Auditory Processing Disorder (APD): Progress in Diagnostics So Far. A Mini-Review on Imaging Techniques

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Auditory processing disorder (APD) is a disorder that affects the perception of sound, both verbal and non-verbal. Patients who are generally diagnosed with APD present with normal audiograms. There is no gold standard investigation for APD and no standardized criteria for diagnosis. Because of its disabling effect and the overlap that exists with other neurodevelopmental disorders, there is an urgent need to develop tools and criteria for appropriate diagnosis. There is a current significant focus in research on imaging techniques that can possibly be used in the future for the appropriate diagnosis of APD. Over the years, several imaging techniques have contributed significantly to defining this disorder. To date, no studies have reported the routine use of imaging for the diagnosis of APD.

KEYWORDS: Auditory processing disorder, APD assessment, APD imaging, neurodevelopmental disorders

INTRODUCTION
The definition that was agreed upon by the British Society of Audiology (BSA), the American Speech–Language–Hearing Association (ASHA), and the American Association of Audiology (AAA) is that auditory processing disorder (APD) is a deficiency in the central auditory nervous system that causes an impairment in the ability of the auditory pathway to integrate appropriately to enable normal sound perception [1]. Patients who are generally diagnosed with APD present with normal audiograms. These patients experience a significant difficulty in perceiving sounds, both verbal and non-verbal. The definition of APD is still a debatable issue. This disorder is diagnosed in both adults and children.

In the 2011 BSA position statement, APD is described as a group of symptoms that may present with other neurodevelopmental disorders, including attention deficit hyperactivity disorder (ADHD) and autism. In fact, several reviews and studies give an indication that APD tends to coexist with learning and language disorders [1]. There is evidence that shows that higher-order cortical functions, particularly attention, play a role in problems with listening, which implies that this is not a problem of the auditory pathway on its own [2, 3].

The auditory deficits involved include the following:

“Sound localisation, auditory pattern recognition, auditory discrimination, temporal processing, processing of degraded signals and processing of auditory signals when embedded in competing acoustic signals” (Bamiou et al., 2001) [4].

These auditory deficits translate into the following problems with verbal instructions and directions: needing repetition; reading problems, with poor handwriting and spelling skills; difficulties in perceiving speech; problems with understanding a fast speaker; difficulties in structuring a sentence and communicating with others as well as following a conversation in background noise; difficulties in localizing a sound; impaired auditory sensations; difficulties in maintaining attention; and difficulties in learning a foreign language and new words. Also, these patients tend to provide inappropriate responses when asked for particular information [4-6]. It has also been reported that children referred for testing for APD generally have other forms of deficiencies, mainly in cognitive function and attention [3].

Current Proposed Classification of APD
In the BSA position statement (BSA, 2011), APD was categorized into three types, namely developmental, acquired, and secondary.

Developmental APD is defined as a case where a child presents with a normal audiogram but is having problems with hearing, although with no significant history. Also, the child would generally be struggling at school. It has been suggested that APD in children could be part of a neurodevelopmental syndrome that develops as the child grows older and demands on higher cortex
functioning increase with changes in the social environment and the addition of academic pressure [2].

The acquired form of APD is diagnosed when a patient presents with abnormal hearing after an incident such as a head injury, vascular event, multiple sclerosis (MS), or infection [7]. A recent study showed that HIV infection or its treatment could be a possible cause of difficulty in perceiving sounds with relatively normal audiometry [8]. A case report in 2004 reported a patient who sustained a significant head injury and was complaining of difficulties in listening, paying attention, and communicating [9]. This patient seems to have had a form of acquired APD.

Secondary APD is when APD results from an initial peripheral hearing problem such as otitis media with effusion [2, 7, 10]. This is hypothesized to be a potential etiological factor in APD because repeated otitis media at a young age leads to repeated episodes of abnormal hearing. However, the effect of otitis media with effusion on children is probably related to the severity of hearing loss, not simply the presence of hearing loss. Bilateral, persistent, as well as severe hearing loss (more so than moderate forms) might impede the normal development of the auditory pathways. Children with a history of otitis media have a long-term risk of functional hearing deficit [11]. The presence of persistent otitis media with effusion may represent an additional significant problem, particularly for a child who already has another existing disability. Such children may have permanently impaired auditory perception [11].

There is no gold standard investigation for APD and no standardized criteria for diagnosis. In fact, a study demonstrated that there were nine different sets of criteria for APD with a diagnosis rate ranging from 7.3% to 96% [12].

A good clinical history is needed from the patient or from parents, teachers, and caregivers in the case of children. Validated questionnaires exist to collect this information [1].

Diagnosis is generally made using the test battery recommended by local guidelines, if available. If at least one core test results in poor performance, a diagnosis of developmental APD is made [11]. Detailed audiometry is necessary to exclude any peripheral ear problems. A set of suggested tests includes the following:

1) SCAN, which assesses auditory processing via four assessment subsets. One test evaluates the patient’s ability to discriminate single words in background noise, the second uses acoustically degraded words, the third subset presents single words dichotically, and finally, sentences are used. In all of these, the patient is asked to repeat what s/he heard. Different versions of this test exist for adults, adolescents, and children;

2) Random Gap-Detection Test (RGDT) determines the gap threshold in frequencies that the patient can detect. This gives an indication of the patient’s auditory temporal resolution;

3) Gap in Noise Test (GIN) is also a measure of auditory temporal resolution, but determines the gap that the patient can detect in white noise;

4) Pitch Patterns Sequence Test (PPT) and Duration Patterns Sequence Test (DPT) determine the ability of the patient to identify an auditory pattern. PPT presents a change in pitch, whereas there is a change in the duration of a tone in DPT. Patients are then asked to describe the changes in the tones [13].

However, psychoacoustic testing is not considered to be a good representation of a patient’s problems [1]. On the other hand, electrophysiological testing, such as for complex auditory brainstem responses (ABR), might give a better indication [2].

In 2011, a survey was performed to discover the most commonly used methods for APD testing. This showed that most clinicians use their test batteries on their experience, reviewing current literature, and the most recent national guidelines available, together with the patient’s age and history [14]. The most commonly used tests were the dichotic listening test (DLT), monaural low-redundancy speech test, and temporal processing tests [14].

### Imaging Techniques Available

To date, imaging has only been used in research, mainly in developmental APD, despite being highly recommended for appropriate clinical diagnosis [15]. None of the current guidelines recommend imaging. Currently, clinical audiologists diagnose auditory deficits and determine reversed language dominance by clinical testing only, with no evidence from imaging or electrophysiological testing [16].

Acquired APD can be indicated via computed tomography (CT) scanning. A vascular event or tumor that is shown on CT and occurs within one of the auditory areas gives evidence that the location of the vascular event/tumor is causing the patient’s hearing impairment.

The main techniques that have revolutionized the way in which we visualize the brain and how it functions are the positron emission tomography (PET) scan, structural and functional magnetic resonance imaging (sMRI and fMRI, respectively) with the diffusion tensor imaging (DTI) technique, magnetoencephalography (MEG), and electroencephalography (EEG) [17]. Near infrared spectroscopy (NIRS) is another technique that may be used, but it is not popular because fMRI and MEG provide superior information [17].

Via the uptake of a radioactive tracer, a PET scan can detect the areas in which the uptake of the tracer is highest and where perfusion is increased, which indicates the areas with the highest activity. Abnormal uptake of the tracer is indicative of decreased activity.

Currently, PET is likely to be used in APD for research purposes and when fMRI cannot be used due to the presence of incompatible materials, as in patients with cochlear implants [18]. This is also true for NIRS [17].

Diffusion tensor imaging is a magnetic resonance technique that is powerful for investigating the microstructure of white matter in vivo. The diffusivity of water is described by diffusion parameters, namely fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD: perpendicular diffusion), and axial diffusivity (AD: parallel diffusion). A high value of FA is indicative of the presence of high fiber density and organization and therefore better fiber myelination. MD indicates the rotational invariant of diffusion and is indicative of increased overall diffusion [19]. White-matter abnormalities generally
result in a decrease in FA and increases in MD and RD. Abnormalities that are detected by DTI are referred to as decreased microstructural integrity [20, 21].

Structural magnetic resonance imaging using the fluid attenuation inversion recovery (FLAIR) technique is an excellent imaging technique for identifying lesions in the brain, as in MS, because it provides good spatial resolution and identification of lesions [22]. sMRI produces an image of the brain’s gross anatomy because it is ideal for imaging soft tissue. MS patients are generally diagnosed by sMRI scanning. This can be the investigation of choice to determine whether plaque lesions that are typical of MS are found in any of the auditory processing areas.

On the other hand, fMRI with blood oxygen level-dependent (BOLD) contrast is what would be used, as suggested by current research, for developmental and secondary APD. BOLD fMRI is what is mostly used in research to identify the auditory processing pathways and abnormalities within them [23]. fMRI in APD will therefore highlight the areas in which there is either abnormal or no neural activity via the production of a very weak signal.

Electroencephalography and MEG record neuronal activity via electric or magnetic fields, respectively. These neuroimaging techniques provide a way to assess cortical networks during perception of a stimulus, such as sound in a background of noise, and the results give a more fine-tuned localization when used in combination. Because their excellent temporal resolution, they are used for connectivity analysis in auditory processing [25, 26]. Compared with EEG, MEG produces less distortion. Because MEG records the magnetic field, which is not affected by bone, separate recordings from both hemispheres can be collected more conveniently [17, 27]. Four reasons that have been suggested as to why this neuroimaging technique is useful include the following: it can provide evidence of the mechanisms of cortical neural activity that occur in central APD (CAPD) and what kind of compensation occurs; it enables visualization of the link between patient performance and neural structures in clinical testing; if neural pathologies are identified, there can be new, better management of the condition based on the indicated neural abnormalities; and it can be used to determine how much restoration of normal neural activity in CAPD occurs via interventional management of CAPD patients [25]. MEG in combination with ABR can track neural activity at the start of a neural signal from the structures just below the midbrain up to the higher auditory cortex [28]. MEG and EEG can assess selective attention because it has been shown that attention causes a significant change in the M100 and N100 potentials, respectively, in normal listeners when attending to a particular signal when two signals are presented at the same time [17]. This is expected to be abnormal in APD, with delayed or absent signals. MEG and EEG provide excellent temporal resolution but poor spatial resolution, whereas fMRI has very good spatial resolution and poorer temporal resolution [17].

Use of Imaging in APD Research

A reported case study of a young adult who had had difficulties in understanding speech and communicating with others since he was a child used 18F-FDG PET with advanced signal analysis using a high-resolution research tomograph (HRRT) (ECAT HRRT; CTI/Siemens) and a 1.5 T MRI scanner (Magnetom Vision Plus; Siemens), with prior testing using pure-tone audiometry (PTA), ABR, and auditory evoked potentials/middle latency responses (MLR) [19]. In this study, normalization of PET images was carried out using the SPM5 software package (Wellcome Department of Imaging Neuroscience, University College London) [19]. The patient’s language functionality was assessed using the Western aphasia battery and his cognitive functioning via the Wechsler adult intelligence scale [19]. Audiology and electrophysiological testing were normal, which indicated that the hearing problem lay beyond the brainstem. Neuropsychological testing showed a deficiency in psychometric intelligence, scoring better on performance IQ than verbal IQ [19]. He underwent resting-state MRI and PET scans. sMRI showed significant bilateral atrophy within the auditory cortex and PET showed symmetrical hypometabolism in these areas, namely, in Heschl’s gyri and the precuneus [19]. There was a relative increase in metabolism in the right caudate and both superior frontal sulci [19].

A study was performed using DTI utilizing a 3 T Tim Trio MRI scanner (Siemens; Erlangen, Germany) to assess children with listening difficulties in comparison with typically developing children [21]. This study revealed that in children with listening difficulties there was abnormal brain connectivity: “frontal distributed atypical white matter microstructure”. It was also noted that in multifocal areas in the white matter within the frontal region and auditory radiation area there was delayed myelination. In general, this study concluded by means of DTI during DLT that both sensory and higher-order deficits cause listening difficulties [21].

Resting-state fMRI using a 3 T Siemens Magnetom Trio Tim MR scanner equipped with a 12-channel matrix head coil and MR-compatible goggles (Nordic NeuroLab Visual System) was used to compare children with CAPD and typically developing children of the same ages [27]. This study showed atypical activity in the resting state in the posterior cingulate gyrus of the children diagnosed with CAPD [27]. The posterior cingulate gyrus is part of the default mode network, which is the area involved in attention in the human brain [27]. These findings were similar to findings in children with ADHD. Unfortunately, fMRI cannot help distinguish between areas used for attention related to listening from those used for general attention [27].

Another study with normal participants using BOLD fMRI scanning with a 1.5 T machine with a head coil (Magnetom Sonata, Siemens AG Medical Solutions, Forchheim/Erlangen, Germany) for testing revealed the areas that were activated by the different tests [28]. MRI data were converted into an analyzing format to be read by the Statistical Parametric Mapping program SPM2 (Functional Imaging Laboratory Methods Group, University College; London, UK) using OSIRIS (Unité d’Imagerie Numérique, Service d’Informatique Médical, Département de Radiologie et d’Informatique Médical, Hôpitaux Universitaires de Genève, Switzerland) and MRicro (7) programs [29]. The Hanover phoneme discrimination test (HPDT), memory span test (MST), and DLT were used in normal adults and normal children [23]. The left middle temporal gyrus (MTG) was activated during the HPDT [23]. In children, the inferior frontal gyrus was also activated, which could be due to working memory processing, not listening per se [23], as was shown in other studies [30]. Because the left MTG exhibited the maximum global responses during the HPDT, it is a possible indication
of phoneme-specific localization [23]. Bilateral activation of the insula possibly indicates that once an auditory stimulus is received there is a process of preparation for speech production, even if this does not actually occur [23]. The insula has previously been associated with overall speech production [29]. DLT is a test that is commonly used in the diagnosis of CAPD. This revealed bilateral activation of the superior or temporal gyrus (STG), although it was the right STG that displayed the most global activation [23]. Also, with the Dichotic listening test there was bilateral activation of the STG [23]. By means of this study it was concluded that the activation patterns that were recorded by BOLD fMRI during this study provided significant data with which scans from children with CAPD can be compared [13].

Another study that compared typically developing children with children with autism spectrum disorders using MEG showed M100 latency when they were presented with pure tones of different frequencies [26]. A whole-cortex 275-channel MEG system (VSM MedTech Inc.; Coquitlam, BC) was used [26]. Raw data were corrected for eye-blinking by applying the pattern search function in the BESA 5.2 program (MEGIS Software GmbH; Gräfelfing, Germany) [26]. A delayed response was indicative of an abnormality in auditory processing pathways.

A study in 2011 that compared children with auditory sensory processing problems with typically developing children used a 32-channel BioSemi Active Two EEG system (BioSemi Inc.; Amsterdam, the Netherlands) to follow event-related potentials (ERPs) to show that there was a significant difference in processing in the cortex between two groups: one of typically developing children and another of children with a sensory processing disorder [30]. ERP signals were recorded while auditory stimuli in the form of clicks and tones of different frequencies and intensities were presented [30]. EEG and ERP signals were analyzed using Brain Vision Analyzer 2 software (Brain Products GmbH; Munich, Germany) [30]. It was concluded that there actually was a statistically significant difference in brain function between the two groups [30].

MEG using a 306-channel Neuromag Vectorview MEG system (Elekta; Helsinki, Finland) was used in a study involving normal young adults, during which mismatch negativity in phrase structuring was used to identify localized areas within the cortex that process language and during which mismatch negativity in phrase structuring was used to identify localized areas within the cortex that process language and the perception of speech signals [31]. Strong signals were recorded in the primary auditory cortex and superior temporal sulcus, which were stronger in the left hemisphere [31]. These strong signals were an indication that the normal brain very quickly picks up any changes in language [31]. Signals with mismatch negativity were significantly reduced in patients with dyslexia when presented with changes in tone frequency [32]. Dyslexia is commonly associated with APD [1].

CONCLUSION
As a result of these studies, it is clear that there is a role for imaging techniques in diagnosing APD. Several areas of abnormal brain activity have been detected, which can provide a more evidence-based diagnosis when imaging is used together with the patient’s history, detailed audiometry, electrophysiological testing, and neuropsychological testing. Some clinical testing might be eliminated if imaging is performed.

In acquired forms of APD, imaging such as CT scans or sMRI can make the diagnosis more efficient and accurate because it provides evidence of a lesion such as a slow-growing tumor or a previous hemorrhagic event. Even in children, a tumor could be a cause of their inability to perceive verbal and non-verbal sounds and impaired speech [33]. If sMRI is not performed in such a case, the tumor could go unnoticed for a very long time; the child could be coping, although with difficulty, because of the brain’s ability to compensate.

The use of MEG, EEG, DLT, and BOLD fMRI (where available) should be increased for difficult cases of developmental and secondary APD in which a patient seems to have other deficits as well as in auditory processing that are difficult to distinguish. If an abnormal area within the cortex can be localized by BOLD fMRI and abnormal neural activity or connectivity detected by MEG, a better diagnosis can be made. A drawback with this is that the anatomy and interactions of the auditory pathways are still not wholly defined and because of an overlap in the attention pathways, a diagnosis of APD may still not be distinct from an attention deficit disorder. This is probably why imaging techniques are still not included in guidelines and clinicians hesitate to use them.

To diagnose a patient with developmental or acquired CAPD, the patient should have a good history taken followed by a series of tests, which requires a multidisciplinary approach [15]. Audiometry, electrophysiological studies, and neuropsychological testing should be performed as well as an appropriate neuroimaging technique to make a definite diagnosis [15]. The routine use of neuroimaging for diagnosing neurodevelopmental disorders may take more time until there is a confirmed map of the cortex and defined abnormalities that can be detected by the different imaging techniques. It seems that a lot of work remains to be conducted.

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