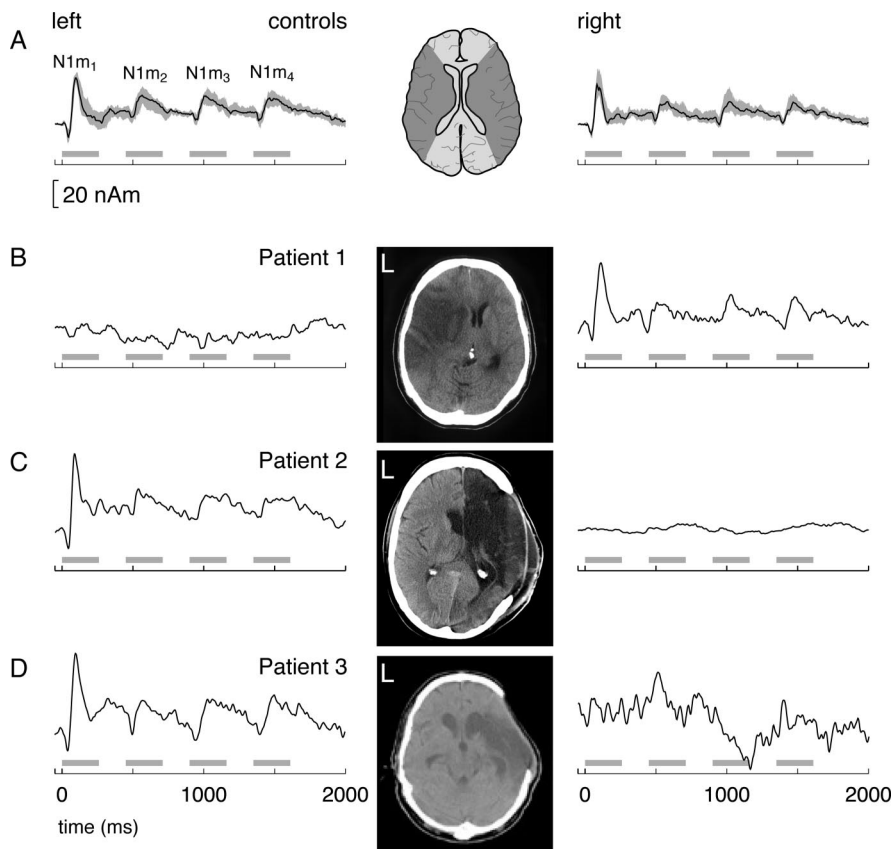


Figure 1. Auditory evoked fields (AEFs) in three patients with middle cerebral artery (MCA) infarction and an age-matched control group of healthy men. (A) Median amplitude (black waveform) as well as upper and lower 95% CIs (gray shading) in the control group. The four consecutive N1m responses are labeled. The boxes below the waveform represent the four rapidly recurring acoustical stimuli (duration of single stimuli, 260 milliseconds). The dark areas in the schematic brain slice represent the territory of the MCA. (B) AEF of Patient 1 (44 years, complete left MCA infarction). (C) AEF of Patient 2 (32 years, complete right MCA and anterior cerebral artery infarction). (D) AEF of Patient 3 (65 years, right MCA infarction). Over the affected hemispheres, no N1m responses are detectable. Normal N1m responses were found over the intact hemispheres of the patients. To demonstrate the extension of the stroke, CT images of the acute phase are shown. Patients 2 and 3 were treated with hemispherectomy (the skull defect is visible over the right hemisphere).

sensory symptoms perceivable by the patients. Accordingly, our patients had no subjective hearing impairment or deficits in pure tone audiometry or speech perception. Auditory evoked responses over the lesioned hemisphere were absent, indicating that the entire auditory processing was performed in the intact auditory cortex. In contrast to our initial hypothesis, however, the contralesional N1m response was indistinguishable from the control group regarding amplitude, latency, and source location. Although these results corroborate a previous report of a single patient with a chronic ischemic lesion in the right auditory cortex and its vicinity,⁴ they stand in sharp contrast to well-established findings for the motor, somatosensory, and language system, where monohemispheric lesions may result in recruitment

of perilesional cortical areas or in activation of contralesional homologs.⁵

In view of the severe neurologic deficits of our patients, we confined ourselves to contralateral stimulation, to keep the measurement time short. Therefore, we cannot exclude that ipsilateral stimulation might have resulted in increased latencies, similar to findings in patients with frontotemporal infarction, in whom the N1m peak latencies after stimulation ipsilateral to the lesioned hemisphere were significantly longer than in healthy controls.⁶ We also might have overlooked neural correlates of the recovery of sound localization. In cats, primates, and humans, it has been shown that unilateral lesions of the primary auditory cortex are often associated with deficits of sound localization.⁷ A behavioral study suggested, however, that patients with an impaired sound localization after early hemispherectomy may recover over time.⁷

The presented results may seem unexpected because several lines of evidence suggest that the neuronal organization of the auditory cortex is plastic throughout life, similar to the motor and other sensory systems. Recent results from rehabilitation science may provide an explanation, suggesting that cortical reorganization is driven by and dependent on meaningful training of impaired functions.⁸ Patients with unilateral lesions of the auditory system do not perform such training because they are typically not aware of hearing deficits, and audiologic examinations mostly fail to reveal manifest disor-

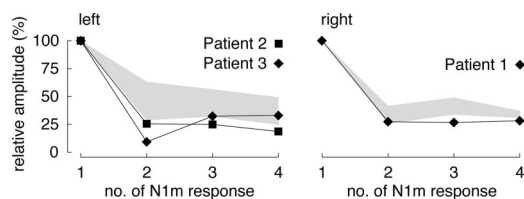


Figure 2. Relative amplitude of the four consecutive N1m responses in three patients with middle cerebral artery infarction and an age-matched control group of healthy men ($n = 12$). The amplitudes of the second, third, and fourth N1m responses were normalized to the amplitude of the first N1m, separately for each subject. The gray area represents the upper and lower 95% CIs for the control group.

ders.⁹ In this respect, they crucially differ from patients with lesions of the sensorimotor strip or the language cortices, who typically experience marked losses of function. In addition, the subcortical structures of the auditory pathways comprise more synapses than the visual or somatosensory pathways, and they exhibit bilateral projections. The more complex organization of the auditory system may result in subcortical changes after MCA infarction, which are not necessarily noticeable as cortical reorganization.

As a result of an acute unilateral brain lesion, cortical excitability may increase in both the perilesional and the homologous contralateral areas of the human brain.¹⁰ To study this aspect in our patients, the short-term decrement of the N1m was evaluated. Consistent with healthy controls, the unaffected hemispheres of our patients showed an amplitude decrease of approximately 50% from the first to the second N1m (figure 2). The relative amplitudes of patients were near the lower 95% CI of controls. Only in one case (Patient 3, second N1m) was the relative amplitude outside the range found in the control group. As this is a statistical evaluation involving multiple comparisons, such an outlier does

not seem remarkable. The current study does not provide evidence for increased excitability in the auditory cortex of patients with chronic stroke. However, an increased auditory decrement in such patients cannot be ruled out.

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