Pergamon

www.elsevier.com/locate/neuroscience

PII: S0306-4522(01)00072-0

Neuroscience Vol. 104, No. 2, pp. 347–358, 2001
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0306-4522/01 $20.00+0.00

EVIDENCE OF PERIPHERAL AUDITORY ACTIVITY MODULATION BY THE AUDITORY CORTEX IN HUMANS

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Abstract—At the auditory periphery, the medial olivocochlear system is assumed to be involved in complex sound processing and may be influenced by feedback from higher auditory nuclei. Indeed, the descending auditory pathway includes fibers coming from the auditory cortex that are anatomically well positioned to influence the superior olivary complex, and thus the medial efferent system. The aim of the present study was to verify the hypothesis of an implied influence of the auditory cortex on the peripheral auditory system. In three rare cases of patients presenting with intractable temporal lobe epilepsy, Heschl's gyrus (i.e. the temporal superior gyrus) was surgically removed in the right hemisphere in two patients and in the left hemisphere in a third patient, in order to minimize epilepsy attacks, as preoperative stereo-encephalography had shown the epileptic focus or tumor to be situated in those locations. In all three cases, several weeks after the operation the medial olivocochlear system was clearly less functional on both sides, but especially on the side contralateral to the resection. In healthy controls, no such pattern was obtained. In four other epileptic patients, who were operated unilaterally at the anterior temporal pole, amygdala and hippocampus with the temporal gyrus partially spared, efferent suppression grew stronger in the ear ipsilateral to surgery.

These results revealed that, in humans, the primary and secondary auditory cortex play a role in modulating auditory periphery activity through direct or indirect efferent fibers. In accordance with previous findings, this descending influence may improve the auditory afferent message by adapting the hearing function according to cortical analysis of the ascending input. © 2001 IBRO. Published by Elsevier Science Ltd. All rights reserved.

Key words: temporal lobe, medial olivocochlear system, auditory descending pathways.

Progressive and sequential information processing takes place along the auditory afferent pathways, from the auditory nerve to the cerebral cortex. This hierarchical organization is superimposed upon a parallel arrangement of auditory pathways that may be specialized in processing particular aspects of acoustic information.[55] It is striking to note that most auditory pathways are reciprocal, which implies that the auditory system is rich in reciprocal descending projections, often quite numerous, so that the function of a given auditory nucleus can be influenced by feedback through another, hierarchically higher, auditory nucleus.

A brief description of the ascending auditory pathway begins with the auditory nerve, which originates in the cochlea and sends its axons to the cochlear nucleus in the brainstem. Ascending inputs, which for the most part cross after the cochlear nucleus, are received by the three contralateral superior olivary complex nuclei. The auditory information then passes through the lateral lemniscus to the inferior colliculus,[1] before reaching the medial geniculate nucleus of the auditory thalamus. Finally, these projections head towards the auditory cortex, which in cats and humans constitutes a large part of the superior temporal gyrus, that corresponds to Brodman area 41 (Heschl's gyrus), the primary auditory cortex,[19] and Brodman areas 42[7] and 22, the associative auditory cortex.

Information that is processed in the auditory cortex is redistributed in subcortical centers. There are also auditory fibers coming from the inferior colliculus that synapse onto the superior olivary complex and cochlear nucleus. These connections are anatomically quite well established in the cat,[3,4,56] but their functional role is much more difficult to demonstrate, especially in humans.

At a peripheral level, the medial superior olivary complex is the target of efferent projections from the CNS.[61] As illustrated in Fig. 1, medial olivocochlear (MOC) neurons receive input from the auditory cortex[18] and from the ipsilateral inferior colliculus,[64,65] the latter being the possible origin of excitatory terminals and a major synaptic station along the descending auditory pathway.[2,27,43,44] The main efferent projections come from the auditory cortex, both to the medial geniculate body of the auditory thalamus and to the inferior colliculus;

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Abbreviations: ANOVA, analysis of variance; ATL, anterior temporal lobe; BAER, brainstem auditory-evoked response; EA, equivalent attenuation; MLR, middle latency response; MOC, medial olivocochlear; MRI, magnetic resonance imaging; T1, superior temporal gyrus; TEOAE, transiently evoked otoacoustic emission.

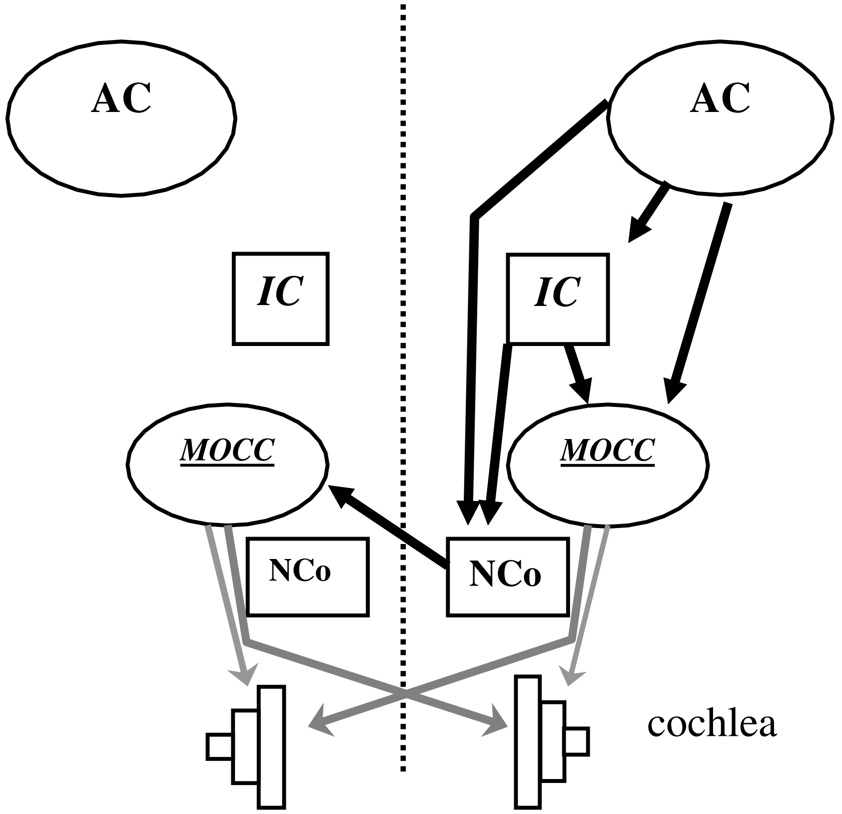

Fig. 1. Main descending auditory pathways. Schematic representation of the main descending auditory pathways susceptible for modulating MOC system activity. AC, auditory cortex; IC, inferior colliculus; MOCC, medial olivocochlear complex; NCo, cochlear nucleus.

from the inferior colliculus, they go to both the cochlear nucleus and the superior olivary complex. It is striking that, from the superior olivary complex, neurons are in direct contact with the outer hair cells of the cochlea. In addition, the medial superior olivary complex receives ascending tonotopically organized bilateral input, both directly and indirectly, from the anteroventral cochlear nucleus.[24,63] In summary, from an anatomical perspective, the MOC efferent system could be modulated by auditory cortical efferents via both the inferior colliculus and the ventral cochlear nucleus, but not via the thalamus.

The methods employed in animals to study descending auditory pathways are often invasive and damaging to the brain.[47,57] Consequently, they are not applicable in humans. However, MOC system activity can be assessed non-invasively through transiently evoked otoacoustic emission (TEOAE) recording, using the method developed by Bray and Kemp.[8] TEOAEs are sounds which arise following an acoustic stimulation; they can be easily measured in the ear canal,[30] and are generally thought to correspond to the active mechanical function of the outer hair cells of the organ of Corti.[9] Given that descending MOC fibers directly synapse these outer hair cells, the functioning of the MOC system originating in the medial superior olive of the brainstem[25] can be precisely assessed by measuring its action on the outer hair cells, in terms of the TEOAE amplitude suppression elicited by contralateral acoustic stimulation which activates the MOC efferent system.[66] This efferent suppression has previously been assessed in animals through the measurement of compound action potentials.[35] Differences as large as 10 dB have been observed between the effective attenuation computed from the compound action potentials and the otoacoustic emissions.[51] However, even if MOC system assessment via otoacoustic emissions[43] results in lesser values, this efferent reflex is equally as strong in humans as it is in animals.[51] As validated in both research and clinical domains,[67] the efferent suppression effect differs quantitatively according to the methods employed, all of which lend to the notion that efferents influence sound-in-noise detection.[21,72] To assess this peripheral suppression, an equivalent attenuation (EA) calculation procedure is classically used.[12,14] We are thus able to measure a peripheral auditory system function in humans: the MOC system, the projections of which are mainly contralateral, crossing at the level of the floor of the fourth ventricle.[69]

Thus, there is much functional and anatomical evidence for an MOC system involvement in feedback loops, including peripheral and central auditory structures.[62] An original approach for evaluating the central influence on the MOC complex consists of testing the influence of a cognitive attention task involving higher centers on MOC performance. Although controversial results have been obtained during visual and auditory attention tasks,[20,37,38,40] these studies suggest the involvement of MOC system activation during these tasks. However, there has been no clear demonstration of the cortical influence on this system, or of the mechanisms and structures which might be involved.

To verify that the olivocochlear bundle, a terminal link in a chain of descending pathways, constitutes the instrument whereby the auditory cortex is able to regulate peripheral processing of auditory information, we decided to test MOC system functioning before and after partial resection of the auditory cortex in humans. Certain cases of intractable temporal epilepsy are remediable only by surgery.[70] In three rare cases of patients with temporal lobe epilepsy, the temporal superior gyrus, including the primary and secondary auditory cortical areas, was partially or totally surgically removed in order to minimize epilepsy attacks, as preoperative stereoencephalography had shown the epileptic focus or tumor to be situated in those locations.

Our aim was then to evaluate the effect of the absence of the auditory cortex in one hemisphere on the MOC systems on both sides, which are the only system regulating the outer hair cells of the cochlea, and thus the onset of auditory processing. The three patients studied were compared to four other patients showing mesial temporal lobe epilepsy operated on unilaterally at the temporal pole, amygdala and hippocampus, with the superior temporal gyrus partially spared, as well as controls with no pathology but tested on two occasions (i.e. before and after surgery) so as to mimic the epileptic patient's auditory tests.

In this manner, we have related MOC dysfunction to drastic cortical alterations that modify the ability to process speech, in order to find new clues regarding efferent function.

EXPERIMENTAL PROCEDURES

Subjects

The consent of patients and healthy volunteers was obtained in accordance with the Declaration of Helsinki, and the non-invasive tests used in this experiment were approved by the Lyon Hospital Ethical Committee. None of the patients had any known auditory disorders.

Unlike in animal studies, it was not possible to test intermediate auditory pathway nuclei, but an attempt was made to control as many parameters as possible so as best to understand the influence of the superior temporal gyrus on auditory structures. Classic clinical magnetic resonance imaging (MRI) made it possible to check, on scans, the precise location of the gliose or tumors and the areas removed. The functional status of the auditory pathway was measured in epileptic patients by recording brainstem auditory-evoked responses (BAERs) and middle latency auditory-evoked potentials, before and after surgery, to assess damage to the higher auditory pathways.[33] Handedness laterality quotient was assessed using the Edinburgh Handedness Inventory.[46] Hemisphere language specialization was determined using the Wada test[34,68] and the alteration of language processing caused by the lesion was assessed, to a certain extent, using a verbal dichotic test.[39]

The preoperative tests were performed within 10 days of surgery, and included the dichotic listening test, MOC system functioning assessment, and BAER and middle latency response (MLR) measurements. A second round of testing was performed two months postoperatively and any process occurring within this delay should yield the same results across all subjects. This phase included the dichotic listening test, BAER and MLR recording, MRI, and measurement of the efferent system suppressive effect.

Electrophysiological recordings

During the electrophysiological recordings, subjects lay down in a sound-proof room and electrodes (A1, A2, C3, C4, F3, F4, Fz) were positioned according to the International 10–20 system.[28] The reference electrode was placed on the earlobe ispsilateral to the acoustic stimulation. For MLR recording (Na and Pa waves), an analogic filter (1500–3000 Hz) was used. Averaging was performed on 2000 samples and the acoustic stimulus was a rarefaction click of 80 dB HL presented at a rate of 9.2 per second. For BAER recording, the stimulus was a 100-μs 80-dB HL click applied to one ear, with a 20-dB HL masking of the contralateral ear by a white noise. The recurrence frequency was 19.3 Hz, bandpass 5–1500 Hz and sweep time 60 ms. Each series averaged 2000 stimulations and at least two series for each stimulation ensured the reproducibility of the traces. Series that were overly contaminated by the myogenic responses were rejected.

Healthy controls

Fifteen healthy right-handed subjects (eight male and seven female) aged from 22 to 27 years (mean age = 23 years, S.E.M. = 1.12) were volunteered for the experiment. They had normal hearing, with less than 20 dB loss for auditory thresholds between 250 and 8000 Hz by octave, measured with the AD28 Diagnostic Audiometer. They were tested once and then again a few weeks later, to reproduce the same conditions as for the epileptic patients.

Anterior temporal lobe epileptic patients

Four patients with intractable mesial temporal lobe epilepsy were tested within 10 days of, and eight weeks after, surgery. The left hemisphere was operated on in one patient (patient 4), a right-handed, 27-year-old male. The other three patients (patients 5–7) were operated on in the right hemisphere; they were right-handed females aged 25, 40 and 54 years. MRI showed that patient 4 had a removal in the left anterior temporal lobe (ATL) including the amygdala and hippocampus. The postoperative MRI images of patient 6 in coronal and horizontal sections are shown in Fig. 2. It can clearly be seen that the unilateral temporal pole, amygdala and hippocampus were surgically resected. Patients 5–7 showed a removal of the right temporal lobe, sparing only the posterior part of the superior temporal gyrus (T1), while retaining the anterior part of T1 (5 cm), the medial temporal gyrus to inferior temporal gyrus (8 cm) from the pole, and the amygdala and hippocampus. These patients took the same anti-epileptic treatment before and after their operations.

Superior temporal gyrus excision patients

Three patients had rare temporal epilepsy with epileptogenic focus precisely located in T1, of the left hemisphere for one right-handed 28-year-old male patient (patient 1), and of the right hemisphere for the two others (patients 2 and 3), a right-handed male and a left-handed male, aged 53 and 27 years, respectively. Patient 1 had a removal of the left T1 (10 cm) and medial temporal gyrus (8 cm from the pole), sparing the amygdala and hippocampus. The postoperative horizontal MRI image of the right superior temporal gyrus resection of patient 2, who had a total removal of the right T1, is shown in Fig. 3, although in patient 3, only the posterior part of the right T1 was removed. These patients received the same anti-epileptic treatment before and after their operations.

Pre- and postoperative auditory test: medial olivocochlear system functioning assessment

The subjects were placed in a reclining position in a silent room. For both ears of each subject, separate magnitude–intensity functions, representing the growth in TEOAE

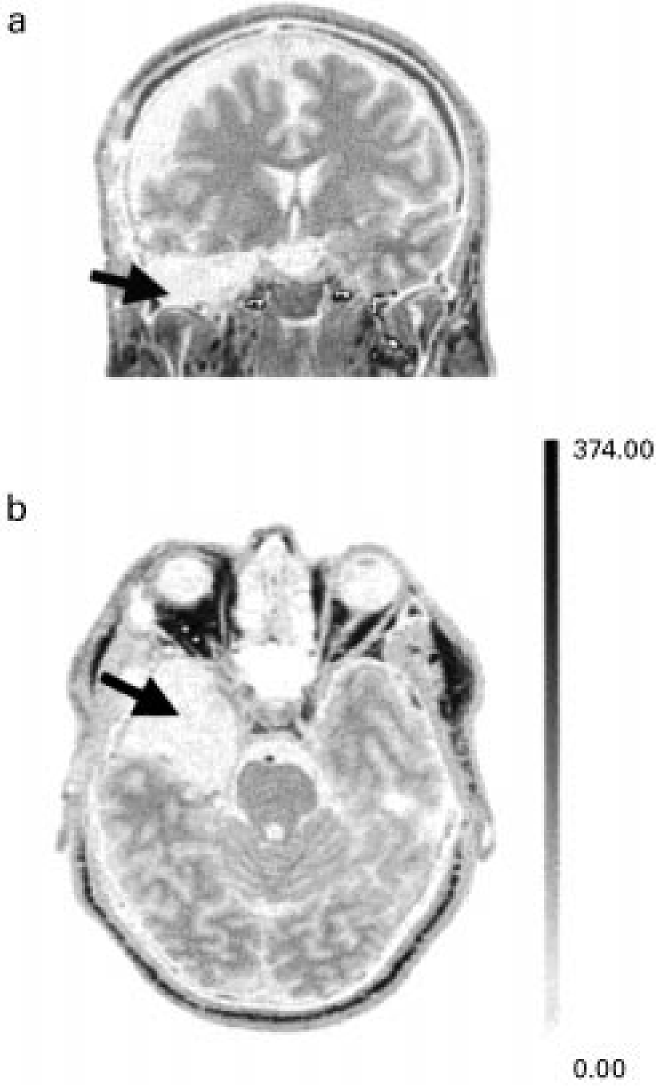

Fig. 2. Scan of patient 6. MRI images in coronal sections of the human temporal lobes in an epileptic patient (number 6) after left hemisphere ATL resection. (a) This ATL ablation is represented in black and indicated with an arrow, in the inferior part of the brain; above, the T1 is clearly visible. (b) The ATL resection as represented in black and indicated with an arrow, in the anterior part of the temporal lobe.

amplitude as a function of stimulus level, were obtained with and without contralateral 30-dB SL broad-band noise (bandwidth: 500–8000 Hz). All TEOAEs were recorded using the ILO88 Otodynamics system (V6.22 software) described in detail by Kemp *et al.*[31] A probe, consisting of a Knowles 1843 microphone and a BP 1712 earphone embedded in a plastic ear plug, was inserted into the subject's ear canal with a foam eartip. Stimuli were non-filtered clicks of 80 μs duration at a rate of 50 per second. Five click intensities were applied (60, 63, 66, 69 and 72 dB intra-meatal peak sound pressure level within 3 dB) in the presence and absence of contralateral acoustic stimulation activating the MOC system of the ipsilateral ear, and thus decreasing TEOAE amplitude when this system functions normally. At these low stimulus levels, the linear acquisition mode (i.e. four clicks of the same polarity and amplitude) was used with a response window set at 3.0–20 ms. In one set of recordings, 250 pairs of responses were averaged and bandpass filtered from 500 to 6000 Hz. The EA corresponding to the reduction in ipsilateral stimulus causing the same TEOAE reduction as a 30-dB SL contralateral acoustic stimulus was calculated.[12,32] The lower the EA value (which is negative when the efferent system inhibits the outer hair cells), the greater the effectiveness of the MOC system.

Pre- and postoperative verbal dichotic listening test

A French language dichotic listening test, sensitive enough to be used in children and patients with temporal cortical seizure,[39] was performed in a quiet room using a list of 50 word-pairs. Subjects were asked to listen to two competing words simultaneously, one arriving in the left ear and one in the right, and to repeat the two words they heard. Each word repeated was scored 2 points, and 1 point when partially repeated. The maximum score per ear was thus 100. Comparison of ear scores thus assessed the ear advantage for verbal material. In order to ensure that a possible inability to repeat words in one ear was not a consequence of hearing loss, the test was also performed monaurally and at the same intensity. Since extinction effects in dichotic conditions were never associated with monaural extinction, the results obtained were deemed reliable. This test was not taken by the control subjects, because it would have been too easy for them, with a 100% success rate.

Statistics

As the test samples were small, a non-parametric version of

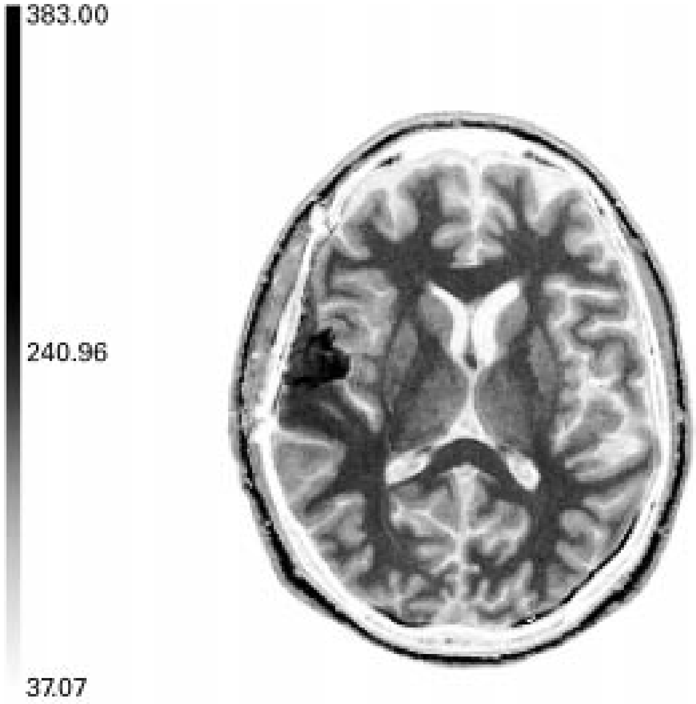

Fig. 3. Scan of patient 2. MRI image in horizontal section of the human temporal lobes, in an epileptic patient (number 2) after right hemisphere T1 resection represented (in white) on the left side of the image, at the superior temporal gyrus locus.

ANOVA was performed on the EA results, considering one non-repeated factor, population (two sorts of epileptic patient according to seizure, plus the healthy controls), and two repeated measures, ear (right or left) and effect of the surgery (before and after operation), or of time (for the healthy controls tested twice). A multiple comparisons procedure (Tukey test) showed significant differences between conditions. A one-way ANOVA was used to compare TEOAE and EA of the three populations, and paired *t*-tests were performed to assess the effect of surgery on the TEOAE, EA, dichotic test scores, BAER and MLR measurements. To compare dichotic scores, BAER pics intervals, and MLR latencies and amplitudes between ATL patients and T1 patients, a *t*-test was used and a Bonferroni correction applied. Pearson's product-moment correlations were calculated to evaluate the relationship between the postoperative change in EA values and in dichotic test results.

For all these analyses, statistical significance was set at a probability level of 0.05.

RESULTS

Amplitudes and latencies of electrophysiological measures

Amplitudes and latencies of the MLR (Na and Pa) for both ears and the results of statistical tests are presented in Table 1. There was no significant difference for these measurements, nor for the I–III and III–V intervals of BAER ($P < 0.05$) (before and after operation), nor between the two populations of patients. All the I–V intervals were normal (less than 4.5 ms).

Influence of the surgical removal on medial olivocochlear system functioning and transiently evoked otoacoustic emissions

No population effect was observed on TEOAE amplitudes (Table 2) and paired *t*-tests showed no statistically significant effect ($P > 0.05$) of the surgery (or of the time).

The operation effects on EA are represented in Fig. 4 as mean EA difference (before minus after surgery) for two groups of epileptic patients, and shows the results for the healthy control group taken at two different testing sessions, in both ears. The results of non-parametric tests showed a statistically significant effect ($F_{2,19} = 4.84$, $P < 0.05$) of the interaction of the three factors, population, ear and surgery (or time), on EA values. Indeed, in healthy controls, no time effect on the EA measure was found for either ear, whereas in T1 epileptic patients, there was a greater EA difference (between pre- and postoperative measurements), as demonstrated by an increase in the left over the right ear after neurosurgery. In contrast, for the ATL epileptic patients, this EA difference, observed postoperatively, was reversed, and greater in the right ear in those cases when this was ipsilateral to the lesion. Thus, it is clear that the influence of the operation (or time) on EA values varies according to the population and the ear considered.

Concerning the EA, preoperatively (first measurement time), there was a statistically significant effect of the factor population on the right ear EA (Table 2), with a tendency for ATL patients to exhibit a greater EA. However, a multiple comparisons test was not statistically significant. Moreover, there was no significant difference for the left ear or for any other time measurement.

On the intracarotid amobarbital test, all the patients, even left-handers, had left hemisphere language dominance. However, as subjects were not operated on in the

Table 1. Results of middle latency responses and dichotic listening test scores

Measurements		Preoperative measures (mean ± S.D.)		Inter-population differences before surgery	Postoperative measures (mean ± S.D.)		Inter-population differences after surgery	Pre/postoperation differences (paired *t*-test)	
Waves	Electrodes	T1	ATL		T1	ATL		T1	ATL
Na latencies (ms)	C3 RE	18.8 ± 0.4	14.1 ± 1.9	NS	22.0 ± 1.6	14.8 ± 3.5	NS	NS	NS
	C4 LE	21.3 ± 3.5	14.7 ± 2.5	NS	17.6 ± 3.6	15.4 ± 3.4	NS	NS	NS
	F3 RE	14.4 ± 5.8	15.5 ± 2.7	NS	19.8 ± 0.3	15.5 ± 2.2	NS	NS	NS
	F4 LE	18.4 ± 0.5	14.9 ± 2.4	NS	20.3 ± 1.1	14.6 ± 3.8	NS	NS	NS
Na amplitudes (μV)	C3 RE	−0.2 ± 0.07	−0.4 ± 0.4	NS	−0.2 ± 0.1	−0.3 ± 0.6	NS	NS	NS
	C4 LE	−0.5 ± 0.04	−0.6 ± 0.3	NS	−0.1 ± 0.02	−0.4 ± 0.4	NS	NS	NS
	F3 RE	−0.3 ± 0.01	−0.6 ± 0.5	NS	−0.3 ± 0.2	−0.5 ± 0.5	NS	NS	NS
	F4 LE	−0.5 ± 0.2	−0.9 ± 0.5	NS	−0.2 ± 0.1	−0.6 ± 0.6	NS	NS	NS
Pa latencies (ms)	C3 RE	38.1 ± 4.1	33.1 ± 1.1	NS	35.0 ± 3.5	36.2 ± 2.1	NS	NS	NS
	C4 LE	35.5 ± 0.4	32.7 ± 2.2	NS	36.2 ± 1.4	33.0 ± 1.5	NS	NS	NS
	F3 RE	35.4 ± 2.3	31.3 ± 1.5	NS	34.3 ± 3.7	35.0 ± 4.1	NS	NS	NS
	F4 LE	34.0 ± 4.2	30.8 ± 2.5	NS	35.3 ± 2.2	31.3 ± 1.0	NS	NS	NS
Pa amplitudes (μV)	C3 RE	0.7 ± 0.02	0.7 ± 0.3	NS	0.3 ± 0.06	0.7 ± 0.2	NS	NS	NS
	C4 LE	0.2 ± 0.1	1.3 ± 0.6	NS	0.6 ± 0.3	1.2 ± 0.7	NS	NS	NS
	F3 RE	0.7 ± 0.2	0.7 ± 0.9	NS	0.4 ± 0.1	0.7 ± 0.9	NS	NS	NS
	F4 LE	0.2 ± 0.4	0.9 ± 0.4	NS	0.6 ± 0.4	1.0 ± 0.7	NS	NS	NS
Dichotic test	RE	57 ± 38.1	82 ± 12.5	NS	62 ± 42.4	91 ± 4.5	NS	NS	NS
	LE	61 ± 38.5	74 ± 14.2	NS	32 ± 46	65 ± 23.1	NS	NS	NS

Means and standard deviations of MLR amplitudes and latencies, and verbal dichotic listening test scores, in both the right ear (RE) and the left ear (LE), and results of their statistical analysis, for T1 and ATL patients. NS, not significant.

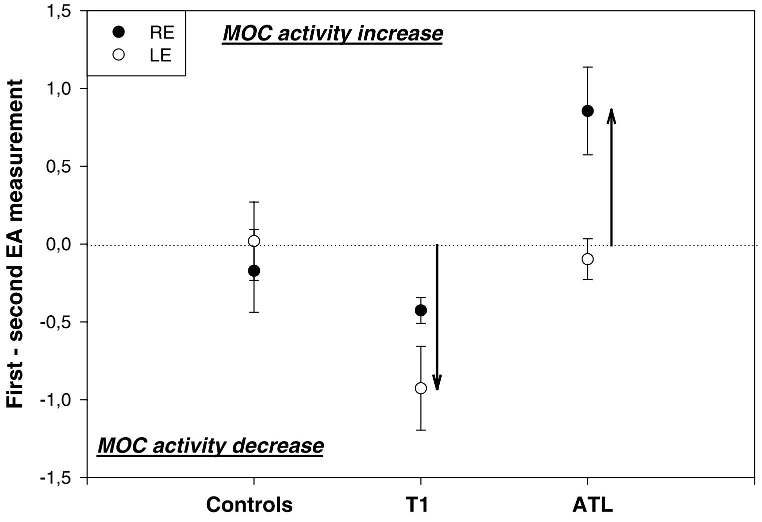

Fig. 4. Effect of surgery on the contralateral suppression effect. Means and standard error bars of EA in both the right ear (RE) and the left ear (LE) before minus after operation, for epileptic patients with T1 ($n = 3$) and ATL ablation ($n = 4$), and the first minus the second testing time, for healthy controls ($n = 15$). Effect of the interaction of the factors: population, ear and surgery (or time) on EA values ($F_{2,19} = 4.84$, $P < 0.05$).

same hemisphere, and had different precise epileptic foci, it was decided to analyse single case results qualitatively, in addition to the statistical analysis.

Epileptic patients with superior temporal gyrus resection

Individual patient EA values are represented in Fig. 5 and individual verbal dichotic listening test scores in Fig. 6.

Patient number 1, who was operated on in the left hemisphere, showed a slightly increased EA (i.e. MOC system functioning decreased) in both ears after the operation. In contrast, patients 2 and 3, who underwent T1 resection in the right hemisphere, had a substantial

Table 2. Measurements of the cochlea and medial olivocochlear system functioning

Measures	First measurement time				Second measurement time			
Populations	T1 (mean ± S.D.)	ATL (mean ± S.D.)	Controls (mean ± S.D.)	Differences between the three populations (one-way ANOVA)	T1 (mean ± S.D.)	ATL (mean ± S.D.)	Controls (mean ± S.D.)	Differences between the three populations (one-way ANOVA)
RE TEOAE	14 ± 3.7	13.5 ± 7	12.5 ± 5	$F_{2,19} = 0.9$, NS	14.6 ± 2.1	13.1 ± 5.6	12.6 ± 4.9	$F_{2,19} = 1.9$, NS
LE TEOAE	12.1 ± 5.5	11.9 ± 5.3	11.8 ± 4.2	$F_{2,19} = 0.6$, NS	8.4 ± 1.2	10.9 ± 3.2	11.7 ± 4.1	$F_{2,19} = 0.05$, NS
RE EA	−1.6 ± 0.2	−0.8 ± 0.7	−3.2 ± 1.8	$F_{2,19} = 4.1$. $P < 0.05$	−1.1 ± 0.3	−1.7 ± 0.3	−3.0 ± 1.8	$F_{2,19} = 2.3$, NS
LE EA	−1.6 ± 0.5	−1.1 ± 0.4	−2.9 ± 2.1	$F_{2,19} = 1.86$, NS	−0.7 ± 0.1	−1.0 ± 0.3	−2.9 ± 2.2	$F_{2,19} = 2.7$, NS

Means and standard deviations of TEOAE and EA in both the right ear (RE) and the left ear (LE), and results of statistical analysis. NS, not significant.

left ear EA increase (contralateral to the resected cortex) and slight right ear EA increase after this resection. However, preoperatively, patients 1 and 3 were the only ones to show extinction on the dichotic listening test (less than 25% of correct responses) in the ear contralateral to the lesion (Fig. 6). Patient 2, who had the stronger EA change postoperatively, also had a stronger dichotic score decrease in the same ear (i.e. contralateral to the resection).

Epileptic patients with anterior temporal lobe resection

As illustrated in Fig. 5, the left anterior temporal lobectomy had no effect on the EA value of patient 4. The three right ATL epileptic patients (5–7) showed an EA decrease (MOC activity increase) in the right ear, which was then ipsilateral to the surgically lesioned side. The left ear EA did not vary after operation, except for a slight increase found in patient 5.

The operation had no extinction effect on the dichotic listening test in the four patients, although patients 5 and 6 had lower scores following surgery in the ear contralateral to removal (Fig. 6).

Links between equivalent attenuation and the verbal dichotic listening test

As shown in Table 1, there was no statistically significant difference for the scores obtained on the dichotic listening test between the populations of patients or pre- and postoperative conditions. As described previously, each individual value for this test is presented in Fig. 6.

To study the link between right and left ear operation effects on EA values on the one hand and on dichotic test scores on the other, pre- minus postoperative EA and dichotic test scores were correlated for both ears.

It appeared (Fig. 7) that the more left ear EA increased (i.e. the MOC system becomes less functional) postoperatively, the more left ear dichotic performance decreased ($r = -0.88$, $P < 0.01$, $n = 7$), whereas in the right ear no statistically significant correlation was found ($r = -0.42$, $P > 0.05$, $n = 7$). Due to the fact that patients 1 and 4 were operated on opposite sites (as compared to other patients), a correlation was performed considering EA differences and dichotic score differences for the right ear in patients 1 and 4 but the left ear for the others, and vice versa. When comparing both left and right side results for the right-side operated patients with those of the remaining two patients, a significant correlation was again found ($r = -0.81$, $P < 0.05$, $n = 7$). Conversely, no significant correlation was obtained ($r = -0.51$, $P > 0.05$, $n = 7$).

DISCUSSION

State of afferent auditory pathways in epileptic subjects

To ensure the reliability of the results obtained with EA, it was necessary to account for any abnormality in brainstem auditory processing, since this may cause a postoperative MOC system change. Our results confirm

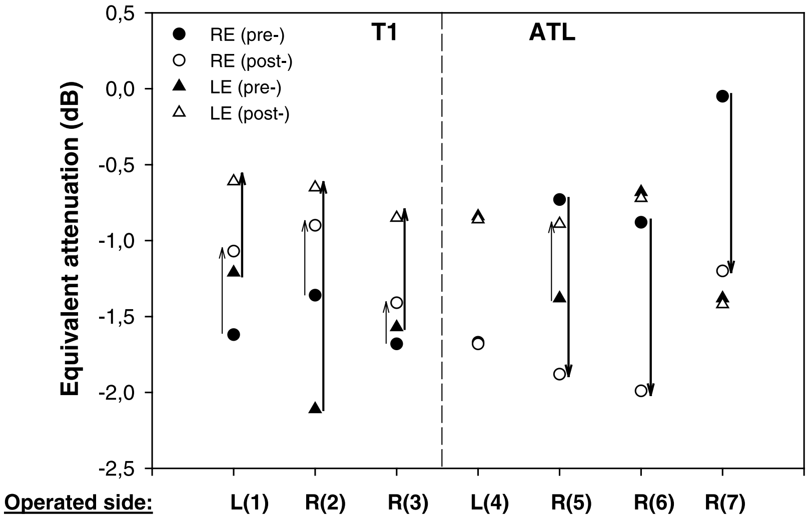

Fig. 5. Efferent suppression for each patient. Individual values of EA in the right ear (RE) and left ear (LE) of the epileptic patients with T1 resection or ATL resection, before (pre-) and after (post-) the operation. The hemispheric side of the operation is indicated by L for left hemisphere and R for right hemisphere. Patients were numbered from 1 to 7 to facilitate references in the text. The lower the EA, the more effective the MOC system.

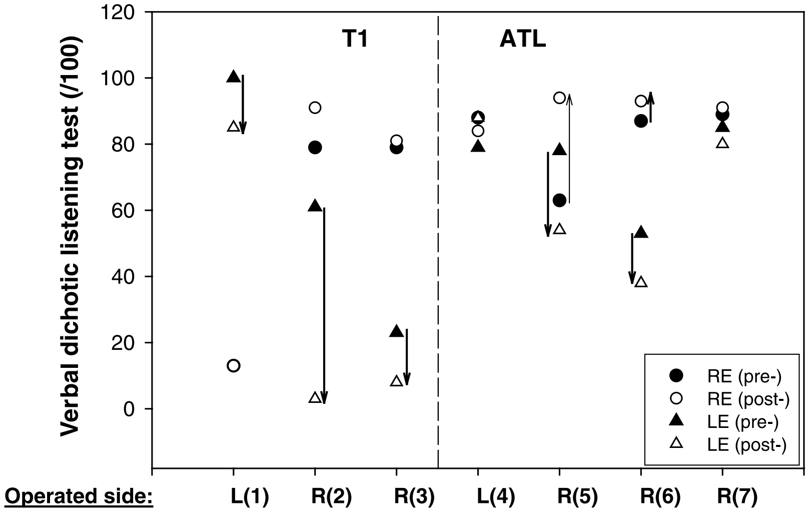

Fig. 6. Dichotic scores for each patient. Individual dichotic listening test scores in the right ear (RE) and left ear (LE) of the epileptic patients with T1 resection or ATL resection, before (pre-) and after (post-) the operation. The hemispheric side of the operation is indicated by L for left hemisphere and R for right hemisphere. Patients have been numbered from 1 to 7 to facilitate references in the text.

this absence of BAER abnormalities and MLR changes postoperatively.

Since the Pa wave is partially generated in the auditory cortex,[59] a significant change of Pa is expected in T1 patients postoperatively. However, this did not occur, potentially due to the preoperative gliosis (which has the potential to alter this wave) that existed before surgery and the minimal number of subjects employed. None the less, patients had normal TEOAEs both before and after cortical removal, which indicates an objective reflection of cochlear functioning.[22] Thus, the objective auditory tests did not reveal any peripheral auditory disorders either pre- or postoperatively. However, the right ear EA was significantly lower (i.e. the MOC system was more effective) in healthy controls than in epileptic patients before the surgery. Such a reduced efferent system activity in temporal epilepsy may be a factor of the anti-epileptic treatment. Indeed, in humans, benzodiazepine (oxazepam) administration decreases the contralateral suppression effect, especially on right TEOAEs.[68] It is of note, however, that all epileptic patients in this study were being treated with drugs containing benzodiazepine and/or its antagonists, which may have a similar effect on the MOC system.

The medial olivocochlear complex: a crossroad in the auditory system

The MOC bundle is not only involved in peripheral loops, but has also been shown to take part in central

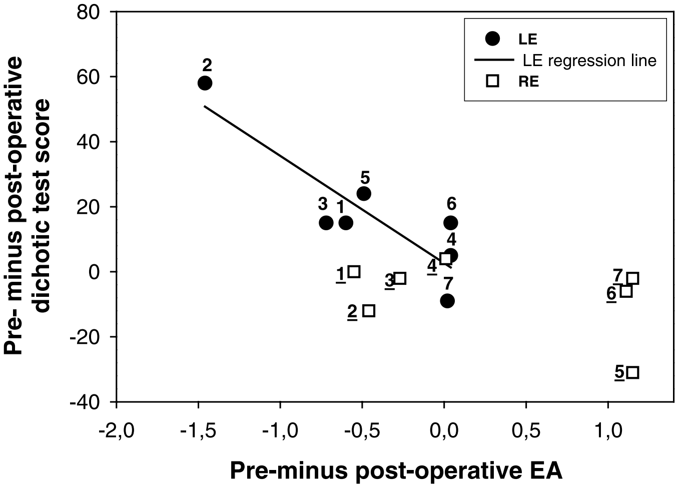

Fig. 7. Correlation between the surgical consequences on the contralateral suppression and the dichotic test score. Relationship between dichotic test score and the difference in the right ear (RE) and left ear (LE) EA before minus after surgery, in the seven epileptic patients, numbered in the figure as in the text. Significant left ear correlation ($r=-0.88$, $P<0.01$, $n=7$) was found.

loops. The function of the efferent pathway between the primary auditory cortex and the cochlear nucleus is unknown. The existence of this direct pathway and the results obtained in the present study suggest, however, that the auditory cortex may be involved in filtering ascending auditory input via the medial efferent system, which intervenes in many auditory functions. Indeed, the projections of the medial superior olivary nuclei, which are myelinated, terminate on the cell bodies of the outer hair cells[36] and play a role by regulating the activity of these contractile cells.[5,10] MOC neurons may enhance signal detection or transduction through an anti-masking effect, by improvement of the signal-to-noise ratio.[15,73] Olivocochlear efferents have also recently been shown to be involved in speech-in-noise intelligibility,[21] and MOC stimulation may further protect the cochlea from noise-induced damage.[52–54] Consequently, cortical regulation of this efferent system could be of importance to hearing functions, such as those involved in the processing of complex signals. Furthermore, the descending influence of the auditory cortex on the MOC system may be fundamental during auditory development, since the MOC system seems to be impaired in pathologies presenting auditory abnormality or communication difficulty, such as autism.[13]

The MOC system modulation seems to come indirectly and directly from the auditory cortex. Indeed, light-optical investigations have shown that the greatest number of corticofugal fibers of the primary and anterior fields of the cat auditory cortex reach the nuclei of the superior olivary complex without relaying either in the medial geniculate body or in the inferior colliculus.[49] More specifically, the auditory cortex of the cat includes the primary, anterior, posterior and secondary auditory fields.[6] Moreover, well-characterized descending projections from the auditory cortex also innervate the inferior colliculus,[3,17,26,71] which projects topographically to lower auditory nuclei of the brainstem, including the nucleus of the superior olive, periolivary nuclei and the cochlear nucleus.[11,57] In the guinea-pig, it was demonstrated using a labeling technique that descending inferior colliculus neurons provide inputs to olivocochlear neurons, which are not, however, the major targets of descending inferior colliculus projections.[64]

Investigations of the effect of the descending system of auditory pathways have been comparatively few in number and their results are contradictory. Nevertheless, it seems that stimulation of the cortex of the primary auditory field inhibits the response of ascending impulse conduction, whereas stimulation of the secondary auditory field potentiates it.[29] The ipsilateral superior olivary complex could then be the target of excitatory and inhibitory descending pathways. Given that all the auditory cortex was resected unilaterally in the three T1 epileptic patients, the two sorts of descending fiber could thus be altered. However, it was demonstrated statistically that the operation produced a change in the efferent system suppression effect. It is important to note that, even if the change in the efferent system does show inter-individual variability, the observed operation effect is unlikely to be due to any corresponding intra-individual variability, which, as seen in the healthy controls, is very slight.

It is also striking to note that MOC system modulation was linked with dichotic test scores, representing alteration in higher center activity. It has already been demonstrated that unilateral temporal lobe damage, especially involving the primary auditory cortex, produces a deficit in the contralateral ear, yielding an overall ipsilateral advantage.[48,58] The decrease of left ear score on the dichotic listening test may thus reflect the degree of damage to auditory pathways and cortices in the right temporal lobe. A greater decrease in the dichotic test score in the ear contralateral to the removal suggests a greater alteration in the auditory cortex and pathways, and a reduced cochleo-cochlear reflex (Fig. 7). This postoperative effect seems to act similarly on MOC system functioning as in the central auditory abilities necessary to perform the verbal dichotic listening test.

Effect of resection of the superior temporal gyrus on medial olivocochlear system functioning

Although the major descending auditory pathways described in the literature are ipsilateral (Fig. 1), in the case of T1 removal, an auditory cortical influence was observed mainly on the contralateral MOC complex, affecting the ear contralateral to the lesion. Along with the descending auditory inputs, the superior olivary complex receives mainly contralateral ascending excitatory input[63,69] from the ventral cochlear nucleus, which is mostly contacted by ipsilateral descending auditory fibers (Fig. 1). The postoperative effect on the contralateral MOC system may be mediated by damage to descending auditory pathways joining the ispilateral cochlear nucleus, in turn modifying the functioning of the contralateral MOC system. This system may be receiving less excitatory inputs and, consequently, it would have less suppressive action on TEOAE amplitude.

In humans, these descending auditory pathways have not been clearly described, and a precise knowledge of these fibers would help to better understand the original results of this study. In all events, the MOC system appears to be partly under auditory cortex control. This control could be of particular importance given that it indirectly reaches the more peripheral part of the auditory system, the outer hair cells of the cochlea involved in the generation of the afferent message. The paradigm of MOC system stimulation used primarily investigates the uncrossed part of the MOC system.[50] However, given the several interactions existing at each stage of the auditory system, it would be an oversimplified view to limit our interpretation to the effect of uncrossed fibers. It is essential to note that the effect described here is minimized, since it is only a part of the consequences of brain damage on MOC system functioning, and thus on cochlea activity.

Effect of anterior temporal lobectomy on medial olivocochlear system functioning

ATL resection had an effect on MOC system performance only where the right hemisphere was concerned. It is hypothesized that such an alteration in MOC system performance may be more attributable to the fact that, in contrast to left resection in patient 4 that was restricted to the ATL, patients 5–7 underwent a partial removal in both the medial and inferior temporal gyrus of the right hemisphere in addition to the ATL. In these patients, the contralateral suppressive action on TEOAE was increased on the side ipsilateral to the lesion. It would appear that ipsilateral descending pathways, which would usually inhibit the medial superior olivary complex, became ineffective and caused an increase in MOC system activity. The ipsilateral inhibitory descending auditory pathways coming from the auditory area[29] could inhibit the ipsilateral MOC system less strongly, thus explaining the increase in its contralateral suppression effect. This effect was reversed in comparison to patients who underwent a complete ablation of T1.

This peripheral effect may also have been due to the fact that the temporo-polar cortex is a potential convergence site for auditory and limbic input,[41] and is involved in auditory information processing. There are arguments to support this hypothesis. Firstly, of nine patients with unilateral anterior temporal lobectomy thought to have spared the primary auditory cortex, all showed a change in ear dominance consistent with the hypothesis that unilateral lobectomy decreases the perceptual salience of the tone presented to the ear contralateral to the lesion.[16] Thus, the ATL appears to take part in specific auditory processing. Secondly, anatomical studies in rhesus monkeys[60] have demonstrated the existence of efferent pathways originating in Heschl's gyrus and planum temporale, and running anteriorly to T1 via several synaptic stages to reach the temporal pole before descending to lower brainstem nuclei. ATL resection would inevitably damage this auditory pathway and consequently may affect MOC system functioning. The absence of a surgical effect on efferent suppression in patient 4 provides no support for this hypothesis. However, no firm conclusion can be drawn from one single case, and an absence of EA change does not necessarily infer an absence of surgical effect.

CONCLUSION

It can be concluded from this study that, in humans, the cochleo-cochlear reflex is modulated by the primary and secondary auditory cortex through direct or indirect efferent fibers. The ATL may also be involved in auditory processing and descending signal regulation. The present experiment confirms the anatomical studies conducted in animals, suggesting that the neocortex may have a direct or indirect influence on the processing of sound at the initial stages, especially in the medial superior olivary complex, which contributes to several auditory functions such as speech-in-noise intelligibility.

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(*Accepted* 13 *February* 2001)