Central auditory pathologies

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This chapter considers specific deficits in auditory processing (‘negative’ disorders) due to neurological conditions and ‘positive’ disorders of central auditory processing caused by abnormal activity in central auditory mechanisms. Recent work focuses on the assessment of auditory processing in disorders that are not specifically auditory. In this case, auditory measurement may provide a ‘window’ into the condition.

This chapter considers disorders of central auditory processing. These are disorders in the processing of sound after the transduction of the sound into neural activity in the cochlea. Such processing involves the characterisation of auditory patterns in frequency or time that are used to identify and localise sound objects. I restrict the term central auditory disorder to deficits in the processing of auditory pattern before the patterns acquire labels or schemata. The attribution of labels after central auditory processing constitutes semantic processing.

The definition of disorders of central auditory processing is broad and can involve a number of brain mechanisms in the ascending auditory pathway and cortex. The initial processing of spectral and temporal patterns occurs in the cochlear nuclei at the ponto-medullary junction, whilst the initial processing of binaural cues for spatial analysis occurs in the superior olives in the pons. On the other hand, processing mechanisms for higher-order patterns in sound occur well beyond the primary auditory cortex located in medial Heschl’s gyrus in the superior temporal plane. Such widely distributed processing mechanisms can be affected by a number of brain processes.

In this chapter, I will describe a clinical approach to the identification of central auditory pathology and describe types of pathology that can be identified using such an approach. The aim is to describe approaches that help diagnosis in typical clinical settings, rather than detailed assessments that are most appropriate for the cognitive neuropsychological studies in the case literature. The initial consideration of methodology concentrates on techniques that are widely available and appropriate for a routine clinical setting. Some research techniques that might in future prove useful in routine clinical practice are also highlighted. This methodological description will also allow readers to consider the thoroughness of assessments used in the case literature.
Clinical assessment of central auditory disorders

The various techniques used in the clinical assessment of central auditory disorders are summarised in Table 1.

History and examination

As with any neurological disorder, the most important aspect of the assessment of central auditory pathologies is a careful history to determine the nature of the disorder. This allows further assessment to be ‘tailored’ to an individual patient, which is important in view of the extensive battery of tests that would be needed to ‘screen’ patients blindly for these disorders. The suggestions here are based on an intuitive approach, and might in future be systematised into structured questionnaires for which the predictive value of different questions could be formally assessed. This would have the added advantage of standardising the clinical approach to a group of disorders that are seen in a number of different specialties (neurology, otolaryngology, speech and language therapy, and audiology). An important aspect of the history is the assessment of any features that might be associated with cochlear or vestibular disorder: difficulty hearing, tinnitus, vertigo, or features of recruitment. Specific deficits in hearing particular classes of sound (speech, music, and environmental sounds) or particular sound attributes (such as location) should also be sought and can often be helpful in pointing towards a particular psycho-acoustic deficit. For example, one subject with particular difficulty in recognising tunes

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<td><strong>History/clinical examination</strong></td>
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where these had a high tempo was demonstrated to have a deficit in the perception of sound sequences with a high tempo. He had a posterior right hemisphere lesion. Another patient with a pontine vascular lesion reported particular difficulty in sound localisation. That patient was found to have a deficit in the detection of interaural phase and intensity cues. This is consistent with the lesion involving the trapezoid body, preventing comparison of the input to the two ears at the superior olives. In both of these examples, the appropriate psychophysical tests were suggested by the history. Neurological examination is also essential in patients with central neurological disorder. This is the case even if high-resolution structural scanning is available, as this might miss small vascular or inflammatory lesions.

Audiometry

Audiometry is a critical part of the assessment of patients with suspected central auditory pathology. Pure-tone audiometry is essential. In subjects with hearing disorders, the presence of normal pure-tone audiometry makes the diagnosis of a central auditory disorder more likely. However, abnormal audiometry is not an exclusion criterion for central auditory pathology, and normal audiometry alone is not a guarantee that a subtle cochlear deficit is not present. Firstly, it is possible for a degree of cochlear or central deafness to co-exist with other disorders, such as auditory agnosia. Secondly, deafness can be a feature of central auditory disorder in its own right (see below). A number of reports describe evolution of central deafness into auditory agnosia. Finally, normal audiometry does not guarantee that there is no cochlear deficit, as it is theoretically possible to have an outer hair cell disorder that could produce deficits in frequency discrimination in the presence of normal pure-tone audiometry. The detection of such deficits requires psychophysical assessment of auditory filter width using a method such as notched noise. Such techniques have been used in research studies of clinical populations, but are not routinely used in most audiology departments.

EEG and evoked potentials

EEG recording is important in the evaluation of children with acquired disorders of complex sound perception and language to exclude the rare condition of Landau Kleffner syndrome (acquired epileptic aphasia). EEG abnormalities in this condition may be subtle, in that they may be present only during sleep, when continuous spike and slow wave activity
can occur. In general, however, there is no specific indication for EEG in the routine evaluation of central auditory disorders in adults. EEG-evoked potentials in response to sound\textsuperscript{10} are useful for the evaluation of the level of the system at which the abnormality occurs. Auditory brain stem responses to clicks can provide a measure to corroborate the presence or absence of cochlear hearing loss, when there will be an alteration in waves I–V. The amplitude of wave V can be used as a measure of threshold in cases of cochlear hearing loss. Dissociation between the early brain stem responses and the middle latency responses to clicks can allow identification of the site of central pathology. The earliest middle latency responses arise from primary auditory cortex in the medial part of Heschl’s gyrus\textsuperscript{11,12}. This response may be absent in patients with central deafness, when the brain stem responses will be preserved. Pre-attentive and attentive responses to acoustic ‘oddball’ stimuli (the mismatched negativity or M M N, and P300 responses, respectively) have also been extensively investigated in clinical conditions. These responses may in future prove to be useful indicators of specific brain activity at and beyond the auditory cortex. The pre-attentive component may in future prove to be the most useful as this does not require the subject to carry out any task. For example, recent studies suggest that the presence of the M M N predicts a better functional outcome from coma\textsuperscript{13,14}. However, the M M N response can be difficult to obtain even in normal, conscious individuals; the general usefulness of this technique remains to be proven if consistent results are only obtainable in laboratories with specific expertise. Other measures of central auditory processing that may prove to be useful are responses to modulated sound. Stefanatos et al\textsuperscript{15} described a specific deficit in responses to frequency-modulated sound in children with receptive language disorder.

**Psycho-acoustic assessment**

Psycho-acoustic evaluation of subjects with central auditory disorders can allow demonstration of deficits that may be related to the symptoms from which the patients suffer. The presence of deficits in acoustic processing in patients with acquired aphasia due to left hemisphere lesions was first suggested nearly 40 years ago\textsuperscript{16}. That work assessed judgements of the temporal order of two tones at different rates of presentation. Subsequent work has assessed temporal order judgement in developmental disorders including dyslexia and specific language impairment (see Bishop\textsuperscript{17} for a review). Recent work has addressed the presence of deficits in modulation processing in developmental and acquired disorders\textsuperscript{18,19}.

There are a number of practical and theoretical problems with the psycho-acoustic evaluation of subjects with central neurological
conditions. The major practical limitation in clinical practice, more than in a research setting, is the amount of time available for testing. Many psycho-acoustic procedures require hundreds of responses to achieve reliable parameters, and were developed using paid volunteers or undergraduates. This will not be appropriate for, say, a 50-year-old subject who has recently had a stroke. This also raises the issue of the appropriate control data to use. Published data based on highly trained young observers may not be appropriate and the use of control data from age-matched controls who are have undergone a similar amount of training are ideal. The other important issue with respect to psychophysical measures is whether deficits that are demonstrated correspond to perceptual deficits or attentional deficits. This is a particular issue in subjects with lesions of the auditory cortices and beyond. With the now widely used and efficient adaptive tracking procedures, it is not possible to say as they yield a single measure for a given task - the threshold. An alternative approach is to use full psychometric functions where the performance at different stimulus levels is estimated. This allows determination of both threshold and whether the subject reaches ceiling performance at \textit{any} stimulus level; this does not occur if the subject shows an attentional deficit. The measurement of full psychometric functions allows a measure of attentional lapses (reflected by the slope\textsuperscript{20,21}). However, this technique is very time-consuming and, therefore, limited for realistic studies of neurological patients.

A battery of psycho-acoustic tasks for the evaluation of neurological patients has been released recently\textsuperscript{22}. The principal purpose of this battery is to provide a tool for research studies of clinical populations where a psycho-acoustic deficit is predicted, but some of the measures may in future prove to be useful in more routine clinical settings. Full psychometric functions are used for all of the tests. The battery systematically assesses temporal processing by measuring thresholds for the perception of the pitch of regular interval sound\textsuperscript{23}, amplitude and frequency modulation processing at different rates, and gap detection\textsuperscript{24}. Binaural processing is also assessed by the measurement of thresholds for the detection of fixed and dynamic interaural amplitude and phase change of a narrow band carrier.

Structural imaging

Structural imaging is essential in the assessment of subjects with suspected disorders of central auditory processing. The history, clinical evaluation and acoustic tests will yield a description of the phenomenology and hypotheses about its cause that can be tested by the use of structural imaging. Vascular and inflammatory lesions are best demonstrated by specific magnetic resonance images (high resolution T2 and proton density weighted) and the
sensitivity may be further increased by the use of gadolinium contrast. Such imaging may be particularly helpful in the evaluation of brain stem lesions to which computerised tomography radiographs are not sensitive. Even the most sensitive MRI may miss small lesions, however.

Functional imaging

Since the first auditory studies in the late 1980s using positron emission tomography (PET), and in the early 1990s using functional MRI (fMRI), there has been a huge increase in our knowledge and understanding of normal human central sound processing. These techniques measure responses related to the brain blood flow following acoustic stimulation. Studies of patients with certain central auditory disorders have been carried out for research purposes to characterise better the conditions. At the present time, these techniques are not suitable for the routine investigation of central auditory disorders.

Types of specific central auditory disorder

Various types of specific central auditory disorder are summarised in Table 2.

Brain stem disorders

Specific disorders of auditory processing (i.e. deficits that occur in the absence of other perceptual or cognitive disorders) are unusual. This is

Table 2 Various types of specific central auditory disorder

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<th>Brainstem disorders (unusual)</th>
<th>Higher-level disorders</th>
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<tr>
<td>Deafness</td>
<td>Central deafness</td>
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<tr>
<td>Temporal-cue detection deficit</td>
<td>Requires bilateral lesions of cerebrum. The older term 'cortical deafness' may be incorrect as the causative lesion may be in auditory radiation. May evolve into auditory agnosia</td>
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<tr>
<td>Binaural-cue detection deficit</td>
<td>Auditory agnosia</td>
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<tr>
<td></td>
<td>Abnormal perception of complex sound in the presence of preserved hearing. Often, but not always, associated with bilateral lesions in region of superior temporal lobe</td>
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<td></td>
<td>Auditory agnosia 1: (pure) word deafness</td>
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<tr>
<td></td>
<td>Inability to perceive oral words</td>
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<td></td>
<td>Auditory agnosia 2: amusia</td>
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<td></td>
<td>Deficit in musical perception</td>
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<td>Auditory agnosia 3: environmental sound agnosia</td>
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<td>Deficit in the perception of environmental sounds</td>
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particularly so in the case of conditions affecting the brain stem. Here, the auditory pathway is closely related to key motor and sensory tracts and nuclei, and the incomplete decussation of the auditory pathway means that the ascending auditory tracts (the lateral lemnisci) transmit information from both ears. It follows from this that many hearing disorders can only be produced by bilateral lesions of the brain stem, which would usually be expected to produce striking neurological features in addition.

Deafness due to disorders of the brain stem is unusual, but has been described due to a vascular lesion\(^2^8\) and is described as occurring in multiple sclerosis (MS). Most neurologists, however, would be very reluctant to ascribe deafness to MS, and would search hard for another cause in patients with this disorder.

The brain stem is the first point of convergence of the input from the two ears, with important points of convergence occurring at the superior olives (in the pons) and between the two inferior colliculi (in the mid-brain). These points of convergence allow binaural processing, the comparison of the phase and intensity of sounds presented to the two ears. A derangement of such processing can occur in MS\(^2^9\)–\(^3^1\) and vascular lesions\(^4\). In the case of MS, the lesions demonstrated by MRI in these patients and associated deficits in brain stem-evoked potentials make it likely that the disease in the brain stem is causal. Many of these patients had psychophysical deficits that were not symptomatic.

Temporal processing deficits are described in MS as well. Early studies suggested deficits in the perception of frequency modulation and formant frequency changes in synthetic speech\(^3^2\),\(^3^3\). It would seem plausible that such deficits might occur as a result of involvement of mechanisms for modulation processing in the ascending pathway in brain stem. Such mechanisms are well described in animal models (see, for example, Rees and Möller\(^3^4\)). Other studies have demonstrated deficits in the detection of temporal gaps in noise in MS\(^3^5\),\(^3^6\). The gap detection studies cannot be interpreted unequivocally in terms of brain stem versus cerebral involvement.

**Higher-level disorders**

Deafness can also occur in lesions of the cerebrum\(^3^7\)–\(^4^1\) and there is a long-standing debate as to whether should be called ‘cortical deafness’ to parallel the better-established cortical blindness. The disorder is always associated with bilateral lesions (usually vascular, see Griffiths et al\(^5\) for detailed description of individual cases in terms of hearing loss, evoked potentials, and lesion). The idea has been controversial, firstly because of debate as to whether the disorder might represent a disorder.
of auditory perception or attention. Many of the patients show an initial profound hearing loss with recovery, which parallels the effect of cortical lesions in the macaque but not lower mammals. For human subjects, variability in the audiograms of affected individuals is consistent with a variable attentional component to the condition, but there is always a degree of deafness after this is taken into account. A second source of controversy has been whether the condition is a truly cortical disorder. Tanaka et al described two cases with partial sparing of Heschl’s gyrus (containing the primary auditory cortex in its medial part) on one or both sides. This suggests the possible importance of projections to the auditory cortex rather than lesions of the cortex itself. For this reason, I have proposed the term central deafness for this condition.

Auditory agnosia is a condition where there is impaired perception of complex sounds with preservation of the pure tone audiogram. The disorder can evolve from central deafness, and is also associated with bilateral lesions of the superior temporal lobes, although cases in association with unilateral lesions are described. Three different forms of auditory agnosia have been described: for words (word deafness), music (amusia) and environmental sounds (environmental-sound agnosia). There is often overlap between the three forms, and I have argued on the basis of this that the disorder can be characterised as an apperceptive disorder. This term is used in the sense of an inability to perceive particular patterns in sound, in distinction to the attribution of meaning to those sounds after initial pattern processing. Common deficits in the analysis of particular stimulus features might on this basis be manifest with a number of different sorts of sound. For example, the slow changes in pitch, intensity and timing of musical sounds have a parallel in prosody or the ‘melody of language’. There is a well-established association between amusia and deficits in prosodic perception, even in cases where language function is otherwise spared. This is consistent with a common deficit in the perception these two sound patterns characterised by features that change at similar rate. Consistent with this, psycho-acoustic studies of one subject with amusia demonstrated a profound deficit in amplitude and frequency modulation perception, that was particularly marked at low modulation rates, corresponding to slow temporal changes. Interestingly, the same subject was still able to detect the emotion in music despite an almost total loss of musical recognition. It is important to stress that this account of apperceptive agnosia does not exclude the existence of associative forms of auditory agnosia, where the spectrottemporal patterns corresponding to an acoustic object are analysed normally but the association of those patterns with semantic labels or schema is lost. Recent functional imaging work suggests the possibility that the...
planum temporale, the part of the superior temporal plane behind Heschl’s gyrus, may be an important locus for such association.

Recent studies of congenital auditory agnosia

There are reports of subjects with ‘tune deafness’ or ‘tone deafness’ going back a century in the absence of any known neurological insult. This disorder may represent a developmental form of amusia, although there are clear differences, such as the absence of any associated deficit in the detection of prosody in speech. The disorder has just been just been systematically described for the first time. Striking deficits in the perception of music were demonstrated in subjects otherwise considered ‘normal’ using the battery of tasks originally developed by Peretz for the characterisation of acquired amusia. Further studies are needed to show how common this disorder is in the population, at what level the deficit lies, and what brain structural and functional brain deficits can be demonstrated. The striking pitch difference limens found (greater than four semitones in one subject) suggests that this is a central rather than a cochlear disorder. In the converse situation, where subjects have good musical skills, interesting brain correlates have been described such as greater structural asymmetry in the planum temporale associated with absolute pitch. It will be interesting to see if anatomical and functional correlates exist at this level.

‘Positive’ disorders of central auditory processing

Tinnitus may be associated with abnormal activity in the ascending auditory system or auditory cortex. Using PET, Lockwood and colleagues studied patients with tinnitus evoked by facial or eye movements, a condition that allows subjects to ‘switch’ the tinnitus on and off to allow demonstration of activity associated with the percept. Gaze-evoked tinnitus was originally thought to be rare, even amongst patients with eighth nerve section for acoustic neuroma, but turned out to be common in this particular group. Unilateral activation of the auditory cortex or auditory pons without auditory input was been demonstrated in these subjects. This pattern would not be seen with actual auditory input even to one ear, due to the incomplete decussation of the auditory pathway. Lockwood has argued that central tinnitus associated with abnormal activity of the auditory cortex or pons might be likened to the phenomenon of alien limb in amputees. A recent fMRI study has examined the basis for tinnitus in more typical tinnitus patients who had not undergone surgery. The use of subjects with
normal hearing and lateralised tinnitus simplified the interpretation. Indirect inference about abnormal activity in the inferior colliculus was made on the basis of less increase in activity with sound stimulation. This effect might be due either to masking of abnormal central activity by external sound or saturation effects when the effect of central activity and external stimulation is combined. In either case, the results support abnormal activity in the central pathway in this more common form of tinnitus.

Musical hallucinations need to be distinguished from tinnitus, but also appear to be due to abnormal central auditory activity\(^26\). This disorder may occur in subjects who are in middle-to-later life with moderate-to-profound hearing loss. More rarely, the condition can also occur due to central lesions, epilepsy or psychosis. In the common form, subjects typically experience melodies that were previously familiar and it can be argued on the basis of the phenomenology that the condition is due to the inappropriate activity of a normal mechanism for musical perception and imagery. Supporting this, functional imaging demonstrated a network of brain areas where activation increased with severity of the hallucination. This network was similar to that shown in normal hearing subjects actually listening to sound sequences. This bilateral network includes the planum temporale and frontal operculum.

**Auditory processing in disorders that are not specific auditory disorders**

Many of the specific disorders with localised pathologies, as described above, are rare. There has been considerable recent interest in assessing central auditory processing in neurological conditions that are not restricted to audition, as a ‘window’ into the condition. In coma due to a variety of causes, EEG-evoked potential studies suggest that the early brain stem responses to click are often preserved, but that their absence correlates with poor survival\(^76-79\). Recent studies mentioned above have shown that the presence of MMN can correlate with a good prognosis at the level of functional outcome. Whilst any conclusion about unique predictive power for auditory tests would be premature, the results to date (and reasoning based on the distributed nature of many auditory cortical processes) suggests a useful application of auditory testing in the intensive care ward.

A PET study of five patients in vegetative state due to diffuse hypoxia has shown activation in primary auditory cortex in the region of Heschl’s gyrus and in the planum temporale in response to click stimuli, despite decreases in resting metabolism\(^80\). These activations occur in a
similar region to that demonstrated in normal controls in the same experiment, and in MEG studies of normal click response\textsuperscript{11}. Less activation in response to clicks was observed in more posterior cortex in the temporoparietal junction in patients compared to controls, and an analysis of functional connectivity showed a functional disconnection between the posterior superior temporal lobe and the inferior parietal lobule, anterior cingulate and hippocampus. This suggests a deficit in connections beyond the auditory cortices in these patients.

Conclusions

Increasingly, systematic assessment of specific deficits in central auditory processing has led to greater understanding of their psycho-acoustic and anatomical basis. Recent work has characterised a developmental form of auditory agnosia, and re-organisation and aberrant activity within the central auditory system is becoming increasingly recognised as a cause of pathology. The use of sound stimuli to probe the unconscious brain is a developing area, with the potential to define distributed brain mechanisms relevant to functional outcome from coma and vegetative state. Auditory stimuli have the potential to probe the integrative function of the brain needed for normal conscious functioning and a challenge for the future is to develop auditory stimuli and techniques that can probe this integrative function in routine clinical settings.

References

5 Griffiths TD, Rees A, Green GGR. Disorders of human complex sound processing. Neurocase 1999; \textbf{5}: 365-78
8 Chinnery PF, Elliott C, Green GR et al. The spectrum of hearing loss due to mitochondrial DNA defects. Brain 2000; \textbf{123}: 82-92
Buchtel HA, Stewart JD. Auditory agnosia: apperceptive or associative disorder? Brain Lang 1989; 37: 12–25
Coslett HB, Brashear HR, Heilman KM. Pure word deafness after bilateral auditory cortex infarcts. Neurology 1984; 34: 347–52
Tanaka Y, Yamadori A, Mori E. Pure word deafness following bilateral lesions. Brain 1987; 110: 381–403
von Stockert TR. On the structure of word deafness and mechanisms underlying the fluctuations of disturbances of higher cortical functions. Brain Lang 1982; 16: 133–46
67 Monrad-Krohn GH. Dysprosody or altered ‘melody of language’. Brain 1947; 70: 405–15
73 Zatorre RJ, Perry DW, Beckett CA, Westbury CF, Evans AC. Functional anatomy of musical processing in listeners with absolute pitch and relative pitch. Proc Natl Acad Sci USA 1998; 95: 3172–7