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The neural correlates of 'deaf-hearing' in man
Conscious sensory awareness enabled by attentional modulation

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Summary
Attentional modulation of normal sensory processing has a two-fold impact on human brain activity: activation of a network of localized brain regions is associated with paying attention, and activation of specific sensory regions is enhanced relative to passive stimulation. The mechanisms underlying attentional modulation of perception in patients with lesions of sensory cortices are less well understood. Here we report a unique patient suffering from extensive bilateral destruction of the auditory cortices (including the primary auditory fields) who demonstrated conscious perception of the onset and offset of sounds only when selectively attending to the auditory modality. This is the first description of such an attentively modulated 'deaf-hearing' phenomenon and its neural correlates, using $H_2{}^{15}O$-PET. Increases in cerebral blood flow associated with conscious awareness of sound that was achieved by listening attentively (compared with identical auditory stimulation presented when the patient was inattentive) were found bilaterally in the lateral (pre)frontal cortices, the spared middle temporal cortices and the cerebellar hemispheres. We conclude that conscious awareness of sounds may be achieved in the absence of the primary auditory cortex, and that selective, 'top-down' attention, associated with prefrontal systems, exerts a crucial modulatory effect on auditory perception within the remaining auditory system.

Keywords: cortical deafness; auditory physiology; functional neuroimaging; attention

Abbreviations: A1 = primary auditory cortex; BA = Brodmann area; N1 = N100 (long-latency component of auditory evoked potentials)

Introduction
In this experiment we were interested in studying how perceptual awareness of sounds can be enabled by volitional attention in the case of a subject with lesioned primary auditory cortices. Historically, bilateral lesions of the primary auditory cortices were thought to cause complete deafness in man (Wernicke and Friedländer, 1883), based on observation of the behaviour of patients with such lesions. Though patients with bilateral lesions of the auditory cortices are still occasionally described as persistently deaf (Graham *et al.*, 1980; Bahls *et al.*, 1988), the majority of human cases in the neuropsychological literature are reported to have auditory recognition deficits rather than deafness. Forty-five out of the 55 patients with central auditory disorder that have been reported in the last 20 years had no difficulty with hearing as such (Oppenheimer *et al.*, 1978; Haguenauer *et al.*, 1979; Metz-Lutz *et al.*, 1980; Michel *et al.*, 1980; Parving *et al.*, 1980; Traugott *et al.*, 1980; Kneebone *et al.*, 1981; Auerbach *et al.*, 1982; Miceli *et al.*, 1982; Rosati *et al.*, 1982; Sato *et al.*, 1982; von Stockert, 1982; Coslett *et al.*, 1984; Lechevalier *et al.*, 1984; Marshall *et al.*, 1985; Buchman *et al.*, 1986; Kanter *et al.*, 1986; Motomura *et al.*, 1986; Ho *et al.*, 1987; Mendez *et al.*, 1988; Yaqub *et al.*, 1988; Buchtel *et al.*, 1989; Hasegawa *et al.*, 1989; Lambert *et al.*, 1989; Fechtelpeter *et al.*, 1990; Kazui *et al.*, 1990; Praamstra *et al.*, 1991; Seliger *et al.*, 1991; Shindo *et al.*, 1991; Baddeley and Wilson, 1993; de la Sayette *et al.*, 1994; Carmona *et al.*, 1995; Engelien *et al.*, 1995; Godefroy *et al.*, 1995; Habib *et al.*, 1995; Kaga *et al.*, 1997). In the largest sample of patients reported to date (Kaga *et al.*, 1997), 10 patients were specifically tested for profiles of residual hearing capacities.

None of these 10 patients was reported to have been deaf or ever behaved as if he or she was deaf. Studies in various mammals (including primates) have repeatedly shown that hearing is not chronically abolished after bilateral ablation of the (primary) auditory cortex (e.g. Heffner and Heffner, 1989, 1990; Beitel *et al.*, 1993).

We observed spontaneous deaf behaviour in patient SB, a 22-year-old right-handed man who had suffered from two consecutive strokes, destroying Heschl's gyri and the insulae bilaterally, with lesions extending widely into both superior temporal gyri. SB showed no orienting or startle response to unexpected, sudden sounds, in contrast to the majority of patients with milder impairment cited above. Consequently a diagnosis of cortical deafness was made. Normal function of the auditory periphery to the inferior colliculus was demonstrated with audiological and neurophysiological measurements. SB has no other clinically apparent neurological or neuropsychological deficit, except for severe speech apraxia.

When SB was explicitly instructed to focus his attention solely to audition and to try to detect the onset and offset of sounds, he achieved conscious awareness of these sounds. Galvanic skin responses to sounds were elicited only when SB focused his attention to audition. The purpose of our functional neuroimaging experiment was to identify the neural correlates of volitional selective auditory attention in this patient, and to identify modulatory effects enabling conscious awareness of sound.

Methods

Case report

SB, a right-handed man and former student of engineering, suffered two consecutive strokes in the territories of the middle cerebral arteries (June 1990, aged 22 years, right hemisphere; May 1991, aged 23 years, left hemisphere). After the first stroke he initially suffered a brachiofacial left-sided sensorimotor paresis that resolved. The second stroke caused a right-sided sensorimotor deficit and global aphasia. His total lack of reactions to spoken speech was first assumed to be part of the global aphasia. The sensorimotor deficit and aphasia improved and communication was resumed with gesturing, facial expression, reading and writing. It then became evident that the patient had no reaction to sounds of spoken speech, music or hand-clapping. Thus, cortical deafness was suspected. The patient was also practically mute (anarthric). Despite intensive speech and language therapy, he was unable to initiate or perform the articulation of syllables or words. However, he showed extensive articulatory searching behaviour, and non-linguistic orofacial motor skills (yawning, chewing, swallowing, coughing, etc.) were preserved. Neurologically, there was no sign of orofacial paresis. He thus suffered from severe, specific apraxia for speech. In contrast, his initial global aphasia recovered very well under therapy. At the time of testing, he was fully able to communicate by writing and reading (with occasional word-finding difficulties and phonemic errors).

The aetiology of the stroke(s) was thought to be a familial deficit in protein C, and the patient was treated with an oral anticoagulant. MRI (T_1-weighted images) in the chronic phase showed a right-sided lesion of the superior temporal gyrus, almost in its complete extent, and of the frontal operculum. On the left, the superior temporal gyrus and part of the supramarginal gyrus were lesioned. The insular cortex was lesioned bilaterally, and this was complete on the right. Part of the left anterior insula was spared. The transverse temporal gyri were completely destroyed on both sides.

Neuropsychological and neurolinguistic examination

Cognitive function was tested with subroutines of the Leistungsprüfsystem (Horn, 1983) and the Corsi Block Tapping Test, which examines working memory function in the visuospatial domain (Milner, 1971). Language functions were measured with the Aachen aphasia test (Huber *et al.*, 1980, 1983, 1984; Willmes *et al.*, 1980, 1983). The subtests dealing with spoken speech and/or auditory input, however, could not be administered. SB was tested for buccofacial apraxia using a questionnaire developed by Lehmkuhl and Poeck (Lehmkuhl and Poeck, 1981). In addition, an extensive investigation of the patient's attentional capabilities was conducted several months later, when his clinical syndrome remained unchanged. The patient was tested in various attentional and memory tasks in the visual domain probing alertness, selective attention, scanning, divided attention and shifting attention. The memory span was also re-examined.

Audiological examination

Pure-tone audiometry was difficult to perform. Initially, under routine conditions widely varying pure tone thresholds in the range of 90–120 dB were obtained. SB needed specific instruction to focus his attention to audition and to listen very carefully to the beginning of sounds. But once he fully concentrated on the task, a complete audiogram with nearly normal thresholds in the range of 250–6000 Hz was obtained and replicated. The acoustic reflexes were also measured.

Neurophysiological and psychophysical examination

Auditory evoked potentials were examined in all latency ranges: brainstem auditory evoked potentials, middle-latency auditory evoked potentials and long-latency auditory evoked potentials, according to standard clinical procedures (Hoke, 1979; Döring, 1984; Grandori *et al.*, 1990). Galvanic skin responses to unattended and attended sound presentation were also examined.

Table 1 *List of complex sounds used for auditory tasks*

Sound category	Sounds
Animals	Cow, dog
Musical instruments	Trumpet, drum
Tools	Saw, hammer
Vehicles	Motorcycle, aircraft
Signals	Table bell, bicycle bell, car horn, alarm clock, telephone ringing
Spoken speech	News-speaker, someone shouting SB's first name

Auditory task performance under selective auditory attention

The detection of onsets and offsets of sounds was tested with a set of 15 sounds. In the first run, the stimulus and interstimulus interval durations were kept constant (30 s each). To avoid a simple rhythmic response strategy, a second run was performed in which stimulus duration was varied between 1 and 30 s. Discrimination between different intensity levels was tested with narrow-band noises centred on 12 underlying carrier frequencies in the range of 315–4000 Hz. Each of these sounds was presented three times with different sound pressure levels (55, 75 and 95 dB). The patient was asked to judge the perceived loudness in a subjective seven-step scale, ranging from 'nothing heard' to 'discomforting loudness'. The ability to discriminate different frequencies was also tested with narrow-band noises in the frequency range of 250–6000 Hz. Eleven comparisons were tested. The instruction was: 'You will hear pairs of sounds. The pitch might be the same or different. Please indicate whether you consider the second pitch the same, lower or higher in comparison to the first one.' Therefore, the probability of guessing correctly was 33% in this task. The ability to localize sound sources was tested in a special audiological laboratory with 12 loudspeakers arranged clockwise around the patient. Sixty tones were given (five from each of the speakers) in a randomized order.

The discrimination of complex sounds was tested twice. Fifteen, mostly non-verbal sounds were used (Table 1). The interstimulus interval was varied between 10 and 2 s, in order to avoid the confounding effects of auditory short-term memory malfunction. The stimulus duration was always 15 s for both the first and the second sound. The ability to identify environmental sounds was tested in three settings. At first, all 15 sounds were presented once, and the task was to match each sound to its corresponding picture. All 15 pictures (black-and-white line drawings of the objects emitting the sounds) were laid out on the table simultaneously for this task. Secondly, SB was asked to identify sounds by writing. The third setting was a forced-choice task in which SB was asked to guess the correct answer from two choices (provided by two pictograms).

Due to the inabilities demonstrated by SB (see Results), no further investigation of finer auditory discrimination was undertaken.

PET activation study

The neural correlates of the residual hearing associated with the volitional attentional state were studied with a highly sensitive $H_2{}^{15}O$-PET technique (Silbersweig *et al.*, 1993) measuring regional cerebral blood flow under defined experimental conditions. The aim of this study was to contrast the passive presentation of sounds with listening to sounds when the subject was paying attention. Our hypothesis was that task-related neocortical activation would be demonstrated only in the attentionally modulated perception condition. Since auditory perception is normally an automated process that cannot be suppressed, such a contrast would not be expected in healthy subjects. We therefore decided not to study a control group with the paradigm specifically tailored to this patient. SB served as his own within subject control in the inattentive state. Eighteen scans were obtained, six each under each of three experimental conditions: attended auditory stimulation, unattended matched auditory stimulation and rest. Written instructions were given to the patient. He was asked to lie still and rest for the 'rest' and 'unattended sound stimulation' conditions. For the 'attended sound stimulation' condition, the patient was asked to focus his attention to audition and listen carefully for all sound onsets and offsets. No overt motor responses were allowed during scanning, and in fact they did not occur. The order of scans was arranged according to a modified Latin square design (ABC BCA CAB CAB ABC BCA). The sounds used for acoustic stimulation were a broad sample of complex, mostly non-verbal, sounds (stimulus length and interstimulus interval durations varied between 6 and 15 s, and there was 60 s of stimulation per scan). These durations and intervals were based upon SB's average reaction time in this task as well as a consideration of the temporal window of the slow bolus $H_2{}^{15}O$-PET measuring technique. The sounds were presented via earphones from a portable Sony TCD-D3 digital audio tape recorder. The same sound tapes were used during unattended and attended conditions, in a semi-randomized fashion (in order to minimize possible order and memory effects).

The images were reconstructed in a three-dimensional fashion. Data processing included realignment in order to correct for head movement and spatial smoothing (Gaussian filter 10 mm^3). Significant changes in regional cerebral blood flow across conditions were assessed according to the General Linear Model, using a voxel-by-voxel *t*-test as provided in the SPM (statistical parametric mapping) software (Friston *et al.*, 1991; Frackowiak and Friston, 1994; Worsley *et al.*, 1995) with a threshold for significance of $P < 0.01$. The study was approved by the local ethics committee of the Hammersmith Hospital and permission to give radioactivity was given by ARSAC (Administration of Radioactive Substances Advisory Committee, UK) of the Department of Health (UK). SB gave written informed permission prior to scanning according to the declaration of Helsinki (Lynoe *et al.*, 1991).

Table 2 *SB's neuropsychological profile*

Test	Percentile rank	Level of performance
WAIS		Normal
LPS		
UT 3 (logical reasoning)	78.8	Normal
UT 7 (mental rotation)	84.1	Normal
Visual memory span (Corsi block tapping)	65.0	Normal
AAT		
Token test	95.0	Normal
Written naming	97.0	Normal
Written comprehension	94.0	Normal
Spontaneous speech	None	Absent
Repetition	None	Absent
Auditory comprehension	None	Absent
Writing on dictation	None	Absent
Spoken naming	None	Absent
Visual attention tasks		
Alertness (simple visual reaction time)	31	Normal
Selective attention (go/no-go task)	62	Normal
Visual scanning	58	Normal
Divided attention reaction time (reaction to specific stimulus characteristics)		Normal
Shifting attention reaction time (letters versus digits)	54	normal

AAT = Aachen aphasia test, standardized for aphasic population; normal range ⩾90 percentile rank; LPS = Leistungsprüfsystem (age- and education-corrected norms were applied); WAIS = Wechsler Adult Intelligence Scale (age- and education-corrected norms were applied).

Results

Neuropsychological examination

The results in the general intelligence and working memory tests all indicated a normal level of performance in SB. A general cognitive deficit and/or general memory span deficit were thus excluded. As regards language, the subtests dealing with spoken speech and/or auditory input of the Aachen aphasia test could not be performed. All other subtests of language function were normal, i.e. they did not indicate aphasia (written naming, written comprehension and the token test. Given that the left premotor cortex, frontal operculum and anterior insula, which are considered important regions for motor speech programming (Dronkers, 1996), were intact, the persistence of the severe speech apraxia in SB is surprising and might underline the importance of afferent components in some types of speech apraxia, as suggested earlier by Luria (Luria, 1966) and Kimura and Watson (Kimura and Watson, 1989). The patient showed normal performance in attentional and memory tasks in the visual domain probing alertness (visual reaction time), selective visual attention (go/no-go paradigm), visual scanning, visual divided attention and shifting visual attention (reaction time for shifts between letters and digits). The visual memory span was also normal. For details of test results, see Table 2.

Audiological examination

Pure-tone audiometry showed that SB had nearly normal hearing levels over the complete frequency range tested (250–6000 Hz) when his attention was focused on the task. The acoustic reflexes were also normal.

Neurophysiological and psychophysical examination

The brainstem auditory evoked potentials were normal, confirming the integrity of the auditory periphery up to the diencephalon. The positive peak with a latency of 6–8 ms corresponds to the preserved wave V on both sides. The middle-latency responses were absent. All late responses were reduced to virtually no response for sound pressure levels of <70 dB. For higher sound pressure levels, small response-like patterns of abnormal pathology were observed in the latency range up to ~150 ms. At ~100 ms latency, no N100 (N1) long-latency component could be identified. Stronger but non-classifiable responses were found in the latency range of 200–400 ms. Galvanic skin responses were elicited by sound onsets only when the sounds were attended to. See Fig. 1 for auditory evoked potentials and galvanic skin responses.

Auditory task performance under selective auditory attention

In the sound onset and offset detection tasks, SB detected 96% of the onsets and 88% of the offsets. The reaction time was significantly longer for the sound offsets (mean reaction time to onset = 1.2 s, SD = 0.6 s; mean reaction time to

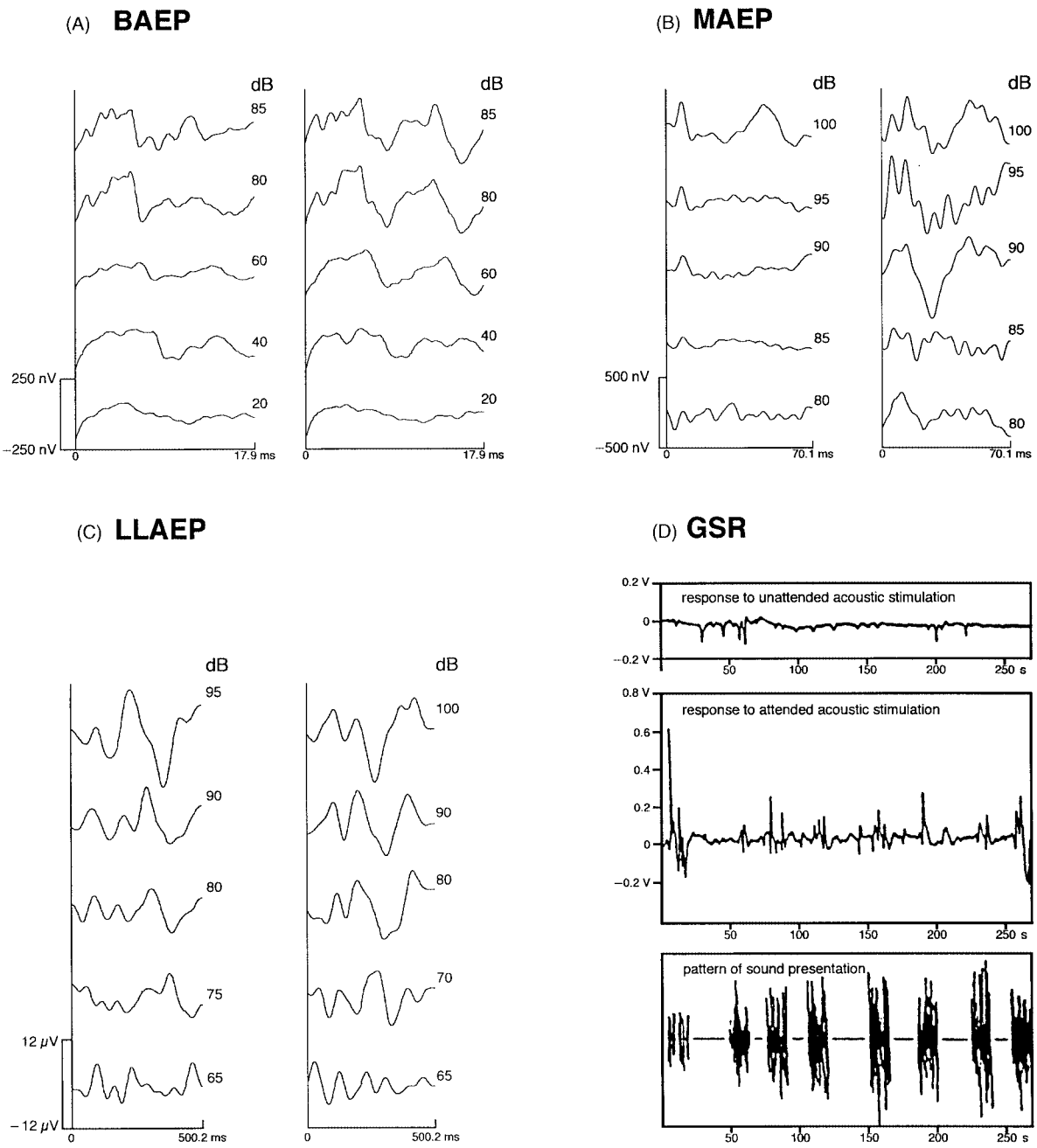

Fig. 1 Auditory evoked potentials (AEP) and galvanic skin responses (GSR) to sound onsets. Electrophysiological data obtained in SB. Auditory evoked potentials recorded according to routine clinical protocols. (**A**) Brainstem or short-latency auditory evoked potentials. (**B**) Middle-latency auditory evoked potentials. (**C**) Long-latency auditory evoked potentials. The data for right ear stimulation are always presented in the left panel and vice versa. Note the absence of middle-latency auditory evoked potentials even with high sound pressure level stimulation, as well as distorted, unclassifiable waveforms in the long-latency range. Note that positivity is upwards, so that the irregular small positivities observed with a latency of ~150 ms are not to be mistaken for a possible N1 component. (**D**) GSR obtained to sound onsets under two conditions identical to those in the PET activation study. In the first part of the experiment (presented in the upper panel), SB was not made aware of any sound stimulation and had no instructions other than to lie still and wait. No specific changes of skin conductance were observed in response to any sound onset. When SB paid selective attention to audition, however, galvanic skin responses were elicited to several sound onsets, as shown in the middle panel. The lower panel shows the pattern of sound stimulation as a reference; any deflection from the centred baseline indicates the presence of sound.

offset = 4.1 s, SD = 3.0 s; $P < 0.0001$, Mann–Whitney U test). SB evaluated 78% of the sound intensity comparisons correctly. In the frequency discrimination task, SB gave correct responses in 64% of the comparisons, but since the probability of guessing correctly was 33% (see Methods), this is not significantly different from a chance level performance according to a simple binomial model (test for non-overlapping confidence intervals) for this small sample (n =

Table 3 *SB's performance in auditory tasks under focused attention*

Task	AC	*n*	% Hits	PG (%)	Latency (s)	
					mean	SD
Detection of sound onsets	0.01	50	96	–	1.2*	0.6
Detection of sound offsets	0.01	50	92	–	4.1	3.0
Discrimination: intensity levels	0.01	36	78	–	–†	–†
Discrimination: frequencies	n.s.	11	64	33‡	–†	–†
Changes of sounds	0.01	45	36	–	6.1	4.1
Localization of sound sources	n.s.	60	12	8	–†	–†
Same–different judgements of complex sounds						
With long interstimulus intervals (10 s)	n.s.	30	43	50	19.2	13.4
With short interstimulus intervals (2 s)	n.s.	44	50	50	22.0	11.0
Identification: sound-to-picture matching	n.s.	15	7	6	32.7	12.8
Identification: written response	n.s.	15	7	–	50.2	29.0
Identification: forced choice (two pictures)	n.s.	90	61	50	16.3	10.0

PG = probability of guessing the correct answer; AC = above chance, indicating whether the patient's performance was above chance level using a simple binomial model (non-overlapping confidence intervals); SD = standard deviation; n.s. = not significant; *n* = number of trials. * Two outliers of 13 and 16 s were not considered in the calculation of mean reaction time and the standard deviation, because the patients forgot to signal on these two occasions. † Reaction time not measured. ‡ The instruction was: 'You will hear pairs of sounds. The pitch might be the same or different. Please indicate whether you consider the second pitch the same, lower or higher in comparison to the first one'. Therefore, only three different answers were possible and the probability of guessing the correct answer was 33%.

11). SB judged the location of the sound correctly for only seven of the 60 stimuli. Out of the 12 possible sound locations, he chose one in particular (that to the right of the posterior midline) in 25% of comparisons, which was probably due to his inability in this task. The pattern of misclassifications was not specific for peripheral auditory system disease that leads to impaired sound localization, i.e. no particular part of auditory space was totally ignored and no systematic shifts in any direction existed. In the same–different judgement task for complex sounds, SB's performance was at chance level for both interstimulus intervals (2 and 15 s). His performance was also at chance level for sound identification in all three task settings (multiple choice, writing and forced choice). For details, see Table 3.

PET activation study

During the state of listening consciously when the patient was focusing his attention on audition rather than unattended auditory stimulation, we found strong bilateral cortical activations. This network comprised the (pre)frontal cortices [Brodmann areas (BA) 6, 8, 9, 10, 11 and 46] and the middle temporal cortices (BA 22 and 21) bilaterally, as well as the left head of the caudate nucleus, right putamen and thalamus, and the cerebellum bilaterally. In contrast, only two minor foci of significant activation in the right posterior parietal and medial superior frontal regions were found during unattended auditory stimulation compared with the resting condition (Table 4, Fig. 2).

Table 4 *Comparison of PET activation sites significant to* $P < 0.01$ *during attended compared with unattended sound stimulation in SB*

	Laterality		Brodmann area
	Left	Right	
Superior/middle frontal gyrus	+	+	6, 8, 9, 10, 11, 46
Frontal operculum		+	45
Superior parietal lobule		+	2, 7
Inferior parietal lobule	+		39
Superior temporal gyrus (posterior)	+	+	42/22
Middle temporal gyrus	+	+	21
Inferior temporal gyrus	+	+	37
Fusiform gyrus	+		20/36
Cuneus	+		17
Posterior cingulate gyrus	+		30
Head of caudate nucleus	+		
Thalamus		+	
Putamen		+	
Cerebellum (medial and vermis)		+	
Cerebellum (lateral)	+		

Discussion

SB spontaneously behaved as if he were deaf after two strokes that had destroyed much of his cortical auditory system bilaterally. We will discuss our findings with respect to a complete destruction of the primary auditory cortical field (AI) after careful consideration of anatomical knowledge specified in detail in Appendix 1. The neurophysiological

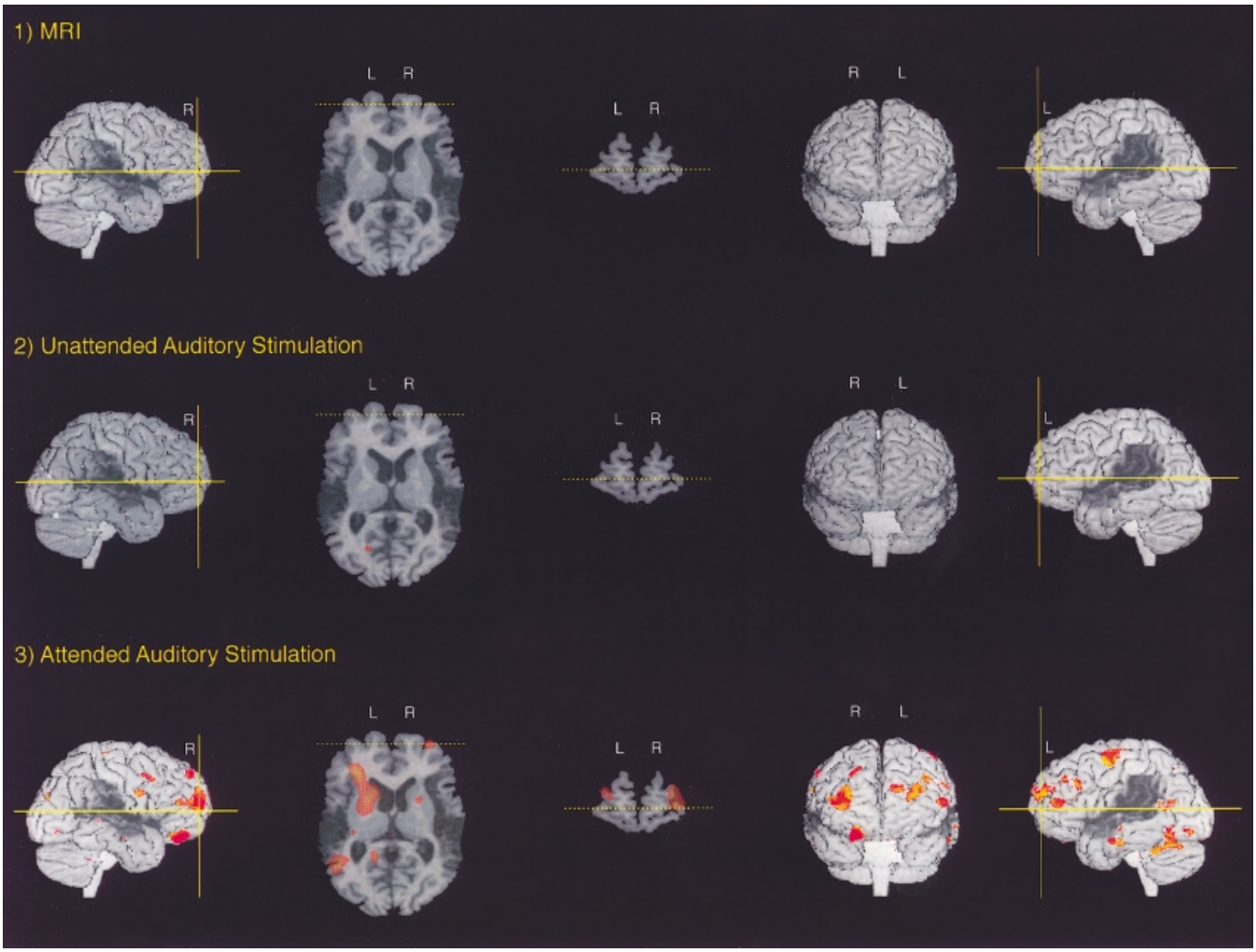

Fig. 2 Structural MRI and PET activation study results in SB. The figure shows the structural MRI scan in SB in the first row and the remaining two rows show the PET activation study results superimposed onto his individual T_1-weighted MRI for two categorical comparisons: unattended stimulation versus no stimulation (rest), and selectively attended versus unattended auditory stimulation. In each row, for these three data sets, the following views are provided (from left to right): lateral surface view in 3D reconstruction of the right hemisphere, horizontal slice parallel to the AC–PC (anterior–posterior commissure) line through the superior temporal gyrus depicting the lesions, coronal slice through prefrontal cortex, frontal view of 3D reconstruction, and lateral surface view in 3D reconstruction of the left hemisphere. The yellow lines indicate where in the volume the horizontal and coronal slices are located. All PET results shown are significant at $P < 0.01$.

examination of auditory evoked potentials further supports this interpretation of complete destruction: the brainstem potentials were normal, whereas the middle-latency potentials, which are most probably generated in the primary auditory cortex (Peronnet and Michel, 1977; Parving *et al.*, 1980; Kileny; 1987; Ibanez *et al.*, 1989; Kaseda *et al.*, 1991; Pantev *et al.*, 1995), were abolished. Only with high sound pressure intensities were some distorted and unclassifiable long-latency responses (200–400 ms) elicited. N1 responses could not be identified. The striking clinical phenomenon in our patient was that he was consciously aware of the presence of sounds only when he paid selective and undivided attention to audition. He showed no hearing when not attending, and only under focused attention was his residual hearing preserved. This syndrome has not been described before and may be labelled as 'deaf-hearing'. This situation cannot be induced in normal hearing subjects, as auditory perception is automatic and mandatory, and cannot be consciously suppressed.

These behavioural findings correlated with a physiological response in which changes in skin conductance were elicited by sound onsets only when SB was paying selective attention to sounds. Even under this condition of focused attention, however, no further discrimination in the sense of same–different judgements or the recognition of sounds or spoken words was possible. A functional neuroimaging experiment was conducted to identify the neural correlates underlying this attentionally modulated 'deaf-hearing', with a paradigm tailored to his unique clinical syndrome. The questions we addressed were (i) whether unattended, unperceived auditory

stimulation would cause cerebral activation, and (ii) how conscious awareness of sound (depending on top-down selective attention) is mediated in a brain lacking the primary auditory cortex.

With our PET activation study we first demonstrated the pathophysiological basis of SB's spontaneous deaf behaviour: unattended auditory stimulation did not lead to substantial cortical activation (two minor activations that were very small in their spatial extent were found). The complete destruction of the right insula (Mesulam, 1985; Habib *et al.*, 1995), in association with the disruption of the reciprocal connections between the primary auditory cortex and the thalamus, might be an important pathophysiological basis for this auditory inattention phenomenon, i.e. the failure of SB to react to unexpected sounds.

In the second part of the PET study, during selective attention and the associated conscious perception of an identical auditory stimulation, we demonstrated prominent bilateral cortical activations, principally in the (pre)frontal and middle temporal regions.

Phenomenological consciousness of sensory stimuli despite complete destruction of the primary sensory cortices (as demonstrated in SB for the auditory modality) is in accord with previous investigations in visual (Barbur *et al.*, 1993) and somatosensory (Bottini *et al.*, 1995) modalities. Barbur and colleagues demonstrated a case of activation of the visual association area labelled V5 (specialized for motion perception), associated with residual perception of moving stimuli despite destruction of the ipsilateral primary visual cortex (Barbur *et al.*, 1993). Parallel afferent pathways to V5 (e.g. Zeki, 1993; Buchner *et al.*, 1997) might account for this phenomenon. Bottini and colleagues demonstrated that additional sensory input in the vestibular modality enhanced activation of touch perception in the spared insular cortex (Bottini *et al.*, 1995). However, in our case of cortical deafness, the modulation of conscious awareness depended not on additional sensory input but rather on attentional modulation. This poses the question of how attention and conscious perception interact.

In healthy human subjects, sustaining attention in the visual domain is associated with right more than left lateral prefrontal and parietal cortex activation (Pardo *et al.*, 1991; Posner, 1994; Posner and Dehaene, 1994; Nobre *et al.*, 1997; Rees *et al.*, 1997*a*; Sturm *et al.*, 1999), and seems to depend on the bilateral prefrontal lobes for the auditory domain (Reinsel *et al.*, 1995; Pugh *et al.*, 1996; Tzourio *et al.*, 1997). Selective attention to a certain modality, stimulus or feature is known to enhance activation in corresponding sensory cortices (Corbetta *et al.*, 1990, 1991; Fink *et al.*, 1996, 1997; O'Craven *et al.*, 1997; Rees *et al.*, 1997b; Tzourio *et al.*, 1997). In another recent PET study, the effect of paying attention to audition versus vision was investigated during bimodal stimulation in which top-down auditory attention was found to be associated with activation in the right thalamus (Frith and Friston, 1996). Bilateral prefrontal and temporal cortex activations may therefore be expected during the attentional processing of auditory material.

Knowledge of the projections from the auditory association cortices to the prefrontal areas is not yet as precise as for the visual domain, where ventral and dorsal stream connections are known to be separate initially and to be integrated later (OScalaidhe *et al.*, 1997; Rao *et al.*, 1997; Courtney *et al.*, 1998). Given that bilateral (pre)frontal cortex activation specifically in BA 8, 9, 10, 45 and 46 has been found previously during sustained auditory attention (Pugh *et al.*, 1996), the activation of these areas in SB may well be associated with the volitional effort to pay selective attention to audition *per se*. Largely symmetrical areas were activated bilaterally in SB. In the light of knowledge derived from other modalities, the bilateral dorsolateral prefrontal activation (BA 46) might also relate to the known working memory functions of these regions (Friedman and Goldman-Rakic, 1994; Klingberg *et al.*, 1997; Braver *et al.*, 1997; Barch *et al.*, 1997; Manoach *et al.*, 1997), since the task of detecting sounds may have entailed monitoring constantly whether a sound signal was still present. An unexpected result was the activation of BA 6, since this is classically considered to be a premotor area. However, McGuire and colleagues demonstrated activation of area 6 during auditory–verbal imagery, and interpreted this evidence as suggesting a role for this executive area in the allocation of attentional resources to the auditory modality in this context (McGuire *et al.*, 1996).

Assuming that the bilateral (pre)frontal activations may be the substrate of the attentional components of the task, the questions arise as to where they exert a modulatory effect, and which cortical structures are mediating the conscious awareness of sounds in the absence of primary sensory cortices Conscious auditory perception is thought to involve (neo)cortical activation (Picton and Stuss, 1994). Crick and Koch argue that the primary sensory cortex activity may not be the substrate of perceptual conscious awareness, but rather activity in higher-order sensory association cortices (Crick and Koch, 1995). Reciprocal connections between the thalamus and neocortex may play a crucial role in conscious awareness, with 40 Hz thalamocortical resonance as a potential neurophysiological basis (Joliot *et al.*, 1994; see also Kinsbourne, 1995; La Berge, 1997).

The extensive reciprocal corticothalamic connections between the primary auditory cortical field (AI) and the medial geniculate body were destroyed in SB. However, the anatomy of the central auditory system differs from that of other sensory systems in that more nuclei lie between the peripheral sensory organ and the primary cortex area. There are also multiple interconnections between the right and left auditory pathways (Nieuwenhuys *et al.*, 1991), as well as parallel afferent pathways to the secondary auditory areas (the so-called 'belt projection'; Celesia, 1976; Pandya, 1995; Kosmal *et al.*, 1997; Kaas and Hackett, 1998; Rauschecker, 1998; see also Appendix I). We infer that part of this system was spared in SB.

The spared middle temporal cortices, which were demonstrated to be active during the attentional state associated with conscious awareness, receive direct afferent projections from more 'diffusely' ascending auditory neurons (Webster and Garey, 1990; P. N. Pandya, personal communication). These neurons do not code for specific acoustic features, for example they do not exhibit frequency-tuning. It seems possible that, under the condition of volitional selective attention, these neurons can successfully mediate the conscious perception of auditory sound 'on' or 'off'. However, as reflected in SB's behavioural syndrome, they cannot mediate more refined discriminations. Therefore, this case demonstrates that for such rudimentary perception the primary fields need not always be an 'obligatory portal for the entry of sensory information into the cortical circuitry' (Mesulam, 1998).

Middle temporal cortex activations have frequently been found in auditory perceptual tasks (e.g. Demonet *et al.*, 1992; Engelien *et al.*, 1995, Binder *et al.*, 1996), thus challenging earlier views that the middle temporal gyrus in man belongs solely to the visual association system (for a recent synthesis, see Mesulam, 1998). We have previously demonstrated that recovery from auditory agnosia after bilateral perisylvian strokes is associated with activation of spared peri-infarct regions in middle temporal gyrus auditory association cortices while listening to environmental sounds (Engelien *et al.*, 1995). The results of this study of a cortically deaf patient now suggest that the recruitment of spared regions in the middle temporal lobe can occur even in the setting of complete, bilateral primary auditory cortex lesions. The residual hearing capacities and middle temporal cortex activations are only associated in this patient under conditions of selective attention.

Within the remaining central auditory system, the modulatory effect of selective attention may take place at many levels. Corticocortical connections with the prefrontal cortices (BA 8, 9, 10 and 46) are well established for the perisylvian auditory association cortices (Streitfeld, 1980; Pandya and Yeterian, 1990). Even though the primary auditory cortices and their recurrent connections with the thalamus were destroyed in SB, components of the auditory system in the thalamus were probably spared. These may include neurons of the parallel auditory belt projection to the secondary auditory cortices directly, and the non-specific auditory projection to the polysensory cortices, which synapse in the small posterior and dorsomedial nuclei of the thalamus, respectively (Rauschecker, 1998). Although the spatial extent of these nuclei is extremely small, a statistically significant activation in the right thalamus was detected in this single-patient analysis. The right thalamus might thus constitute an important locus of the top-down attentional modulation for audition, in accord with the findings of Frith and Friston (Frith and Friston, 1996), even when the projection to the primary auditory cortex is lesioned. Anatomically, the dorsomedial nuclei of the thalamus also project to the prefrontal cortices, again suggesting possible interactions of attentional and auditory processing mechanisms in the (pre)frontal lobes.

Ahissar and Ahissar, in an essay on plasticity of the auditory cortical circuitry (Ahissar and Ahissar, 1994), argue that attention might be necessary to induce certain types of cortical plasticity, so that in principle the attentional effort may not only have the short-term effect of compensation, but may also promote more substantial and long-lasting recovery. However, no qualitative change was observed over 2 years in SB, and the proposal of Ahissar and Ahissar thus remains to be empirically tested for the auditory modality.

Additional subcortical activations were found in the head of the caudate nucleus, the putamen and the cerebellum. Anatomical circuits parallel to the known motor pathways in the basal ganglia, connecting the dorsolateral prefrontal and posterior parietal association cortex via the head of the caudate nucleus and putamen to the thalamus and back to the prefrontal cortex, are known to exist (Alexander *et al.*, 1990). Their functional significance has yet to be fully understood, but cognitive operations have been suggested by multiple lines of evidence, including neurobehavioural findings in patients with basal ganglion dysfunction (Owen *et al.*, 1992, 1997; Dubois *et al.*, 1994; Poncet and Habib, 1994; Robbins *et al.*, 1994; Saint-Cyr *et al.*, 1995; Darvesh and Freedman, 1996; Dubois and Pillon, 1997; Wascher *et al.*, 1997), animal models (Rolls, 1994; Graybiel, 1995), and recent functional imaging studies during cognitive task demands (Alivisatos and Petrides, 1997; Mentzel *et al.*, 1998).

Subcortical activation of the head of the caudate nucleus in SB was strikingly asymmetrical (occurring only on the left), raising the possibility of a functional significance of this laterality. The perisylvian lesion impinging on the frontal operculum and insula was more extended into the frontal white matter adjacent to the right head of the caudate nucleus, so that the lack of activation in the right hemisphere might be due to a disconnection from (pre)frontal cortices. Considering that there was left $>$ right asymmetry not only in the caudate nucleus, but also in the neocortical activation in the spared posterior perisylvian cortex, this might imply a possible verbal components for mediation of the task. However, if internal speech was a strong component in this task, one might also have expected activation in Broca's area in the left hemisphere. No significant activation was observed in this region.

Regardless of laterality, our results suggest a role for the basal ganglia in auditory sensory processing under the condition of selective attention, or participation in the mediation of attentional modulatory effects. As regards the cerebellum, accumulating evidence suggests that its function is not limited to the motor system but also includes a significant role during cognitive tasks (Jenkins and Frackowiak, 1993; Leiner *et al.*, 1993; Schmahmann, 1997). Direct anatomical projections exist between the cerebellar dentate gyrus and prefrontal cortices, and may be a substrate for the participation of the cerebellum in cognitive operations. In the cat, a direct afferent auditory pathway from the inferior

colliculi into the cerebellum has been demonstrated (Kudo and Niimi, 1980). Similar projections might exist in the human, and may have functional significance particularly in the case of auditory cortex lesions. To what degree these structures may also be important for compensation and recovery from such a severe perceptual deficit cannot yet be fully assessed.

Conclusion

Localizing the source of sounds, discriminating between simple and complex patterns and identifying sounds or words are all impossible for SB, even when he makes a volitional effort to use the enhancing effect of selective attention (e.g. in order to detect the doorbell when expecting friends). It therefore seems that, although conscious awareness of sounds can be achieved despite destruction of the primary auditory cortices in man, preservation of at least a small portion of the core projections to the primary auditory cortex in one hemisphere may be necessary in order to enable recovery of more complex auditory discrimination and identification (Engelien *et al.*, 1995).

The work reported here is based on only one patient with unique lesions. However, the careful examination and characterization of SB in terms of his behaviour and the neuroanatomy and neurophysiology of his lesions, in combination with the use of specific functional neuroimaging probes to identify the neural substrates of his attentionally modulated 'deaf-hearing', may shed some light on the attentional modulation of lesioned cerebral sensory systems and on the functional anatomy of human cortical auditory areas beyond the traditionally studied fields in the superior temporal gyrus. Further studies may examine the effect on reinforced selective attention in systematic therapeutic efforts to ameliorate such central auditory disorders after stroke.

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Appendix I

Primary auditory cortex is a cytoarchitectonic definition (e.g. Galaburda and Sanides, 1980), although it was shown a long time ago that it is also possible to identify these fields with physiological criteria (Merzenich *et al.*, 1976). It is thus, in principle, impossible to be absolutely sure of complete destruction of the primary auditory cortex (AI) after a stroke lesion *in vivo*. However, it seems extremely likely that primary auditory cortices were indeed destroyed bilaterally in SB, having taken the available anatomical literature into account. Traditionally, the primary auditory cortex is conceived of as the one field (AI) occupying the medial part of Heschl's gyrus in man (Galaburda and Sanides, 1980; Liegeois-Chauvel *et al.*, 1995; Penhune *et al*., 1996). Recently, two or three primary auditory fields have been suggested in different primate species based on functional properties (Morel *et al.*, 1992, 1993; Kaas and Hackett, 1998; Rauschecker, 1998). The first empirical evidence in man suggests that multiple tonotopic maps with specific orientations can be detected (Pantev *et al.*, 1995; Talavage *et al*., 1997), with a possible analogue to the primate rostral field (R), in the lateral part of Heschl's gyrus in man (Rauschecker, 1997). Both of Heschl's gyri were completely destroyed in SB, and the lesions even extended significantly into the superior temporal gyri, where auditory association areas are located. Therefore, we think it is justified to discuss our findings with respect to the complete destruction of primary auditory cortex.