ABNORMAL ANATOMY OF THE AUDITORY CORTEX IN SCHIZOPHRENIC BRAINS WITH AUDITORY HALLUCINATIONS: A SYSTEMATIC REVIEW

By

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Audiology Doctoral Project Submitted to the Faculty of the

DEPARTMENT OF SPEECH, LANGUAGE, AND HEARING SCIENCES

In Partial Fulfillment of the Requirements

For the Degree of

DOCTOR OF AUDIOLOGY

In the Graduate College

THE UNIVERSITY OF ARIZONA

2022

THE UNIVERSITY OF ARIZONA
GRADUATE COLLEGE

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titled: Abnormal Anatomy of the Auditory Cortex in Schizophrenic Individuals with Auditory Hallucinations: A Systematic Review and Synthesis.

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Final approval and acceptance of this Audiology Doctoral Project is contingent upon the candidate's submission of the final copies of the Audiology Doctoral Project to the Graduate College.

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ACKNOWLEDGEMENTS

I would like to express the deepest appreciation to my committee chair and Neuroaudiology lab mentor, Dr. Frank Musiek for his devotion to promoting excellence, providing guidance, and encouraging us to dig deeper. To Dr. David Velenovsky, for sharing his endless curiosity and passion for all things audiology (or audiology-adjacent). And to Dr. Linda Norrix, for nurturing my growth as both a clinician and researcher. Your support has inspired another class of exceptional audiologists.

Further, I would like to recognize my fellow lab members, Aaron Whiteley, Au.D., and Barrett St. George, B.S., for their foundational contributions and technical skills that allowed for the completion of this research project and many others.

Most of all, I would like to thank Jillian Bushor, my research partner, for her dedicated work in producing this complimentary research project. I could not have asked for a better teammate.

DEDICATION

To my Echo, without whom I would never have made it this far, and the many soulmates we have acquired along the way.

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Abstract

Background: Due to the high prevalence of auditory hallucinations in schizophrenic individuals (60-80%; Lim et al., 2016), this review will focus on evidence of neuroanatomical abnormalities found in key auditory structures of this clinical population. Identifying atypical anatomy of these areas can inform our understanding of the mechanisms underlying the experience of auditory hallucinations as well as potential deficits in central auditory processing, providing a rationale for the involvement of audiologists in diagnosis and treatment of auditory hallucinations.

Purpose: The goal of this review is to describe the auditory neuroanatomical differences in schizophrenic individuals who experience auditory hallucinations compared to normal individuals who do not. Further, it will also explore how these differences in neuroanatomy may be related to central auditory processing dysfunction and auditory hallucinations.

Methods: A review of existing literature published from 1960-2020 was conducted to summarize and compare neuroanatomical abnormalities of key auditory structures in schizophrenic brains. Relevant studies published between the years of 1960 and 2020 were identified using the following online databases: Google Scholar, PubMed, PSYCnet, and Mendeley, as well as books, chapters, and bibliographies. For each of the listed databases, search terms included “schizophrenia” AND “auditory hallucinations” AND “auditory cortex” AND “anatomy” AND “Sylvian fissure” OR “superior temporal gyrus” OR “Heschl’s gyrus” OR “planum temporale” OR “(central) auditory processing dysfunction” OR “dichotic listening”.

Results: Findings from previous anatomical studies are in strong agreement, having identified structural abnormalities of Heschl’s gyrus, planum temporale, and the Sylvian fissure in schizophrenic brains, suggesting that these auditory structures potentially play a role in the experience of auditory hallucinations.

Conclusion/Discussion: This review summarizes and compares available evidence of neuroanatomical abnormalities in the auditory cortex of individuals with schizophrenia who experience auditory hallucinations. Anatomical studies investigating auditory structures in schizophrenic brains indicate abnormalities of Heschl’s gyrus, planum temporale, and the Sylvian fissure, particularly a reduction in hemispheric asymmetries. These anatomical deviations have implications for functional auditory processing. Evidence of the involvement of these key auditory structures provides rationale for audiologists to collaborate with psychiatrists in the diagnosis and treatment of auditory hallucinations. This review also suggests the need for future research to investigate potential correlations between neuroanatomical variances in schizophrenic brains and audiological findings.

Key Words: Auditory Hallucinations, schizophrenia, auditory cortex, structure, anatomy, superior temporal gyrus, Heschl’s gyrus, planum temporale, Sylvian fissure, central auditory processing, dichotic listening

Abbreviations: Auditory hallucinations (AH), auditory verbal hallucinations (AVH), central auditory nervous system (CANS), inner speech model (ISM), corpus callosum (CC), superior temporal gyrus (STG), Heschl’s gyrus (HG), planum temporale (PT), gray matter (GM), gray matter volume (GMV), white matter (WM), white matter volume (WMV), anterior cingulate cortex (ACC), temporo-parietal junction (TPJ), right ear advantage (REA)

Background

Auditory Hallucinations and Schizophrenia

Hallucinations can occur unimodally in any of the senses (visual, somatic/tactile, olfactory, auditory), but the most commonly experienced are multimodal hallucinations (53% compared to 27%). Notably, auditory hallucinations (AH) were the most common in both the unimodal (68%) and multimodal hallucination groups (88%), followed by visual, somatic, and finally olfactory hallucinations (Lim et al., 2016). For the purpose of this review, we will focus on auditory hallucinations, which have been defined as perceptions of sounds experienced in the absence of a corresponding external stimulus (Nazimek et al., 2012). This definition is not exclusive to AH; it is also used to describe tinnitus, a common symptom for many individuals with hearing loss. However, there is some distinction in the characteristic and treatment of the sounds individuals experience. Tinnitus is more often reported as a tonal stimulus (i.e., clicking, buzzing, ringing) and is addressed by otolaryngologists or audiologists; whereas AH tend to be more complex (i.e., voices, music; Musiek et al., 2007) and are primarily triaged by psychiatrists.

The perception of AH can be internal (originating within the head) or external (outside the head) and may be perceived on one or both sides of the body, or from another body part all together (McCarthy-Jones et a., 2014; Slotema, et al., 2012). The most typical AH are auditory verbal (AVH) and musical hallucinations (41% music; Jain, 2013). Though AVH are generally more prevalent, women over the age of 60 years tend to experience musical hallucinations at higher rates than men (Evers et al., 2004). Research has also identified “three independent dimensions in AH: spatial location, language complexity, and self-other misattribution” (Stephane et al., 2003; Plaze et al., 2009).

While this territory is fairly new for audiologists, the basis for this research is not unwarranted. Most audiologists will have patients with AH at some point in their career (Linszen

et al., 2019) and recently, there has been a call for audiologic evaluation in the psychiatric literature discussing schizophrenic and psychosis populations that experience AH (Baumeister, D., et al., (2017). Existing literature from clinical reports, lesion studies, and neuropsychology has largely been supported by functional imaging studies which suggest that the auditory system is key for understanding the origin and mediation of AH (Blom, 2015). The central auditory nervous system (CANS) and auditory cortex have been strongly implicated in the involvement of AH. Functional imaging and cadaver brain dissections have reported decreased auditory cortex volumes in individuals with AH, which could be indicative of less neural substrate, myelination, and/or interconnectivity that is necessary to modulate neural responses to acoustic stimuli, causing distorted perceptions (Highly et al., 1999).

Prevalence of AH in the general population ranges from about 4-21% occurrence for those over the age of 18 years, though the frequency and impact may vary greatly. Auditory hallucinations have been reported in multiple populations, including children who will generally have diminished symptoms with aging (9% prevalence in 7-8 yr old; Bartels-Velthuis et al., 2011; Linscott & Van Os, 2013), the elderly (32%; Cole et al., 2002; Tien, 1991), and individuals with hearing loss (16.2%; Linszen et al., 2019); interestingly, individuals with hearing impairment seem to have an increased prevalence of AH with greater severity of hearing impairment (Linszen et al., 2019). Of note, it has been documented that, unlike psychosis-related AH, AH can be remediated in individuals with hearing impairment if hearing sensitivity can be improved (Marneros et al., 1997). It is important to remember that prolonged auditory deprivation that might occur as a result of hearing loss, and elderly patients have an increased risk for AH due to social isolation (Evers et al., 2004).

We know that AH are experienced by many atypical populations with neurologic disorders (i.e., trauma, tumors, strokes, degenerative disorders, etc.). Though they make up

less than 1% of the general population, schizophrenics have the highest prevalence of AH, estimated to be between 60% and 80% (Lim et al., 2016), making them the ideal population in which to investigate these experiences. Auditory hallucinations are one of the main symptoms considered in the diagnosis of schizophrenia, and thus have mainly been studied by psychiatrists and psychologists, while only a small percentage of the literature has been put forth by the audiological community. Auditory hallucinations can still be hard to categorize for people with schizophrenia, as the characteristics associated with the disorder are heterogenous within the population, and each individual will present with a complex constellation of symptoms (Musiek et al., in press).

There is a substantial amount of literature proposing theoretical models that aim to explain AH, notably the Inner Speech Model (ISM) and the connectivity model. The ISM proposes that people with schizophrenia have a propensity to misinterpret internal acoustic perception (AH) as external acoustic stimuli, while the connectivity model asserts that abnormal central auditory processing in this population may result in neurological dysfunction affecting the cognitive and speech systems. However, when considered alone, it is unlikely that either model sufficiently explains the mechanisms underlying AH. Thus, the combination model was developed, which theorizes that the misperception of acoustic stimuli due to abnormal central auditory processing is carried through to the regions of the brain responsible for cognition and speech, where we see the misattribution of that original acoustic stimuli (Musiek et al., in press).

Although many researchers have focused their attention on developing these theoretical models, a growing body of evidence is emerging demonstrating neuroanatomical abnormalities in the auditory cortex of schizophrenic patients, which may be involved in the generation of AH (Blom, 2015). The possibility of atypical auditory anatomy in this clinical population prompted this review of the available literature to summarize and compare the findings presented by

researchers in the last six decades. This review will focus on anatomical differences in the auditory cortex between schizophrenic and control populations, particularly in three key structures: Heschl's gyrus, planum temporale, and the Sylvian fissure. Because all three structures are known to play significant roles in audition, it is possible that abnormalities in their formation could be part of a system of underlying contributors in the manifestation of AH, specifically in schizophrenic brains. There will also be discussion regarding the effects of anatomy on functional listening, including deficits demonstrated by those with schizophrenia.

Psychiatric Approaches to Diagnosis & Treatment

Historically, the diagnosis and treatment of people with schizophrenia has primarily been the responsibility of psychiatrists. The Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5), classifies the presence of "two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be (1) delusions, (2) hallucinations, or (3) "disorganized speech (e.g., frequent derailment or incoherence)." See Table 6 for a summary of symptoms. Diagnosis of schizophrenia is determined by first administering physical examinations and screeners (i.e., bloodwork, CT, MRI) to rule out the influence of physical illness or substance abuse. Further testing consists of a thorough psychiatric evaluation of interview and observation, along with a variety of screening questionnaires (Table 7) to assess relevant symptomology with respect to the DSM-5 criteria. (American Psychiatric Association, 2013)

Schizophrenia is associated with positive, negative, and disorganized symptoms. Positive symptoms refer to abnormally present symptoms, like delusions, hallucinations, paranoia, and distorted perceptions of reality or beliefs. Negative refers to symptoms that are characterized by a deficit, like a reduced ability to speak, express emotions, or initiate plans. Disordered symptoms include difficulty with logical reasoning, bizarre behavior, confusion, and

disordered thinking and speech. These symptoms can influence cognition, concentration, attention, and memory. Though male brains mature slower than female brains (Penrose, 1991), there is evidence that men are more likely to experience earlier onset of symptoms, a predictor of poorer outcomes (Eaton et al., 1992), which may be due to neural developmental differences in men and women (Delvecchio et al., 2017).

Methods

Identifying Relevant Literature

This review identifies and summarizes and when appropriate, compares the existing literature regarding auditory neuroanatomy in schizophrenic individuals who experience auditory hallucinations. I will review findings from multiple disciplines, including research presented by audiologists, psychologists, psychiatrists, and neuroanatomists. Relevant studies published between the years of 1960 and 2020 were identified using the following online databases: Google Scholar, PubMed, PSYCnet, and Mendeley, as well as books, chapters, and bibliographies. For each of the listed databases, search terms included “schizophrenia” AND “auditory hallucinations” AND “auditory cortex” AND “anatomy” AND “Sylvian fissure” OR “superior temporal gyrus” OR “Heschl’s gyrus” OR “planum temporale” OR “(central) auditory processing dysfunction” OR “dichotic listening”.

Results

Structural Auditory Neuroanatomy in Schizophrenic Brains

The primary auditory cortex, found within the Sylvian fissure, lies on the latero-medial plane of the superior temporal gyrus (STG). Visualization of the superior temporal plane (STP) allows us to identify its various components: Heschl’s gyrus, planum temporale, and posterior aspects of planum polare. Other key structures involved in AH include the insula, which is nested within the most medial aspect of the cortex; the corpus callosum, which connects the two hemispheres; and subcortical structures including the amygdala, hippocampus, cerebellum, and thalamus. To begin, this review will summarize neuroanatomical abnormalities broadly affecting the STG that have been detected in schizophrenic/hallucinatory patients. The same measurement techniques used have also been implemented to assess more distinct portions of

the STG, i.e., Heschl's gyrus (HG) and planum temporale (PT), which are considered primary and secondary auditory areas, respectively.

Data reported in these studies may include each structure independently or in combination with others, but they are responsible for different aspects of auditory processing. It is important to identify anatomical boundaries and delineate the purposes of each region to understand which specific functional processing abilities are undermined by the deficits of a particular structure. After narrowing down and presenting results related specifically to HG and PT, this review will shift focus away from gray matter to a third auditory structure: the Sylvian fissure (SF), followed by a brief overview of other structures believed to contribute to AH.

Relevant schizophrenia and AH literature also contains reports regarding a number of fMRI studies of schizophrenic brains. The majority of these researchers observed disturbed physiological function corresponding to anatomical deviations of each of these structures, evidence to suggest that the underlying reduction in the normal hemispheric asymmetry driven by left-lateralized deficits is related to the abnormal brain activity in patients with AH (Pearlson, 1997; Hickok & Poeppel, 2000; O'Daly et al., 2007; Hubl et al., 2008). These findings have implications for divergent dorsal and ventral processing streams. However, these studies are outside the scope of this review, so the following sections will primarily discuss specific structural findings and discuss the relationship between abnormal auditory anatomy, hallucinations, and functional dichotic listening.

Superior Temporal Gyrus

Researchers have employed various imaging modalities to measure the auditory cortex bilaterally in schizophrenic patients and controls and compare data in terms of overall volume and degree of asymmetry. While gray matter volume (GMV) is the most common metric analyzed, cortical thickness and surface area changes have also been studied (Mørch-Johnsen

et al., 2017). Over 100 years ago, Southard (1915) published the first qualitative post-mortem report about the superior temporal gyrus (STG) in schizophrenic patients, noting observed structural “peculiarities” in the left hemisphere (LH). Since then, a number of studies evaluating changes in anatomy have had similar findings, compiling evidence to support LH STG deficits in people with schizophrenia and AH (Jakob et al., 1989; Barta et al., 1990; Bilder et al., 1994; Crow, 1997; DeLisi et al., 1997; Niznikiewics et al., 2003; Neckelmann et al., 2006; Takahashi et al., 2009; Panaliyappan et al., 2012).

The majority of evidence endorses a left STG GMV deficit in schizophrenia brains, reducing L > R asymmetry compared to normals, which has negative implications for hemispheric dominance and functional listening that will be reviewed later (Table 1). However, this claim of left-sided insufficiency has not gone uncontested. Some researchers have observed a decreased asymmetry created by the opposite hemisphere, thus attributing the reduction to GMV abnormalities of the right STG (DeLisi et al., 1994; Pearlson, 1997; Sommer et al., 2001, 2019; Garcia-Martí et al., 2008; Delvecchio., 2017). Even more contradictory, other researchers have failed to confirm an asymmetry difference of any kind, either because a subject exhibits overall STG GMV comparable to controls, or they have a proportionate bilateral deficit that maintains the typical left-right asymmetry (Ohi et al., 2016). These results illustrate different patterns of neuroanatomical deviations, but collectively suggest that auditory structures in both hemispheres are involved in the structural pathology of AH (Modinos et al., 2013).

As research developed, patterns of asymmetry began to emerge implicating more specific regions of the STG, like the posterior STG (pSTG). Again, the details of these findings are not consistent, suggesting that the pSTG has either a right- (Sommer et al., 2019) or left-lateralized deficit (Wise et al., 2001). Wise et al. (2001) explains that the left pSTG is a key structure in processing the temporal sequence of sounds for externally and internally generated

words. The right STG is believed to contribute to discourse comprehension and production, understanding indirect requests, metaphors, humor, and emotional prosody; thus, an abnormality of the right STG may be an underlying source of negative symptoms which are present in schizophrenia (Mitchell & Crow, 2000; Delvecchio et al., 2017).

Table 1. Structural Abnormalities of the Superior Temporal Gyrus

SUPERIOR TEMPORAL GYRUS		
HEMISPHERE	**MEASUREMENT**	**REFERENCES**
REDUCED ASYMMETRY		
LH	↓**GMV**	Southard (1915); Jakob et al. (1989); Barta et al. (1990); Bilder et al. (1994); Crow (1997); DeLisi et al. (1997); Niznikiewics et al. (2003); Neckelmann et al. (2006); Takahashi et al. (2009); Panaliyappan et al. (2012)
LH (pSTG)	↓**GMV**	Wise et al. (2001)
RH	↑**GMV**	Pearlson (1997); Sommer et al. (2001, 2019); Garcia-Martí et al. (2008); Delvecchio. 2017)
RH (pSTG)	↓**GMV**	Anderson et al. (2002); Sommer et al. (2019)
BILATERAL	↑↓**GMV**	Modinos et al. (2013)
NORMAL ASYMMETRY		
BILATERAL	↓**GMV**	Ohi et al. (2016)
NO SIG DIFFERENCES		DeLisi et al. (1994)

Heschl's Gyrus (HG)

The patterns of reported GMV deficits in Heschl's gyrus (HG) are similar to those documented in the STG, with deficits in the LH compared to controls result in a reduction of the hemispheric asymmetry (Hirayasu et al., 2000; Kasai et al., 2003; Gaser et al., 2004; Modinos

et al., 2013). Again, this is a controversial finding (Table 2). In the first manual volumetry study on HG contrasting schizophrenic patients with or without AH, Hubl et al. (2010) also documented an attenuated asymmetry, this time due to an increased HG volume in the right hemisphere (RH) of hallucinators. They posit that this relatively larger volume "may be interpreted as compensatory plastic adaptations of contralateral regions." While Yamasaki et al. (2007) found GMV deficits of the STG, the reductions were localized to PT bilaterally and the normal. volume of HG was preserved. Chance et al. (2008) reviewed 34 MRI and 5 post-mortem studies, half of which reported a LH deficit and a relatively larger HG in the RH.

Other studies have chosen to collect data on the cortical thickness and surface area of HG, but there is a paucity of research evaluating these variables and the results are highly inconsistent. Chen et al. (2015) found that patients with AH had a reduced cortical thickness in the right HG compared to normals and non-hallucinating patients, but thinner cortex has also been documented in the left HG (Mørch-Johnsen et al., 2017). The reductions seen in cortical volume may either be related to reduced cortical thickness or surface area, potentially reflecting different neuropathologies. In 2017, Mørch-Johnsen and colleagues found that AH were associated with a thinner cortex of the left HG, but not with a smaller surface area.

Due to the lack of definitive evidence, another comparison we were interested in investigating in our experimental partner study was the number of HG present in schizophrenics and controls. Heschl's gyrus is generally thought to be a single transverse gyrus, but it is possible to have duplications. A common stem duplication is present when Beck's intermedius (a sulcus) divides HG partially, extending anterolaterally to posteromedially towards (but not through) the medial aspect. A complete duplication is present when Beck's intermedius extends, fully dividing HG. (St. George et al., 2017) Though the findings are still largely uncorroborated,

Hubl et al. (2010) and Takahashi et al. (2021) have documented higher rates of HG duplications in schizophrenic patients with AH.

Table 2. Structural Abnormalities of Heschl's Gyrus

HESCHL'S GYRUS		
HEMISPHERE	**MEASUREMENT**	**REFERENCES**
REDUCED ASYMMETRY		
LH	**↓GMV**	Hirayasu et al. (2000); Kasai et al. (2003); Gaser et al. (2004); Modinos et al. (2013); Chance et al. (2008)
	↓CT	Mørch-Johnsen et al. (2017)
RH	**↑GMV**	Hubl et al. (2010); Chance et al. (2008)
	↓CT	Chen et al. (2015)
NORMAL ASYMMETRY		
NO SIG DIFFERENCES		Yamasaki et al. (2007)

Planum Temporale (PT)

In a landmark study, Geschwind and Levitsky (1968) performed a post-mortem study investigating the temporal lobe in each hemisphere of the brain. The superior temporal plane is home to the structures that are the primary and secondary auditory areas of the brain, Heschl's gyrus and planum temporale. What Geschwind and Levitsky (1968) found (as well as many other investigators since) was a significant asymmetry, where the left planum temporale was larger in surface area and one-third longer than its counterpart on the right in 65% of brains. The documentation of this asymmetry would be the basis for deeper investigations of the temporal lobe to understand how this structural difference between the two sides could contribute to

different functional responsibilities for each hemisphere. Following this seminal research many studies over the years have continued to explore the nature of this asymmetry observed in the auditory cortex. Chi et al. (1977) reported evidence of auditory cortex asymmetry, specifically PT, already present as early as 29-30 weeks of gestation in a typically developing fetus.

In pathologic populations such as those with formal thought disorder, psychosis, or schizophrenia there is a greater degree of variability regarding asymmetry of auditory cortex. While some researchers have reported no changes in asymmetry for neuropathologic populations (Kleinschmidt et al., 1993; DeLisi et al., 1994; Barta et al., 1997; Shapleske et al., 2001) others argue that there is a variable degree of asymmetry that can be attributed to severity of the condition (Rossi et al., 1994; Petty et al., 1995; Sommer et al., 2001). In a study of first episode psychosis patients with either schizophrenia or manic psychosis (bipolar disorder) compared to normal controls, Hirayasu et al. (2000) found temporal lobe GMV differences among all three groups, where the LH PT GMV was significantly reduced for SZ relative to the other groups, results corroborated by Kasai et al. (2003). Contradictory evidence of reductions in PT of the RH have linked GMV deficits to functional increases in delusions (Yamasaki et al., 2007). Other studies have also found abnormalities (both left deficits and right increases) resulting in a reversal of normal asymmetry in either GMV or surface area (Falkai et al., 1995; Petty et al., 1995; Kwon et al., 1999).

Sex differences in the structure of PT have also been explored, demonstrating different patterns of symmetry in male and female patients that support the theory that neural maturation divergences between the sexes can impact the onset and severity of schizophrenic symptoms (Falkai et al., 1995; Shapleske et al., 2001; Delvecchio et al., 2017; Wong et al., 2020). Sex-specific characteristics of schizophrenia and AH are still understudied, but evidence suggests

that patterns of asymmetry may be related, revealing a promising avenue for future research that may inform approaches diagnosis and management.

Gray matter volume measurements are a feature of many studies, while others evaluate cortical thickness or surface area. Recall that, Mørch-Johnsen et al. (2017) found that AH were associated with a thinner cortex of HG, but not with a smaller surface area. Barta et al. (1995, 1997) encouraged skepticism about disparate measurement techniques of PT surface area, as it is a mistake to assume PT is flat considering the complex folding of its surface that is altered in schizophrenia. Chance et al. (2008) found reduced PT surface area asymmetry due to a left-lateralized deficit but failed to identify age-associated changes that are normally observable in PT (and HG). The authors reported that reduced PT surface area was also associated with cortical thinning, suggesting a failure of adult neuroplasticity that hinder the brain's processing of anomalous events and other cognitive demands, the effects of which could lend to schizophrenic patients' vulnerability to symptoms.

Table 3. Structural Abnormalities of Planum Temporale

PLANUM TEMPORALE		
HEMISPHERE	**MEASUREMENT**	**REFERENCES**
REDUCED ASYMMETRY		
LH	**↓GMV**	Hirayasu et al. (2000); Kasai et al. (2003)
	↓CT	Chance et al. (2008)
	↓SA	Chance et al. (2008)
RH	**↓GMV**	Yamasaki et al. (2007)
REVERSED ASYMMETRY		

LH	↓**GMV**	Petty et al. (1995); Kwon et al. (1999)
RH	↑**GMV**	Falkai et al. (1995)
NORMAL ASYMMETRY		
NO SIGNIFICANT DIFFERENCES		Kleinschmidt et al. (1993); DeLisi et al. (1994); Barta et al. (1997); Shapleske et al. (2001)

Sylvian Fissure (SF)

Though some controversy remains, a substantial majority of existing evidence is congruent, showing that schizophrenic patients exhibit a significant reduction in the normal structural asymmetries of the STG and, more specifically within its boundaries, HG and PT. However, these key structures are not unique in their asymmetry. In fact, the asymmetry of the Sylvian fissure (SF) was the first to be identified in normal brains, with the SF being significantly longer in the LH (Eberstaller, 1884). Especially given previous cortical findings, questions were raised about whether or not researchers would also identify abnormalities in schizophrenic brains for the SF (a sulcus) as they did for the gyri. The results of these studies are also generally in agreement that schizophrenic patients demonstrate a reduced asymmetry, but in comparison to the gyral studies discussed, not only is there more disagreement about the details, but researchers have also debated the existence of a reduction at all.

Falkai et al. (1992) obtained post-mortem images of schizophrenic brains and used a surface view to create manual tracings of the SF length bilaterally. Their findings were analogous to those from gyral studies; the authors reported a significant asymmetry abnormality between hemispheres, which they attributed to a reduction in the length of the LH SF. That same year, Hoff et al. (1992) also reported a significant reduction in asymmetry in patients. Though they agreed with Falkai et al. (1992), instead of a shorter left SF, the authors attributed

the lack of asymmetry to a relative increase in length of the right SF. However, their findings have been both supported (Crow et al., 1992, 1994, 1997; Bilder et al., 1997; Sommer et al., 2001) and contested (DeLisi et al., 1997; Shapleske et al., 2001; Falkai et al., 2002).

More than one study has failed to identify significant reductions in SF asymmetry in schizophrenic patients, but perhaps the most well-known contradictory findings came from Bartley et al., 1993, who investigated this abnormality in a monozygotic twin study. The neuroanatomy of one twin with schizophrenia and one without did not indicate a difference, with both twins exhibiting normal asymmetry. Though these two siblings were the only participants in the study, Bartley et al. (1993) were among the few to evaluate relatives and their reports do not support a genetic association with abnormal asymmetry. A later study by Falkai et al. (2002) explored genetic influences by separating subjects based on their family history of schizophrenia. Patients either came from a uni-affected family, where there was no history of psychosis over the past three or more generations, or a multiply-affected family, where they did have close relatives with a history of psychosis. Notably, their results both confirmed and denied the presence of an asymmetry in schizophrenic patients. They only found a reduced asymmetry in those who came from uni-affected families, where those from multiply-affected families demonstrated the normal left sided SF asymmetry seen in controls. These findings haven't been replicated, but the two groups displayed heterogeneous patterns of structural disturbances, encouraging additional explorations of patients from uni- and multiply-affected families.

Other studies looked beyond the diagnosis and family history, with results suggesting that there are even more details that might be related to decreased asymmetries. In terms of patient characteristics, a decreased asymmetry in SF length was reported in female first-episode schizophrenics (Hoff et al., 1992), providing evidence that the abnormality was present at the onset of the disorder. This finding suggests that the abnormality is more likely a

developmental disturbance opposed to a consequential change related to the chronic disease process. DeLisi et al. (1994) used the same cohort to complete another MRI study on SF and this time changed their measurement approach. In controls, the left SF was longer than the right when taking measurements from an anterior slice, but the opposite was true when using a posterior slice. Compared to the controls, first-episode schizophrenic participants had reduced L>R asymmetry in anterior slices, and females (but not males) with schizophrenia showed a trend toward less R>L asymmetry in the posterior slices. These asymmetries were corroborated by volumetric measurements obtained by Honer et al. (1995), who found the posterior (but not anterior) third of the SF to be larger in the RH for controls and the LH for schizophrenic patients. Collectively, the authors' observations of both control and schizophrenic brains indicate that the "normal" hemispheric asymmetry of the SF is variable based on the approach to measurements, underscoring the importance of clearly detailing your process and supporting the development of standardized measurement techniques.

After comparing and contrasting the findings of these varied studies, the majority of authors report on reduced SF asymmetry in schizophrenic people as leaning towards a LH reduction, but these findings are controversial. Each patient exhibits heterogeneous symptoms, which increases the challenge faced by the authors to identify a relatively *homogeneous* experimental group within the population (Bartley et al., 1993). This is difficult not only for one set of authors recruiting a study group, but for subsequent researchers to identify groups that are similar to other participants. This barrier has to be kept in mind when trying to compare these studies that have all approached the subject with specific questions in mind, because these researchers sought participants with a certain profile to target their variable of interest. Based on the multitude of contributing factors that have been correlated with changes in the SF, there are too many influential factors to reach a decisive conclusion with the existing body of

evidence. Additional research is needed to replicate the results from these studies and further probe the strength of relationships between these different characteristics and potential structural abnormalities.

Table 4. Structural Abnormalities of the Sylvian Fissure

SYLVIAN FISSURE		
HEMISPHERE	**MEASUREMENT**	**REFERENCES**
REDUCED ASYMMETRY		
LH	↓**LENGTH**	Falkai et al. (1992); Crow et al. (1992, 1994, 1997); Bilder et al. (1997); Sommer et al. (2001); Falkai et al. (2002)* **Uni-affected families*
RH	↑**LENGTH**	Hoff et al. (1992)
	↑**VOL**	Honer et al. (1995)** ***Posterior (but not anterior) third*
NORMAL ASYMMETRY		
NO SIGNIFICANT DIFFERENCES		Bartley (1993); DeLisi et al. (1997); Shapleske et al. (2001); Falkai et al. (2002)* **Multiply-affected families*

Other Anatomy Implicated

While they are not the focus of this review, there are a number of other neuroanatomical structures that have been assessed for potential correlations with schizophrenia and/or AH. Notably, not all of the structures implicated are auditory in nature. The wide variety of structural abnormalities identified in these studies is indicative of a much larger, dispersed network of connectivity that influences both the generation and perception of AH which extends well

beyond the auditory cortex (Table 5). Because we understand that this expansive network of structures and processes throughout the brain contribute to normal processing of external auditory stimuli (Allen et al., 2008), the involvement of these structures in processing of *internally generated* auditory events is not surprising, as we know schizophrenic patients are unable to differentiate between the two (Plaze et al., 2009).

Insula Concurrent with previous GMV studies, the left insular cortex is also abnormal. In schizophrenic patients with AH and patients without AH, those with AH have deficits in GMV bilaterally, typically greater in the LH (Shapleske et al., 2002; Garcia-Martí et al., 2008; Chen et al., 2015). The reduction of the insula is likely not generalizable to all schizophrenic patients, rather it has a relationship with the symptom of AH specifically. The insula has been identified as a key structure in auditory processing (Bamiou et al., 2006) and a larger "salience network" (Menon & Uddin, 2010), contributing to the integration of salient sensory and interoceptive information (Kurth et al., 2010) and the articulatory planning of speech (Dronkers, 1996). Dysfunction of the insular cortex may impact a patient's capacity to accurately process internal speech within the context, so they attribute unwarranted "proximal salience" to ordinarily insignificant stimuli, which Panalniyappan and Liddle (2012) believe promotes perceptual and cognitive distortions, as well as deficits in auditory and information processing.

Amygdala and Hippocampus Along with the insula, the amygdala is a key structure for emotional regulation; it works to heighten a person's processing of information when they are in an emotional state, thus the insula is involved in processing the emotional load that accompanies AH (Anderson et al., 2002; Alba-Ferrara et al., 2012). The negative symptom of poor emotional regulation may be a consequence of GMV deficits of the amygdala in schizophrenic patients (Garcia-Martí, et al., 2008; Allen et al., 2008). The amygdala is also connected to another structure, the hippocampus, involved in learning and memory. In

conjunction, they are sometimes referred to as the amygdala-hippocampus-complex, also found to have reduced volume and disturbed asymmetry (Falkai et al., 2002; Shenton et al., 2002).

The Temporo-parietal Junction Gray matter volume deficits have also been documented in the parietal lobe, a key region for the integration of sensory information, and activity is associated with the experience of somatic hallucinations (Nenadic et al., 2010). But, structural GMV abnormalities alone cannot explain the AH, prompting the expansion of research into white matter structures and functional connectivity. Several researchers have explored the relationships between schizophrenia/AH and the right and left temporo-parietal junctions (TPJ), a region containing many auditory fibers (Wise et al., 2001; Vercamman et al., 2009, 2010; Plaze et al, 2009). Their findings indicate anatomic abnormalities in both hemispheres that are related to functional deficits of processing internally and externally generated speech. The right TPJ is involved in the 'where' auditory pathway that informs the perceived spatial location of AH. In the LH, the posterior STG is important for temporal sequencing and the middle TPJ has a role in the repetition of words and sounds (Wise et al., 2001).

Interestingly, patients with outer space AH had significantly decreased white matter volumes in the right STG near the TPJ compared to those with inner space AH, who actually had increased white matter volume compared to controls (Plaze et al., 2009). In addition to the white matter deficits, the TPJ in both hemispheres were found to have reduced functional connectivity (Wise et al., 2001; Vercammen et al., 2010, 2012; Plaze et al., 2009). In the LH, schizophrenics demonstrated connectivity deficits between the left TPJ and the right equivalent of Broca's area. Neural coupling deficits between the left TPJ and the anterior cingulate and amygdala bilaterally (two areas involved in emotion processing) were correlated with more severe AH (Mechelli et al., 2007; Vercamman et al., 2010).

Anterior Cingulate Cortex (ACC) Similar to the right TPJ, the cingulate cortex, particularly the anterior portion, seems to be involved in the 'where' of the auditory pathway. A number of functional studies have found that the ACC (involved in attention) was active during AH (McGuire et al., 1993; Suzuki et al., 1993; Silbersweig et al., 1995; Szechtman et al., 1998; Shergill et al., 2000a); this activity was present in response to an external auditory stimulus and during active hallucinations, but not if the patients were only imagining the sound (Allen et al., 2008). Resting activity in the ACC has also been positively correlated with positive symptoms and decreased activity is related to source-monitoring and misattribution of self-speech in AH patients (Northoff & Bermpohl, 2004; Allen et al., 2008).

Other In schizophrenic brains, a widely distributed network of structural and functional connectivity deficits has been identified underlying the experience of AH. Note that these additional anatomical findings have been documented within the relevant literature reviewed regarding the auditory cortex. These studies have some contradictory results thus this brief overview is intended to serve as a general summary of the findings rather than a comprehensive analysis. For more information on these structures, see referenced reviews on multiple areas of involvement (Anderson et al., 2002; Gaser et al., 2004; Neckelmann et al., 2006; O'Daly et al., 2007; Allen et al., 2008, 2012; Garcia-Martí et al., 2008; Panaliyappan et al., 2012; Steinmann et al., 2014; Sommer et al., 2019).

Table 5. Other Structural Abnormalities

OTHER ANATOMY		
STRUCTURE	**MEASUREMENT**	**REFERENCES**
REDUCED ASYMMETRY		
L FRONTAL GYRUS	↓**GMV**	Garcia-Martí et al. (2008)
L THALAMUS	↓**GMV**	Allen et al. (2008)
L SMG	↓**GMV**	Gaser et al. (2004); Allen et al. (2008)
L MTG	↓**GMV**	O'Daly et al. (2007)
R FRONTAL GYRUS	↓**GMV**	Gaser et al. (2004); Allen et al. (2008)
	↑**GMV**	Shin et al. (2005)
R FUSIFORM GYRUS	↓**GMV**	O'Daly et al. (2007)
R HIPPOCAMPUS	↓**GMV**	Allen et al. (2008)
R MTG	↓**GMV**	Niznikiewics et al. (2003), Zhao et al. (2018)
	↑**GMV**	O'Daly et al. (2007)
BILATERAL INSULA (L>R)	↓**GMV**	Shapleske et al. (2002); Garcia-Martí et al. (2008); Chen et al. (2015)
BILATERAL TPJ	↓**GMV**	Allen et al. (2008)
BILATERAL ACC & PCC	↓**GMV**	Niznikiewics et al. (2003); Northoff & Bermpohl, (2004); Allen et al. (2008)
BILATERAL CEREBELLUM	↓**GMV**	Neckelmann et al. (2006); Allen et al. (2008)
BILATERAL PRECUNEUS	↓**GMV**	Allen et al. (2008)

Correlations with Auditory Hallucination Severity and/or Characteristics

There is a paucity of studies investigating the structural abnormalities found in schizophrenic brains in which the authors have evaluated multiple different groups presenting with similar characteristics. Though some studies describe only the neuroanatomy of disordered brains, it is typical to compare the schizophrenic brains to normal controls. However, as the literature has developed over time, it has become more standard practice for researchers to make neuroanatomical comparisons past the expected group of normal controls. Currently, there are a few studies that have compared structural abnormalities related to schizophrenia to potential diversions in other non-schizophrenic psychotic (e.g., bipolar disorder) or hallucinating (e.g., elderly) populations. These studies have concluded that the disturbances found in schizophrenic brains are unique to this clinical population, as they have failed to demonstrate these same abnormalities in similar populations (Ellison-Wright et al., 2003; Ratanather et al., 2013)

Though the confirmation of schizophrenia-related abnormalities is important in our understanding of the underlying changes, arguably even more important is the comparison between structures in schizophrenic individuals who are AH positive (AH+) and those who are AH negative (AH-). Although this population generally has the highest prevalence of AH, symptoms of the disorder are heterogenous and not all individuals have experienced AH. In essence, the AH- groups serve as an additional level of control in this investigation. This comparison between groups is critical to help us determine whether these abnormalities are related to schizophrenia as a disorder, or if they're related specifically to AH as a symptom.

Anderson et al. (2002) investigated other markers by searching for potential differences between schizophrenics who experience predominantly positive symptoms (hallucinations, delusions, etc.) and those who experience predominantly negative symptoms (attention deficits,

social withdrawal, etc.), that the distinction between a profile of positive or negative symptomatology is better described as dimensional rather than categorical. Though many have documented correlations with specific positive/negative symptoms, no one else has explored this exact comparison. Beyond simply considering the presence or absence of AH, researchers have also attempted to identify correlations between structural asymmetries and symptom severity/characteristics. Some researchers have failed to uncover any relationship between structural abnormalities and AH (DeLisi et al., 1994; Zipursky et al., 1994; Marsh et al., 1997; Havermans et al., 1999; Shapleske et al., 2001). However, more recent literature has emerged reporting disturbed anatomy in many different regions of the schizophrenic brain that are significantly correlated with the severity of their individual symptoms/hallucinations. Structural and functional imaging studies have demonstrated both positive and negative correlations between abnormalities and AH severity/characteristics (Table 8). Evidence suggests that many of these changes are likely specific to the symptomatology of AH rather than the underlying disorder of schizophrenia (Hubl et al., 2008).

In another interesting analysis, Løberg et al. (2004) sought to determine if the relationship between AH and functional listening deficits was due to more “state-” or “trait-” factors by separating those with ongoing AH and those with previous AH into groups based on their responses on the PANSS hallucination item (severity rating: 1-7). In this context, state-factors refer to the influence of the symptoms the patient has at the time of evaluation on test performance, whereas trait-factors refer to the profile of symptoms experienced by that patient that may or may not be active. Though their results have not been replicated, they found that patients who had AH in the past had similar performances to controls. However, the patients with ongoing AH performed significantly worse compared to both groups. Their results suggest

that state-dependent factors may have more significant influence on a patient's ability to process external acoustic information presented to the LH of their brains.

Discussion

Impact of Structural Deficits on Auditory Function

Asymmetry and Hemispheric Dominance

Normal Listeners Doreen Kimura (1961a, 1961b) was the first to document a functional asymmetry in auditory perception between the two hemispheres. The neural representation of auditory stimuli arriving from either ear is stronger in the hemisphere contralateral to that ear, attenuating the ipsilateral left ear input (Kimura, 1967). Although there are both contralateral and ipsilateral pathways connecting each ear to both hemispheres, the contralateral pathway is dominant because they contain the bulk of auditory fibers (5:1 ratio; Musiek & Baran, 2020). Furthermore, in this seminal work, Kimura (1961a, 1961b) proposed that along with the RH being dominant in gestalt and music processing, the LH is predominantly analytic and focused on language processing, explaining the better representation of speech processing in the left temporal lobe yielding a right ear listening advantage for language.

Schizophrenics with Auditory Hallucinations The left temporal lobe is a locus for speech perception and dichotic listening is capable of tapping into the structure's functional integrity, particularly that of the STG (Hugdahl et al., 1999, 2002). Crow (1997) reported reduced cortical GMV asymmetry, a change that was more noticeable in patients with an early onset of schizophrenia. He describes schizophrenia as "an anomaly of the function of language, shown in failures of linguistic processing for semantic, syntactic, and discourse structure." It is clear that structural deficits related to schizophrenia are neurodevelopmental in nature (Crow et al., 1991, 1997; Falkai et al., 1992; Pearlson, 1997; Rojas et al., 1997; Sommer et al., 2001; Plaze et al., 2009; Delvecchio et al., 2017). Based on the patterns of evidence, Crow's (2007)

evolutionary theory hypothesizes that a normal hemispheric asymmetry is the basis for neurodevelopment of language for both speech perception (L>R) and motor speech output (R>L), thus the failure to develop cortical asymmetry is what underlies the pathophysiology of schizophrenia and AH.

Dichotic Listening

Normals and Temporal Lobe Lesions One of the most common tasks used to assess the integrity of the central auditory nervous system (CANS) and its processing abilities is dichotic listening. A dichotic listening test involves presenting auditory stimuli to each ear simultaneously and asking the participant to repeat back what they've heard in both ears, typically in the form of digits, words, or consonant-vowel (CV) syllables (Musiek & Pinheiro, 1985). Kimura (1961a, 1961b) utilized a dichotic digit test to assess the functional differences of the auditory cortices in both hemispheres. For the test by Kimura (1961a, 1961b), the participants were presented with three numbers to each ear, simultaneously. The participant was then asked to repeat back all six numbers that were heard. She administered the dichotic digits test to both normal individuals and individuals with temporal lobe lesions in either hemisphere. What she found was that all groups correctly repeated more digits presented to the right ear than the left ear, regardless of whether or not they had a lesion. Even within the group with auditory cortex lesions, there was a contralateral ear advantage regardless of the hemisphere in which the lesion was located (Kimura, 1961b; Hugdahl et al., 1998; Baran & Musiek, 1999; Musiek & Chermak, 2014).

Schizophrenics with Auditory Hallucinations Understanding the relationship between both structural and functional asymmetries of the auditory cortex leads us to question whether the reduction of structural asymmetry reported in those with schizophrenia correlates with the dichotic listening abilities of this clinical population. One of the most highly referenced studies

regarding dichotic listening in schizophrenia was published by Green et al. (1994), who found a significant decrease in the REA in patients with schizophrenia. Though many studies have documented this reduction in lateralization, not all dichotic listening abnormalities found have been in complete agreement. Sommer et al. (2001) reviewed a set of studies assessing the REA in schizophrenia but found no significant reduction. However, the tests used for the evaluation were varied, which was likely a source of the disagreement, as the heterogeneity of the study methods made it difficult for the reviewers to draw conclusions.

Some studies found that schizophrenic subjects performed significantly poorer than controls on triad and word-monitoring tasks that require repetition of stimuli presented to both ears, but controls tend to encounter a ceiling effect with symmetric scores (Hatta et al., 1984; Carr et al., 1992; Seidman et al.,1993; Sakuma et al., 1996). The authors found that using dichotic digits failed to identify any reduction in REA, but that a significant reduction in lateralization emerged once the dichotic listening tests were restricted to consonant-vowel or fused-word tasks for which they asked subjects to respond only to the most clearly discriminated stimulus. In fact, one study found that the REA was absent for schizophrenics even in a forced-attention condition (Løberg et al., 1999), and some patients have even demonstrated a left ear advantage (Conn & Posey, 2000). Anatomically, most schizophrenic patients who do not exhibit the REA are likely to demonstrate significant reductions in GMV in the left temporal lobe (Neckelmann et al., 2006; Garcia-Martí et al., 2008).

Opportunities for Audiological Involvement

Auditory Evoked Potentials

Auditory evoked potentials have been utilized in many areas of study to identify objective neurologic dysfunction. However, these measures are limited to detection of dysfunction, and are not sensitive to specific etiologies. Powerful auditory tests of the peripheral ear (otoacoustic

emissions), the brainstem (auditory brainstem response, auditory steady state response, the thalamocortical pathway (middle latency response), and cortex (late potentials, N1, P2; mismatch negativity potential; P300 auditory evoked potential) have all yielded abnormalities in schizophrenic populations. Albeit there are many factors that could contribute to these abnormalities including: cascading effects from early CANS structures (Lindstrom et al., 1987); variability in test design; duration and severity of psychosis; comorbid factors such as attention, memory, other cognitive influences, reduced neural substrate, or subcortical interactions (Youn et al., 2001; Papageorgiou et al., 2004). Therefore, these tests are somewhat limited in their ability to provide replicable results needed for understanding the underlying mechanisms of AH and associated neuroanatomical factors. (Musiek et al., in press)

Behavioral Central Auditory Processing Tests

Behavioral central auditory tests have proven to be more useful for assessing individuals' functional abilities and CANS integrity in general, the most widely recognized of these tests being dichotic listening tasks. However, other central tests have also revealed a functional reduction in normal asymmetry and significant deficits in schizophrenic patients with AH, implicating more than one underlying auditory processing deficit in these patients (McKay et al., 2000). These findings only underscore the importance of employing a battery of central auditory tests when evaluating patients with AH to determine which specific processes are deficient. The role of CANS evaluation should encourage spreading awareness, so audiologists become more knowledgeable about schizophrenia and AH. There is great potential for audiologists to be involved in the assessment of auditory function in patients with schizophrenia, as well as audiologic management and monitoring when appropriate (Musiek et al., in press).

Conclusion

Emerging AH research provides insights and rationale for audiological collaboration with psychiatry. Neuroanatomical findings from studies of key auditory (and non-auditory) structures across the years have been largely congruent: in the brains of patients with schizophrenia, there is a significant reduction of the asymmetry between hemispheres that has been established in normal brains. It is likely that this failure to develop normal cerebral asymmetry is the ultimate underlying cause of hallucinations (Allen et al., 2010). The reduction of asymmetry in the auditory cortex results in a lack of the normal LH dominance for speech, exhibited as loss of the REA in schizophrenic/hallucination patients (Green et al., 1994). The auditory abnormalities reviewed underlie a further widespread network of structural deficits, of which divergences have implications for functional processing of information.

Various systems demonstrating structural abnormalities have been linked to a number of functional deficits that contribute to AH, including but not limited to relaying and integrating sensory information (thalamus, fusiform gyrus), self-monitoring (cerebellum), spatial memory (hippocampus/parahippocampal gyrus, precuneus, fusiform gyrus, caudate nucleus), volitional auditory perception (frontal lobe), and emotion processing (insula, amygdala, amygdala-hippocampus-complex, caudate nucleus). Though not all AH are speech, these deficits reflect disturbed auditory processing that leads to failed inhibition and inaccurate attribution of salience for internal speech (Modinos et al. 2013).

Evidence has not only linked structural and functional abnormalities to schizophrenia and AH, but also to the specific characteristics (e.g., locus, positive/negative symptoms, subscales, duration) and severity of the AH. However, more research is needed to corroborate any associations, as AH symptoms exist on a dimensional rather than categorical scale (Nenadic et al., 2010). Another interesting avenue of research would be to assess if auditory

structural and functional deficits manifest differently in those with AH unimodal vs multimodal. Hallucinations are regulated by sensory specific deficits (Lim et al., 2016); there are more sensory systems affected by multimodal hallucinations, but it is unknown whether the presence of other sensory deficits influences the manifestation of deficits within the auditory system.

Future studies investigating the mechanisms of AH should focus on including larger sample studies of more homogeneous groups to make more specific AH vs non-AH comparisons in schizophrenia. Many studies have documented schizophrenia-specific deficits, while others have related them specifically to AH as a symptom (Hubl et al., 2008). Further considerations should also include sex, as early neurodevelopmental differences between the sexes may modulate brain morphology and subsequent lateralization (Rojas et al., 1997; Delvecchio et al., 2017), which has implications for symptom onset and severity that may inform clinical treatment. Finally, investigating possible age-related changes in hallucinatory brains may provide insight into neural plasticity in this population; there is some evidence that these changes do not occur, resulting in a decreased capacity for reorganization that could contribute to abnormal activation patterns and a patient's vulnerability to symptoms.

Table 6. DSM-5 Diagnosis Criteria for Schizophrenia (APA, 2013)

DSM-5 DIAGNOSIS CRITERIA FOR SCHIZOPHRENIA
A. Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be (1), (2), or (3): 1. Delusions 2. Hallucinations 3. Disorganized speech (e.g., frequent derailment or incoherence) 4. Grossly disorganized or catatonic behavior 5. Negative symptoms (i.e., diminished emotional expression or avolition). B. For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning). C. Duration: Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences). D. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either (1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or (2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness. E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition. F. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).

Specify if: The following course specifiers are only to be used after a 1-year duration of the disorder and if they are not in contradiction to the diagnostic course criteria.

- First episode, currently in acute episode: First manifestation of the disorder meeting the defining diagnostic symptom and time criteria. An acute episode is a time period in which the symptom criteria are fulfilled.
- First episode, currently in partial remission: Partial remission is a period of time during which an improvement after a previous episode is maintained and in which the defining criteria of the disorder are only partially fulfilled.
- First episode, currently in full remission: Full remission is a period of time after a previous episode during which no disorder-specific symptoms are present.
- Multiple episodes, currently in acute episode: Multiple episodes may be determined after a minimum of two episodes (i.e., after a first episode, a remission and a minimum of one relapse).
- Multiple episodes, currently in partial remission
- Multiple episodes, currently in full remission
- Continuous: Symptoms fulfilling the diagnostic symptom criteria of the disorder are remaining for the majority of the illness course, with subthreshold symptom periods being very brief relative to the overall course.
- Unspecified

Specify if:

- With catatonia (refer to the criteria for catatonia associated with another mental disorder for definition).

Specify current severity:

- Severity is rated by a quantitative assessment of the primary symptoms of psychosis, including delusions, hallucinations, disorganized speech, abnormal psychomotor behavior, and negative symptoms. Each of these symptoms may be rated for its current severity (most severe in the last 7 days) on a 5-point scale ranging from 0 (not present) to 4 (present and severe). (See Clinician-Rated Dimensions of Psychosis Symptom Severity in the chapter “Assessment Measures.”) *Note: Diagnosis of schizophrenia can be made without using this severity specifier.*

Table 7. Questionnaires for Rating Auditory Hallucinations (Hugdahl et al., 2009)

NAME	PURPOSE	FORMAT
Brief Psychiatric Rating Scale (BPRS) Overall and Gorham (1988)	Scale for assessing the positive, negative, and affective symptoms of individuals who have psychotic disorders, especially schizophrenia	The BPRS consists of 18-24 symptom constructs that are scored 1-7. The symptom constructs cover positive and negative symptoms of somatic concern, anxiety, and depression
Positive and Negative Syndrome Scale (PANSS) Kay et al. (1987)	Scale for assessing degree of positive, negative symptoms, and general psychopathology in schizophrenia patients	The PANSS consists of a Positive scale (7 items), Negative scale (7 items), and a General Psychopathology scale (16 items). Each item is scored 1-7
Scale for Negative Symptoms (SANS) Andreasen (1990)	The SANS was designed primarily as descriptive instruments that are useful for encoding negative symptoms commonly observed in psychiatric patients	Clinical interview scale with five dimensions: affective flattening or blunting, alogia, avolition-apathy, anhedonia-associability, attention, with 3-5 items for each dimension. Each item is scored 0-5
Scale for Positive Symptoms (SAPS) Andreasen (1990)	The SAPS was designed primarily as descriptive instruments that are useful for encoding positive symptoms commonly observed in psychiatric patients	Clinical interview scale with five dimensions: hallucinations, delusions, bizarre behavior, formal positive thought disorder, inappropriate affect, ranging from 1-13 items for each dimension. Each item is scored 0-5
Beliefs About Voices Questionnaire - Revised (BAVQ-R) Chadwick et al. (2000)	The BAVQ-R measures beliefs, feelings, and behavior related to AH for schizophrenia	The BAVQ-R is a self-report questionnaire with 35 items. Separate sub-scales malevolence, benevolence, and omnipotence of the content of the voices
Psychotic Symptom Rating Scale (PSYRATS) Haddock et al. (1999)	Clinical interview scale for identification of AH and delusions in psychotic patients	The PSYRATS consists of two dimensions: AH and delusions, each with 11 and 6 items, respectively, scored 0-4

Table 8. Structural Correlations with Auditory Hallucination Severity and/or Characteristics

AUDITORY HALLUCINATIONS: PRESENCE, SEVERITY, AND/OR CHARACTERISTICS			
STRUCTURE	**CORRELATION**	**MEASUREMENT**	**REFERENCES**
REDUCED ASYMMETRY			
LH STG	Severity	↓**GMV**	Barta et al. (1990); Flaum et al. (1992); Levitan et al. (1999); Rajarethinam et al. (2000); Anderson et al. (2002); Neckelmann et al. (2006)
	Severity (+) > (-)	↓**GMV**	Shenton et al. (1992)
	AH	↓**WMV**	Shin et al. (2005); O'Daly et al. (2007)
	AH	↑**WMV**	Shapleske et al. (2002)
RH STG	Severity	↓**GMV**	Shenton, et al. (1992); O'Daly et al. (2007); Garcia-Martí et al. (2008)* **Symptom severity but not AH severity*
	PANSS: Poor Attention	↓**GMV**	Anderson et al. (2002)
	Outer Spaced	↑**GMV**	Plaze et al. (2009)
	Inner Spaced	↓**WMV**	Plaze et al. (2009)
	AH	↑**WMV**	Shin et al. (2005)

BILATERAL STG	Severity	↓**GMV**	Nenadic et al. (2010); Modinos et al. (2013); Mørch-Johnsen et al. (2017)
	Persistence of AH	↓**GMV**	Milev et al. (2003)
LH HG	SAPS: Delusions	↓**GMV**	Gaser et al. (2004)
	Positive Symptoms	↓**GMV**	Delvecchio et al. (2017)
	Illness Duration	↓**GMV**	Lieberman et al. (2001); Mathalon et al. (2001); Thompson et al. (2001)
RH HG	Severity	↓**CT**	Chen et al. (2015)
	AH	↓**GMV**	Hubl et al. (2010)
	Positive Symptoms (Female)	↓**GMV**	Delvecchio et al. (2017)
LH PT	Severity	↓**GMV**	Nenadic et al. (2010); Mørch-Johnsen et al. (2017)
RH PT	AH	↓**GMV**	Mørch-Johnsen et al. (2017)
	Delusional Behavior	↓**GMV**	Yamasaki et al. (2007)
NORMAL ASYMMETRY			
NO SIGNIFICANT DIFFERENCES			DeLisi et al. (1994); Zipursky et al. (1994); Marsh et al. (1997); Havermans et al. (1999); Shapleske et al., 2001)

References

Alba-Ferrara, L. Fernyhough, C., Weis, S., Mitchell, R.L.C., & Hausmann, M. (2012). Contributions of emotional prosody comprehension deficits to the formation of auditory verbal hallucinations in schizophrenia. *Clinical Psychology Review, 32*(4):244-250. doi:10.1016/j.cpr.2012.02.003.

Allen, P., Larøi, F., McGuire, P.K., & Aleman, A. (2008). The hallucinating brain: A review of structural and functional neuroimaging studies of hallucinations. *Neuroscience and Biobehavioral Reviews, 32*:175-191. doi:10.1016/j.neubiorev.2007.07.012

Allen, P., Modinos, G., Hubl, D., Shields, G., Cachia, A., … & Hoffman, R. (2012). Neuroimaging auditory hallucinations in schizophrenia: From neuroanatomy to neurochemistry and beyond. *Schizophrenia Bulletin, 38*(4):695-703. doi:10.1093/schbul/sbs066

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). doi:10.1176/appi.books.9780890425596

Anderson, J.E., Wible, C.G., McCarly, R.W., Jakab, M., Kasai, K., & Shenton, M.E. (2002). An MRI study of temporal lobe abnormalities and negative symptoms in chronic schizophrenia. *Schizophrenia Research, 58*:123-134. doi:10.1016/S0920-9964(01)00372-3

Antonova, E., Kumari, V., Morris, R., Halari, R., Anilmukar, A., … & Sharma, T. (2004). The relationship of structural alterations to cognitive deficits in schizophrenia: A voxel-based morphometry study. *Biological Psychiatry, 58*:457-467. doi:10.1016/j.biopsych.2005.04.036

Bamiou, D.E., Musiek, F.E., Stow, I., Stevens, J., Cipolotti, L., ... & Luxon, L.M. (2006). Auditory temporal processing deficits in patients with insular stroke. *Neurology, 67*:614-619. doi:10.1212/01.wnl.0000230197.40410.db.

Barta, P.E., Pearlson, G.D., Powers, R.E., Richards, S.S., & Tune, L.E. (1990). Auditory hallucinations and smaller superior temporal gyral volume in schizophrenia. *American Journal of Psychiatry, 147*:1457-1462. doi:10.1176/ajp.147.11.1457

Barta, P.E., Petty, R.G., McGilchrist, I., Lewis, R.W., Jerram, M., … & Pearlson, G.D. (1995) Asymmetry of the planum temporale: Methodologic considerations and clinical associations. *Psychiatry Research in Neuroimaging, 61*:137-150. doi:10.1016/0925-4927(95)02650-M

Barta, P.E., Pearlson, G.D., Brill, L.B., Royall, R., McGilchrist, I., … & Petty, R.G. (1997). Planum temporale asymmetry reversal in schizophrenia: Replication and relationship to gray matter abnormalities. *American Journal of Psychiatry, 154*(5):661-667. doi:10.1176/ajp.154.5.661

Bartley, A.J., Jones, D.W., Torrey, E.F., Zigun, J.R., & Weinberger, D.R. (1993). Sylvian fissure

asymmetries in monozygotic twins: A test of laterality in schizophrenia. *Biology Psychiatry, 34*:853-863. doi:10.1016/0006-3223(93)90053-g

Bartels-Velthuis, A.A., van de Willige, G., Jenner, J.A., van Os, J., & Wiersma, D. (2011). Course of auditory vocal hallucinations in childhood: 5-year follow-up study. *British Journal of Psychiatry, 199*(04):296–302. doi: 10.1192/bjp.bp.110.086918

Baumeister, D., Sedgwick, O., Howes, O., & Peters, E. (2017). Auditory verbal hallucinations and continuum models of psychosis: A systematic review of the healthy voice-hearer literature. *Clinical Psychology Review, 51*:125-141. http://dx.doi.org/10.1016/j.cpr.2016.10.010

Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., & Damasio, A.R. (1995). Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. *Science, 269*(5227):1115-8. doi: 10.1126/science.7652558.

Bellani, M., Marzi, C.A., Savazzi, S., Perlini, C., Cerruti, S., … & Brambilla, P. (2010). Laterality effects in schizophrenia and bipolar disorder. *Experimental Brain Research, 2*:339–344. doi:10.1007/s00221-009-2021-0

Bilder, R.M. Wu, H., Bogerts, B., Degreef, G., Ashtari, M., … & Lieberman, J.A. (1994). Absence of regional hemispheric volume asymmetries in first-episode schizophrenia. *American Journal of Psychiatry, 151*(10):1437–1447. https://doi.org/10.1176/ajp.151.10.1437

Brasic, J.R., & Perry, R. (1997). Unilateral auditory hallucinations in a boy with ipsilateral conductive hearing loss. *Journal of Neurology, Neurosurgery, and Psychiatry, 62*(3):302. doi:10.1136/jnnp.62.3.302

Carr, B., Wale, J., Dewis, S., & Stephan, L. (1992). The effect of illness duration on perceptual asymmetry in schizophrenia. *Schizophrenia Research, 7*:211-216. doi: 10.1016/0920-9964(92)90014-v.

Celesia, G.G. (1976). Organization of auditory cortical areas in man. *Brain, 99*:403-414. doi:10.1093/brain/99.3.403

Chance, S.A., Casanova, M.F., Switala, A.E., & Crow, T.J. (2008). Auditory cortex asymmetry, altered minicolumn, spacing and absence of ageing effects in schizophrenia. *Brain, 131*:3178-3192. doi:10.1093/brain/awn211

Chen, X., Liang, S., Pu, W., Song, Y., Mwansisya, T.E., … & Xue, Z. (2015). Reduced cortical thickness in right Heschl's gyrus associated with auditory verbal hallucinations severity in first-episode schizophrenia. *BioMed Central Psychiatry, 15*:152. doi:10.1186/s12888-015-0546-2

Chi, J.G., Dooling, E. C., & Giles, F. H. (1977). Gyral development of the human brain. *Annals of Neurology, 1*:86-93. doi:10.1002/ana.410010109

Chitnis, X., & Elison-Wright, T. (2003). New directions in structural imaging. In M.A. Ron & T.W. Robbins (Eds.), Disorders of the Brain and Mind, 2. Cambridge, UK: Cambridge University Press.

Cole, M.G., Dowson, L., Dendukuri, N., & Belzile, E. (2002). The prevalence and phenomenology of auditory hallucinations among elderly subjects attending an audiology clinic. *International Journal of Geriatric Psychiatry, 17*(5):444–452. doi: 10.1002/gps.618

Conn, R., & Posey, T.B. (2000). Dichotic listening in college students who report auditory hallucinations. *Journal of Abnormal Psychology, 109*(3):546–549. doi:10.1037/0021-843X.109.3.546

Crow, T.J., Ball, J., Bloom, S.R., Brow, R., Bruton, C.J., … & Roberts, G.W. (1989) Schizophrenia as an anomaly of development of cerebral asymmetry: A postmortem study and a proposal concerning the genetic basis of the disease. *Archives of General Psychiatry, 46*:1145-1150. doi:10.1001/archpsyc.1989.01810120087013

Crow, T.J., Brown, R., Bruton, C.J., Frith, C.D., & Gray, V. (1992). Loss of Sylvian fissure asymmetry in schizophrenia: Findings in the Runwell 2 series of brains. *Schizophrenia Research, 6*:152–153. doi:10.1016/0920-9964(92)90230-3

Crow, T.J. (1997). Schizophrenia as a failure of hemispheric dominance for language. *Trends in Neuroscience, 20*:339-343. doi: 10.1016/s0166-2236(97)01071-0

Crow, T.J. (2007). Genetic hypotheses for schizophrenia. *British Journal of Psychiatry, 191*:180. doi:10.1192/bjp.191.2.180

DeLisi, L.E., Hoff, A. L., Neale, C., & Kushner, M. (1994). Asymmetries in the superior temporal lobe in male and female first-episode schizophrenic patients: Measures of the planum temporale and superior temporal gyrus by MRI. *Schizophrenia Research, 12*:19-28. doi:10.1016/0920-9964(94)90080-9

DeLisi, L.E., Stritzke, P., Riordan, H., Holan, V., Boccio, A., … & Anand, A. (1997). The timing of brain morphological changes in schizophrenia and their relationship to clinical outcome. Biological Psychiatry, 31:241–254. doi:10.1016/0006-3223(92)90047-4

Delvecchio, G., Pigoni, A., Perlini, C., Barillari, M., Ruggeri, M., … & Brambilla, P. (2017). Sexual dimorphism of the planum temporale in schizophrenia: A MRI study. *Australian & New Zealand Journal of Psychiatry, 5*(10):1010-1019. doi:10.1177/0004867417702748

Dronkers, N.F. (1996). A new brain region for coordinating speech articulation. *Nature, 384*(6605):159-61. doi:10.1038/384159a0.

du Feu, M., & McKenna, P.J. (1999). Prelingually profoundly deaf schizophrenic patients who hear voices: A phenomenological analysis. *Acta Psychiatrica Scandinavica, 99*:453-459. doi:10.1111/j.1600-0447.1999.tb00992.x

Eaton, W.W., Bilker, W., Haro, J.M., Herrman, H., Mortensen, P.B., … & Burgess, P. (1992).

Long-term course of hospitalization for schizophrenia: Part II. Change with passage of time. Schizophrenia Bulletin, 18: 229–41. doi:10.1093/schbul/18.2.229

Eberstaller, O. (1884). Zur Oberflächenanatomie der grosshirnhemisphären. *Wiener Medizinische Blätter, 7*:479–482.

Ellison-Wright, I., & Bullmore, E. (2010). Anatomy of bipolar disorder and schizophrenia: A meta-analysis. *Schizophrenia Research, 117*:1-2. doi:10.1016/j.schres.2009.12.022

Falkai, P., Bogerts, B., Greve, B., Pfeiffer, U., Machus, B., … Ovary, I. (1992). Loss of sylvian fissure asymmetry in schizophrenia: A quantitative postmortem study. Schizophrenia Research, 7: 23-32. doi:10.1016/0920-9964(92)90070-l

Falkai, P., Bogerts, B., Schneider, T., Greve, … & Ovary, I. (1995). Disturbed PT asymmetry in schizophrenia: A quantitative post-mortem study. *Schizophrenia Research, 14*:161-76. doi:10.1016/0920-9964(94)00035-7

Falkai, P., Honer, W.G., Alfter, D., Schneider-Axmann, T., Bussfeld, P., … & Tempest, R. (2002). The temporal lobe in schizophrenia from uni- and multiply affected families. *Neuroscience Letters, 325*:25-28. doi:10.1016/S0304-3940(02)00224-0

Fiszdon, J.M., Cardenas, A., & Bell, M.D. (2005). Predictors of remediation success on a trained memory task. *Journal of Nervous & Mental Disease, 193*(9):602-608. doi:10.1097/01.nmd.0000177790.23311.ba

Flaum, M.A., Swayze, V.W., Gupta, S., O'Leary, & Andreasen, N.C. (1992) Symptom domains and neural substrates of schizophrenia: A magnetic resonance imaging study. Abstract, American College Neuropsychopharmacology, 31st Annual Meeting, San Juan, Puerto Rico. December 14-18, 1992.

Garcia-Martí, G., Aguilar, E.J., Lull, J.J., Martí-Bonmati, L., Escarti, M.J., … Sanjuan, J. (2008). Schizophrenia with auditory hallucinations: A voxel-based morphometry study. *Progress in Neuro-psychopharmacology & Biological Psychiatry, 32*:72-80. doi:10.1016/j.pnpbp.2007.07.014

Gaser, C., Nenadic, I., Volz, H., Büchel, & Sauer, H. (2004). Neuroanatomy of 'hearing voices': A frontotemporal brain structural abnormality associated with auditory hallucinations in schizophrenia. Cerebral Cortex, 14:91-96. doi:10.1093/cercor/bhg107

Geschwind, N., & Levitsky, W. (1968). Human brain: left-right asymmetries in temporal speech region. *Science, 161*(3837):186-7. doi:10.1126/science.161.3837.186.

Gloor, P. (1986). The role of the human limbic system in perception, memory and affect. In: B.K. Doane, K.E. Livingston (eds.), The Limbic System. Raven Press; New York.

Green, M.F., Hugdahl, K., & Mitchell, S. (1994). Dichotic listening during auditory hallucinations in schizophrenia. *American Journal of Psychiatry, 151*:357–362. doi:10.1176/ajp.151.3.357

Hatashita-Wong, M., & Silverstein, S.M. (2003). Coping with voices: Selective attention training for persistent auditory hallucinations in treatment refractory schizophrenia. *Psychiatry, 66*:255–261. doi:10.1521/psyc.66.3.255.25162

Hatta, T., Ayetani, N., & Yoshizaki, K. (1984). Dichotic listening by chronic schizophrenic patients. *International Journal of Neurosciences, 23*:75-80. doi:10.3109/00207458408985347

Havermans, R., Honig, A., Vuurman, E.F., Krabbendam, L., Wilmink, J., … & van Praag, H.M. (1999). A controlled study of temporal lobe structure volumes and P300 responses in schizophrenic patients with persistent auditory hallucinations. *Schizophrenia Research, 17*:151–158. doi:10.1016/s0920-9964(99)00006-7

Hickock, G., & Poeppel, D. (2000). Towards a functional neuroanatomy of speech perception. *Trends in Cognitive Science, 4*(4):131-138. doi:10.1016/s1364-6613(00)01463-7

Highley, J.R., McDonald, B., Walker, M.A., Esiri, M.M., & Crow, T.J. (1999). Schizophrenia and temporal lobe asymmetry: A post-mortem stereological study of tissue volume. *British Journal of Psychiatry, 175*:127-134. doi:10.1192/bjp.175.2.127.

Hirayasu, Y., McCarly, R.W., Salisbury, D.S., Tanaka, S., Kwon, J.S., … & Shenton, M.E. (2000). Planum temporale and Heschl's gyrus volume reduction in schizophrenia. *Archive of General Psychiatry, 57*(7):692-699. doi:10-1001/pubs.Arch Gen Psychiatry-ISSN-0003-990x-57-7-yoa9242

Hoff, A.L., Riordan, H., O'Donnell, D., Stritzke, P., Neale, C., … & DeLisi, L.E. (1992). Anomalous lateral sulcus asymmetry and cognitive function in first-episode schizophrenia. *Schizophrenia Bulletin, 18*(2):257–272. doi:10.1093/schbul/18.2.257

Honer, W.G., Bassett, A.S., Squires-Wheeler, E., Falkai, P., Smith, G.N., … & Lang, D.J. (1995). The temporal lobes, reversed asymmetry and the genetics of schizophrenia. *Neuroreport, 7*(1):221-224. doi:10.1097/00001756-199512290-00053

Hubl, D., Dougoud-Chauvin, V., Zeller, M., Federspiel, A., Boesch, C., … & Koenig, T. (2010). Structural analysis of Heschl's gyrus in schizophrenia patients with auditory hallucinations. *Neuropsychobiology, 61:*1-9. doi:10.1159/000258637

Hugdahl, K., & Andersson, L. (1986). The 'forced-attention paradigm' in DL to CV-syllables: A comparison between adults and children. *Cortex, 22*:417–432. doi:10.1016/S0010-9452(86)80005-3

Hugdahl, K., Brønnick, K., Law, I., Kyllingsbæk, S., & Paulson, O. B. (1999). Brain activation during dichotic presentations of consonant–vowel and musical instruments stimuli: a 15O-PET study. *Neuropsychologia, 37*:431–440. doi:10.1016/S0028-3932(98)00101-8

Hugdahl, K. (2002). Dichotic listening in the study of auditory laterality. In K. Hugdahl & R.J. Davidson (eds.), The asymmetrical brain (pp. 441–478). Cambridge,

MA: MIT Press.

Hugdahl, K., Løberg, E., & Nygard, M. (2009). Left temporal lobe structural and functional abnormality underlying auditory hallucinations in schizophrenia. *Frontiers in Neuroscience, 3*(1):34-36. doi:10.3389/neuro.01.001.2009

Idowu, O.E., Soyemi, S., & Atobatele, K. (2014). the right [4,10,11]. Morphometry, asymmetry and variations of the Sylvian Fissure and sulci bordering and within the pars triangularis and pars operculum: An autopsy study. *Journal of Clinical and Diagnostic Research, 8*(11):AC11-AC14. doi:10.7860/JCDR/2014/9955.5130

Jakob, H., & Beckmann, H. (1989). Gross and histological criteria for developmental disorders in brains of schizophrenics. *Journal of the Royal Society of Medicine, 82*:466-69. PMCID: PMC1292251

Kasai, K., Shenton, M.E., Salisbury, D.F., Hirayasu, Y., Onitsuka, T., … & McCarley, R.W. (2003). Progressive decrease of left Heschl's gyrus and planum temporale gray matter volume in first-episode schizophrenia. *Archives of General Psychiatry, 60*:766-775. doi:10.1001/archpsyc.60.8.766

Kimura, D. (1961a). Some effects of temporal-lobe damage on auditory perception. *Canadian Journal of Psychology, 15*(3):156-165. doi:10.1037/h0083218

Kimura, D. (1961b). "Cerebral dominance and the perception of verbal stimuli". *Canadian Journal of Psychology, 15*(3): 166–171. doi:10.1037/h0083219

Kimura, D. (1967). Functional asymmetry of the brain in dichotic listening. *Cortex, 3*:163–168. doi:10.1016/S0010-9452(67)80010-8

Kimura, D. (1993). Neuromotor mechanisms in human communication. New York: Oxford University Press.

Kleinschmidt, A., Falkai, P., Huang, Y., Schneider, T., First, G., & Steinmetz, H. (1994). In vivo morphometry of planum temporale asymmetry in first-episode schizophrenia. *Schizophrenia Research, 12*:9-18. doi:10.1016/0920-9964(94)90079-5

Kurth, F., Zilles, K., Fox, P.T., Laird, A.R., & Eickhoff, S.B. (2010). A link between the systems: functional differentiation and integration within the human insula revealed by meta-analysis. *Brain Structure and Function, 214*(5-6):519-34. doi:10.1007/s00429-010-0255z

Kwon, J.S., McCarley, R.W., Hirayasu, Y., Anderson, J.E., Fisher, I.A., … & Shenton, M.E. (1999). Left planum temporale volume reduction in schizophrenia. *Archive of General Psychiatry, 56*:142-148. doi:10.1001/archpsyc.56.2.142

Lennox, B.R., Park, S.B., Medley, I., Morris, P.G., & Jones, P.B. (2000). The functional anatomy of auditory hallucinations in schizophrenia. *Psychiatry Research, 100*:13–20. doi:10.1016/s0925-4927(00)00068-8

Levitan, C., Ward, P.B., & Catts, S.V. (1999). Superior temporal gyral volumes and laterality correlates of auditory hallucinations in schizophrenia. *Biological Psychiatry, 46*:955–962. doi:10.1016/s0006-3223(98)00373-4

Lieberman, J.A., Chakos, M., Wu, H., Alvir, J., Hoffman, E., … & Bilder, R. (2001). Longitudinal study of brain morphology in first episode schizophrenia. *Biological Psychiatry, 49*(6):487–499. doi:10.1016/s0006-3223(01)01067-8

Lim, A., Hoek, H.W., Deen, M.L., & Blom, J.D. (2016). Prevalence and classification of hallucinations in multiple sensory modalities in schizophrenia spectrum disorders. *Schizophrenia Research, 176*(2-3):493–499. doi:10.1016/j.schres.2016.06.010

Linscott, R.J., & van Os, J. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: On the pathway from proneness to persistence to dimensional expression across mental disorders. Psychological Medicine, 43(6):1133-49. doi:10.1017/S0033291712001626.

Linszen, M.M.J., van Zanten, G.A., Teunisse, R.J., Brouwer, R.M., Scheltens, P., & Sommer, I.E. (2019). Auditory hallucinations in adults with hearing impairment: A large prevalence study. *Psychological Medicine, 49*(1):132–139. doi:10.1017/S0033291718000594

Løberg, E.M., Hugdahl, K., & Green, M.F. (1999). Hemispheric asymmetry in schizophrenia: A "dual deficits" model. *Biological Psychiatry, 45*(1):76-81. doi:10.1016/s0006-3223(98)00219-4.

Marneros, A., Beyenburg, S., & Berghaus, A. (1997). Unilateral hallucinations and other psychotic symptoms due to otosclerosis. *Psychopathology, 30*(2), 89–92. doi:10.1159/000285034

Marsh, L., Harris, D., Lim, K.O., Beal, M., Hoff, A.L., … & Pfefferbaum, A. (1997). Structural magnetic resonance imaging abnormalities in men with severe chronic schizophrenia and an early age at clinical onset. Archives of General Psychiatry, 54:1104–1112. doi:10.1001/archpsyc.1997.01830240060009

Mathalon, D.H., Sullivan, E.V., Lim, K.O., & Pfefferbaum, A. (2001). Progressive brain volume changes and the clinical course of schizophrenia in men: A longitudinal magnetic resonance imaging study. *Archives of General Psychiatry, 58*(2):148–157. doi:10.1001/archpsyc.58.2.148

McCarthy-Jones, S., Trauer, T., Mackinnon, A., Sims, E., Thomas, N., & Copolov, D.L. (2012). A new phenomenological survey of auditory hallucinations: Evidence for subtypes and implications for theory and practice. *Schizophrenia Bulletin, 40*(1):225-235. doi:10.1093/schbul/sbs156

McGuire, P.K., Shah, G.M., & Murray, R.M. (1993). Increased blood flow in Broca's area during auditory hallucinations in schizophrenia. *Lancet, 342*:703–706. doi:10.1016/0140-6736(93)91707-s

McKay, C.M., Headlam, D.M., & Copolov, D.L. (2000). Central auditory processing in patients with auditory hallucinations. *American Journal of Psychiatry, 157*(05):759–766. doi:10.1176/appi.ajp.157.5.759

Mechelli, A., Price, C.J., Friston, K.J., & Ashburner, J. (2005). Voxel-based morphometry of the human brain: Methods and applications. *Current Medical Imaging Reviews, 1*(2):105-113. doi:10.2174/1573405054038726

Menon, R.R., Barta, P.E., Aylward, E.H., Richards, S.S., Vaughn, D.D., … & Pearlson, G.D. (1995). Posterior superior temporal gyrus in schizophrenia: grey matter changes and clinical correlates. *Schizophrenia Research, 16*(2):127-135. doi:10.1016/0920-9964(94)00067-I

Milev, P., Ho, B.C., Arndt, S., Nopoulos, P., & Andreasen, N.C. (2003). Initial magnetic resonance imaging volumetric brain measurements and outcome in schizophrenia: A prospective longitudinal study with 5-year follow-up. *Biological Psychiatry, 54*:608–615. doi:10.1016/S0006-3223(03)00293-2

Mitchell, R.L.C., Crow, C.J. (2005). Right hemisphere language functions and schizophrenia: the forgotten hemisphere? *Brain, 128*:963–978. doi:10.1093/brain/awh466

Modinos, G., Costafreda, S.G., van Tol, M., McGuire, P.K., Aleman, A., & Allen, P. (2013). Neuroanatomy of auditory verbal hallucinations in schizophrenia: A quantitative meta-analysis of voxel-based morphometry studies. *Cortex, 49*:1046-1055. doi:10.1016/j.cortex.2012.01.009

Mørch-Johnsen, L., Nesvag, R., Jørgensen, K.N., Lange, E.H., Hartberg, C.B., … & Agartz, I. (2017). Auditory cortex characteristics in schizophrenia: Associations with auditory hallucinations. *Schizophrenia Bulletin, 43*: 75-83. doi:10.1093/schbul/sbw130

Musiek, F.E. & Pinheiro, M.L. (1985). Dichotic Speech Tests in the Detection of Central Auditory Dysfunction. In M.L. Pinheiro and F.E. Musiek (Eds.), Assessment of Central Auditory Dysfunction: Foundations and Clinical Correlates, (pp. 201-218). Baltimore, MD: Williams and Wilkins.

Musiek, F.E., & Chermak, G.D. (2014). Auditory Neuroscience and Central Auditory Processing Disorder: An Overview. Handbook of Central Auditory Processing Disorder. San Diego: Plural Publishing.

Musiek, F.E., Morris, S., Ichiba, K., Clark, L., & Davidson, A.J. (in press). Auditory hallucinations: An audiological horizon? *Journal of the American Academy of Audiology*. doi:10.1055/s-0041-1722989.

Nazimek, J.M., Hunter, M.D., & Woodruff, P.W.R. (2012) Auditory hallucinations: Expectation-perception model. *Medical Hypotheses, 78*:802-810. doi:10.1016/j.mehy.2012.03.014

Neckelmann, G., Specht, K., Lund, A., Ersland, L., Smievoll, A.I., … & Hugdahl, K. (2006). MR morphometry analysis of grey matter volume reduction in schizophrenia: Association with hallucinations. *Intern. J. Neuroscience, 116*:9-23. doi:10.1080/00207450690962244

Nenadic, S.S., Schlosser, R.G.M., Sauer, H., & Gaser, C. (2010). Auditory hallucinations and brain structure in schizophrenia: Voxel-based morphometric study. *The British Journal of Psychiatry, 196*:412-413. doi:10.1192/bjp.bp.109.07044

Niznikiewics, M.A., Kubicki, M., & Shenton, M.E. (2003). Recent structural and functional imaging findings in schizophrenia. *Current Opinion in Psychiatry, 16*:123–147. doi:10.1097/01.yco.0000058610.61505.6b

Northoff, G., & Bermpohl, F. (2004). Cortical midline structures and the self. Trends in Cognitive Science, 8:102–107. doi:10.1016/j.tics.2004.01.004

O'Daly, O.G., Frangou, S., Chitnis, X., & Shergill, S.S. (2007). Brain structural changes in schizophrenia patients with persistent hallucinations. *Psychiatry Research: Neuroimaging, 156*:15-21. doi:10.1016/j.pscychresns.2007.03.001

Ohi, K., Matsuda, Y., Shimada, T., Yasuyama, T., Oshima, K., … & Kawasaki, Y. (2016). Structural alterations of the superior temporal gyrus in schizophrenia: Detailed subregional differences. *European Psychiatry, 35*:25-31. doi:10.1016/j.eurpsy.2016.02.002

Panaliyappan, L., Balain, V., Radua, J., & Liddle, P.F. (2012). Structural correlates of auditory hallucinations in schizophrenia: A meta-analysis. *Schizophrenia Research, 137*:169-173. doi:10.1016/j.schres.2012.01.038

Pearlson, G.D. (1997). Superior temporal gyrus and planum temporale in schizophrenia: A selective review. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 21*:1203-1229. doi:10.1016/s0278-5846(97)00159-0

Penrose, L.S. (1945). Survey of cases of familial mental illness. European Archives of Psychiatry and Clinical Neuroscience, 240:315–24. doi:10.1007/BF02279760

Petty, G., Barta, P.E., Pearlson, G.D., McGilchrist, I.K., Lewis, R.W., … & Powers, R.E. (1995). Reversal of asymmetry of the planum temporale in schizophrenia. *American Journal of Psychiatry 152*(5):715-721. doi:10.1176/ajp.152.5.715

Petty, R.G. (1999). Structural asymmetries of the human brain and their disturbance in schizophrenia. *Schizophrenia Bulletin, 25*(1):121-139. doi:10.1093/oxfordjournals.schbul.a033360

Plaze, M., Paillère-Martinot, M., Penttilä, J., Januel, D., de Beaurepaire, M., … & Cachia, A. (2009). "Where do auditory hallucinations come from?" - A brain morphometry study of schizophrenia patients with inner or outer space hallucinations. *Schizophrenia Bulletin, 37*(1):212-221. doi:10.1093/schbul/sbp081

Pollmann, S., Maertens, M., von Cramon, D. Y., Lepsien, J., & Hugdahl, K. (2002). Dichotic listening in patients with splenial and nonsplenial callosal lesions. *Neuropsychology, 16*:56–64. doi:10.1037//0894-4105.16.1.56.

Prasad, K.M., Rohm, B.R., & Keshavan, M.S. (2004). Parahippocampal gyrus in first episode psychotic disorders: A structural magnetic resonance imaging study *Progress in Neuropsychopharmacology and Biological Psychiatry, 28*:651-658. doi:10.1016/j.pnpbp.2004.01.017

Rajarethinam, R.P., DeQuardo, J.R., Nalepa, R., & Tandon, R. (2000). Superior temporal gyrus in schizophrenia: A volumetric magnetic resonance imaging study. *Schizophrenia Research, 41*:303–312. doi:10.1016/s0920-9964(99)00083-3

Ratanather, J.T., Poynton, C.B., Pisano, D.V., Crocker, B., Postell, E., … & Barta, P.E. (2013). Morphometry of superior temporal gyrus and planum temporale in schizophrenia and psychotic bipolar disorder. *Schizophrenia Research, 150*:476-483. doi:10.1016/j.schres.2013.08.014

Rojas, D.C., Teale, P., Scheeder, J., Simon, J., & Reite, M. (1997). Sex-specific expression of Heschl's gyrus functional and structural abnormalities in paranoid schizophrenia. *American Journal of Psychiatry, 154*:12. doi:10.1176/ajp.154.12.1655

Rossi, A., Serio, A., Strata, P., Petruzzi, C., Schiazza, G., … & Casacchia, M. (1994). Planum temporale asymmetry and thought disorder in schizophrenia. *Schizophrenia Research, 12*:1-7. doi:10.1016/0920-9964(94)90078-7

Sakuma, M., Hoff, A.L., & DeLisi, L.E. (1996). Functional asymmetries in schizophrenia and their relationship to cognitive performance. *Psychiatry Research, 65*:1:13. doi:10.1016/0165-1781(96)02818-1

Seidman, L.J., People, J.R., Faraone, S.V., Kremen, W.S., Green, A.I., … & Tsuang, M.T. (1993). Neuropsychological performance in chronic schizophrenia in response to neuroleptic dose reduction. *Biological Psychiatry, 33*(8-9):575-84. doi:10.1016/0006-3223(93)90095-u.

Shapleske, J., Rossell, S.L., Woodruff, P.W., & David, A.S. (1999) The planum temporale: A systematic, quantitative review of its structural, functional and clinical significance. *Brain Research Review, 29*(1):26–49. doi:10.1016/s0165-0173(98)00047-2.

Shapleske, J., Rossell, S.R., Simmons, A., David, A.S., & Woodruff, P.W.R. (2001). Are auditory hallucinations the consequence of abnormal cerebral lateralization? A morphometric MRI study of the sylvian fissure and planum temporale. *Society of Biological Psychiatry, 49*:685-693. doi:10.1016/s0006-3223(00)01006-4

Shapleske, J., Rossell, S.L., Chitnis, X.A., Suckling, J., Simmons, A., … & David, A.S., (2002). A computational morphometric MRI study of schizophrenia: effects of hallucinations. *Cerebral Cortex, 12*:1331–1341. doi:10.1093/cercor/12.12.1331

Shenton, M.E., Kikinis, R., Jolesz, F.A., Pollak, S.D., LeMay, M., … & McCarley, R.W. (1992). Abnormalities of the left temporal lobe and thought disorder in schizophrenia. *The New England Journal of Medicine, 327*(9):604-612. doi:10.1056/NEJM199208273270905

Shin, S.E., Lee, J.S., Kang, M.H., Kim, C.E., Bae, J.N., & Jung, G. (2005). Segmented volumes of cerebrum and cerebellum in first episode schizophrenia with auditory hallucinations. *Psychiatry Research, 138*:33–42. doi:10.1016/j.pscychresns.2004.11.005

Silbersweig, D.A., Stern, E., Frith, C., Cahill, C., Holmes, A., … & Schnorr, L. (1995). A functional neuroanatomy of hallucinations in schizophrenia. *Nature, 378*:176–179. doi:10.1038/378176a0

Sommer, I., Aleman, A., Ramsey, N., Bouma, A., & Khan, R. (2001). Handedness, language lateralisation and anatomical asymmetry in schizophrenia: Meta-analysis. *British Journal of Psychiatry, 178:* 344-351. doi:10.1192/bjp.178.4.344

Sommer, I., & Hugdahl, K. (2019). Auditory hallucinations in schizophrenia: Where are we now and where do we go from here? A personal commentary. *Schizophrenia Research, 212*:1-3. doi:10.1016/j.schres.2019.07.017.

Southard, E.E. (1915). On topographical distribution of cortical lesions and anomalies in dementia praecox, with some account of their functional significance. *American Journal of Insanity, 71*:383-405, 603-671. doi:10.1176/ajp.71.3.603

Steinmann, S., Leicht, G., & Mulert, C. (2014). Interhemispheric auditory connectivity: Structure and function related to auditory verbal hallucinations. *Neuroscience, B*(55). doi:10.3389/fnhum.2014.00055

Stephane, M., Thuras, P., Nasrallah, H., & Georgopoulos, A.P. (2003). The internal structure of the phenomenology of auditory verbal hallucinations. *Schizophrenia Research, 61*:185–193. doi:10.1016/s0920-9964(03)00013-6

St. George, B., DeMarco, A.T., & Musiek, F. (2017, April 13). Modern views on the anatomy of planum temporale. 29th annual AudiologyNOW! Meeting, Indianapolis, IN.

Sumich, A., Chitnis, X.A., Fannon, D.G., O'Ceallaigh, S., Doku, V.C., … & Sharma, T. (2005). Unreality symptoms and volumetric measures of Heschl's gyrus and planum temporale in first-episode psychosis. *Biological Psychiatry 57*:947–950. doi:10.1016/j.biopsych.2004.12.041

Suzuki, M., Yuasa, S., Minabe, Y., Murata, M., & Kurachi, M. (1993). Left superior temporal blood flow increases in schizophrenic and schizophreniform patients with auditory hallucination: a longitudinal case study using 123I-IMP SPECT. *European Archives of Psychiatry and Clinical Neuroscience, 242*:257–261. doi:10.1007/BF02190383

Szechtman, H., Woody, E., Bowers, K.S., & Nahmias, C. (1998). Where the imaginal appears real: A positron emission tomography study of auditory hallucinations. Proceedings of National Academy of Sciences USA, 95:1956–1960. doi:10.1073/pnas.95.4.1956

Takahashi, T., Wood, S.J., Yung, A.R., Soulsby, B., McGorry, P.D., … & Pantelis, C. (2009). Progressive gray matter reduction of the superior temporal gyrus during transition to psychosis. *Archives of General Psychiatry, 66*(4):366-376. doi:10.1001/archgenpsychiatry.2009.12

Thompson, P.M., Vidal, C., Giedd, J.N., Gochman, P., Blumenthal, J., … & Rapoport, J.L. (2001). Mapping adolescent brain change reveals dynamic wave of accelerated grey matter loss in early-onset schizophrenia. *Proceedings of the National Academy of Science of the United States, 98*:11650–11655. doi:10.1073/pnas.201243998

Tien, A. (1991). Distributions of hallucinations in the population. *Social Psychiatry and Psychiatric Epidemiology, 26*:287–292. doi:10.1007/BF00789221.

Vercammen, A., Knegtering, H., den Boer, J.A., Liemburg, E.J., & Aleman, A. (2010). Auditory hallucinations in schizophrenia are associated with reduced functional connectivity of the temporo-parietal area. *Biology Psychiatry, 67*L912-918. doi:10.1016/j.biopsych.2009.11.017

Waters, F., Allen, P., Aleman, A., Fernyhough, C., Woodward, T.S., … & Laroi, F. (2012). Auditory hallucinations in schizophrenia and nonschizophrenia populations: A review and integrated model of cognitive mechanisms. *Schizophrenia Bulletin, 38*(4):683-692. doi:10.1093/schbul/sbs045

Wible, C.G., Shenton, M.E., & McCarley, R.W. (1997). Functional neuroanatomy of the limbic system and the planum temporale. In: Rama Krishnan KR, Doraiswamy PM, editors. Brain Imaging in Clinical Psychiatry. Marcel Dekker; New York.

Wise, R.J.S., Scott, S.K., Blank, S.C., Mummery, C.J., Murphy, K., & Warburton, E.A. (2001). Separate neural subsystems within `Wernicke's area'. Brain, 124(1):83–95. doi:10.1093/brain/124.1.83

Witelson, S.F. (1989). Hand and sex differences in the isthmus and body of the corpus callosum: A postmortem morphological study. *Brain, 112:*799-835. doi:10.1093/brain/112.3.799

Wong, B.M., & Musiek, F.E. (2020). Morphological variance and related taxonomy of the planum temporale. *Journal of Hearing Science, 10*(4):9-19. doi:10.17430/JHS.2020.10.4.1

Yamasaki, S., Yamasue, H., Abe, O., Yamada, H., Iwanami, A., … & Kasai, K. (2007). Reduced planum temporale volume and delusional behavior in patients with schizophrenia. *Archive of Psychiatry Clinical Neuroscience, 257*:318-324. doi:10.1007/s00406-007-0723-5

Zhao, W., Guo, S., He, N., Yang, A.B., … & Tsai, S. (2018). Callosal and subcortical white matter alterations in schizophrenia: A diffusion tensor imaging study at multiple levels. *Neuroimage: Clinical, 20*: 594–602. doi:10.1016/j.nicl.2018.08.027

Zipursky, R.B., Lim, K.O., Sullivan, E.V., Brown, B.W., & Pfefferbaum, A. (1994). Widespread cerebral grey matter volume deficits in schizophrenia. Archives of General Psychiatry, 49:195-205. doi:10.1001/archpsyc.1992.01820030027004