While there are several hypotheses on the working mechanisms of hallucinations, one specific idea is quite an intriguing concept to me; namely that our brain can be “bored” and just finds a way to entertain itself by creating random activity, or as the quote phrased it by throwing a “little surrealist party”. This quote essentially describes one of the major topics of this thesis; the deafferentation theory or the theory behind the working mechanism of hallucinations in sensory impairment. When I first encountered this type of hallucinations, I was fascinated by the fact that the brain recreates something that has essentially been taken from it. However, I soon realized that this is actually a normal part of perception. Our bodies are not made to get every detail of the world from the outside, but rather rely strongly on input from our brain. It uses our memories and our experiences to perceive the world. Optical illusions are a great example of this mechanism. Maybe there are little surrealist parties in all of us trying to make us hallucinate - but some bodies are better equipped to ignore them than others.

Intrigued as I was, I set out to learn more about this unusual perception, better known as deafferentation hallucinations, only to discover that much about their occurrence and working mechanisms was still unknown. This inspired me to give this phenomenon the attention it deserves and provide new insights into auditory deafferentation hallucinations.

However, the more I learned about one type of hallucinations, the more I wondered whether my newfound knowledge also applies to other types. Therefore, this thesis also touches upon hallucinations in various other clinical as well as non-clinical groups. By going beyond the populations typically studied in the context of hallucinations I hope to contribute to our understanding of hallucinations. In doing so, my aim has been to identify subtypes of hallucinations and describe some of the neurobiological mechanisms involved in specific populations.

Before delving into the research presented in this thesis, a general introduction to the topic of hallucinations will be provided with an emphasis on the populations studied in this thesis.
What are hallucinations?

In this thesis I aim to assess the working mechanisms and phenomenology of hallucinations in and across various populations. This way I hope to provide a comprehensive picture of this phenomenon. Hallucinations are defined as sensory perceptions in the absence of a corresponding stimulus, separating them from veridical perception and illusions (see Figure 1). Even though the experience of a hallucination is metaphysically different, it is often phenomenally similar to a real percept. As a result, to the person experiencing the hallucination it can be indistinguishable from a true perception if not further investigated. However, not every person hallucinating is convinced that their experience is real; some can distinguish their hallucination from reality.

![Figure 1](image.png)

**Figure 1**: Comparison between perception (left), hallucinations (middle), and illusions (right).
Hallucinations can occur in every sensory modality, i.e., visual, auditory, tactile, olfactory, gustatory, or a combination thereof. For some they are limited to one sensory modality, whereas for others they take form across multiple modalities or have multisensory qualities (Chesterman and Boast, 1994). Having hallucinations in multiple modalities means that a person can experience hallucinations in several senses without an overarching theme, e.g., hear voices and smell flowers, whereas multisensory indicates a thematic connection, e.g., hearing voices and seeing faces corresponding to the voices (Montagnese et al., 2021; Toh et al., 2022).

Hallucinations are often associated with a negative impact on a person’s life. In many cases hallucinations are not only related to social isolation and decreased quality of life, but also worse long-term outcomes (Freeman et al., 2019; Kjelby et al., 2015; Slotema et al., 2017; Vukicevic and Fitzmaurice, 2008). Not only do hallucinations occur in the context of many disorders including a variety of psychiatric disorders (schizophrenia spectrum disorders and bipolar disorder) and neurologic disorders (dementia with Lewy bodies and Parkinson’s disease psychosis) but they can also occur during altered states of consciousness, such as following drug use or sleepiness (Fénelon et al., 2010; Fletcher and Frith, 2009; Nichols, 2004; Shinn et al., 2012; Waters et al., 2014a). Hallucinations are also known to occur as a consequence of sensory impairment (Ffytche, 2009, 2005; Linszen et al., 2019), and can be induced by sensory deprivation (Heron, 1961, 1957; Lilly, 1956; Lilly and Shurley, 1961). They happen sporadically in otherwise healthy individuals, for example when they are falling asleep (Bless et al., 2021), but there are even healthy individuals who experience them regularly (Baumeister et al., 2017). In essence, hallucinations can be experienced by a wide variety of people and may have various underlying reasons. If you were ever convinced that your phone rang but nobody else heard it, you may have experienced a hallucination.

Even though this list probably does not cover all causes that may produce hallucinations, it points out that hallucinations arise in a very heterogenous group of people under the influence of a very heterogenous set of causes. The large variability suggests that hallucinations may not necessarily be a symptom of a specific disease, but a fundamental property of the human mind. Yet there are certain disorders in the context of which hallucinations have been more prominently studied throughout the years (see Figure 2). The underrepresentation of particular types of hallucinations within the scientific literature may, therefore, have led to a rather limited picture of the experience of hallucinations throughout
the whole population. For example, schizophrenia spectrum disorders are often associated with auditory verbal hallucinations. Considering the high prevalence of this type of hallucinations in patients diagnosed with schizophrenia, it is an obvious choice to study this phenomenon in this patient group. Nevertheless, auditory hallucinations are also often encountered outside of psychiatry, as several neurological disorders are characterized by this symptom (Amar et al., 2014; Eversfield and Orton, 2019; Llorca et al., 2016). Besides that, they are experienced in other groups, such as hearing-impaired individuals and healthy individuals.

Figure 2: Distribution of the number of scientific publications related to hallucinations and several disorders found on the search engine PubMed in August 2022. It can be seen that the publications on schizophrenia and hallucinations outnumber all of the other disorders.
On top of that, even within one diagnostic group hallucinations do not always show a lot of similarity. Staying with the example of schizophrenia spectrum disorders, it has been suggested that the content of the auditory verbal hallucinations is diverse. Therefore, classifying them into subtypes instead of generalizing all of them as a symptom of this specific disorder may be necessary (Jones, 2010; McCarthy-Jones et al., 2014; Sommer et al., 2018). Indeed, some evidence supports the idea of thematic subtypes in the content of auditory verbal hallucinations (Corona-Hernández et al., 2022; McCarthy-Jones et al., 2014).

Additionally, a substantial part of patients with schizophrenia spectrum disorders experience hallucinations in modalities other than the auditory domain. For instance, McCarthy-Jones et al. (2017) reported that 23–31% of these patients experience visual, 9–19% tactile, and 6–10% olfactory hallucinations. Similar prevalence levels for the visual domain, namely 27%, were extracted in a review by Waters et al. (2014a), suggesting this to be a relatively common phenomenon. Nevertheless, there has been a tendency within research to neglect these other modalities when examining hallucinations (Langdon et al., 2011; McCarthy-Jones et al., 2017; Waters et al., 2014a).

Needless to say, the experience of hallucinations comes with a lot of heterogeneity and differs strongly between individuals, diagnoses, and modalities. This raises many questions, such as: Do these hallucinations among different diagnoses have a similar phenomenology? Do they all have the same underlying mechanism? Would the typical treatment of hallucinations in schizophrenia also alleviate the symptom in other disorders? Therefore, to fully understand hallucinations and test whether there is an intrinsic unity combining these experiences across individuals, it is essential to not only focus research on the most common types of hallucinations.

Earlier studies have undertaken the task of answering some of these questions for example by reviewing the effect of different treatments on hallucinations with a specific content (e.g., Coebergh et al., 2015) or comparing hallucinations between psychiatric and neurodegenerative diseases (e.g., Dudley et al., 2019; Rollins et al., 2019; Sommer et al., 2012; Waters & Fernyhough, 2017). Still, there is much more to discover. With this thesis I aim to contribute to our understanding of hallucinations by 1) investigating hallucinations in lesser studied populations, namely in hearing-impaired individuals and in healthy or non-clinical voice hearers, as well as 2) examining the phenomenology of hallucinations across and beyond diagnostic labels.
Chapter 1

Hallucinations in hearing impairment

Deafferentation theory

Hallucinations that develop as a consequence of limited sensory input are commonly referred to as deafferentation hallucinations. Deafferentation hallucinations tend to occur in individuals who experience sensory impairment. This thesis will specifically address the auditory variant of deafferentation, complex auditory hallucinations due to hearing impairment. Depending on the sensory domain affected by the deterioration, the hallucination tends to resemble the perception debilitated (Mohan and Vanneste, 2017). In other words, a person with visual impairment may have visual hallucinations whereas a person who lost their ability to smell may have olfactory hallucinations. Yet the mechanisms underlying these hallucinations are assumed to be the same regardless of the afflicted sensory domain (de Ridder et al., 2014; Mohan and Vanneste, 2017). The theory behind this mechanism, also referred to as deafferentation, attributes the hallucination to deviations in sensory pathways that can be traced back to the basic principles of perception. Normal perception can be considered to consist of two streams, the bottom-up information, and the top-down processing, which contribute to an internal model of the outside world (Alink et al., 2010; Friston, 2010, 2009; Hesselmann et al., 2010); see the top part of Figure 3 for a simple depiction of auditory perception). The bottom-up part of perception describes the information acquired by the senses and is processed via the primary sensory cortices. This information is then used by higher order areas of the brain to make inferences about the world around oneself (Friston, 2010; Hesselmann et al., 2010). These higher order areas contribute to the top-down part of perception by employing learned information from previous experiences, such as memories, to reduce uncertainty1 (Alink et al., 2010; Quartz and Sejnowski, 2003). In a way, our brains predict the world around us and use the sensory input to update and confirm these predictions (Friston, 2010).

In sensory deprivation, for example due to sensory impairment the amount of information available to the brain decreases. In order to regain homeostasis, the brain is assumed to adapt to this lack of input, either by lowering the threshold to detect activity in the sensory pathways or reducing the inhibition of spontaneous activity (de Ridder et al., 2014; Mohan and Vanneste, 2017; Vanneste et al., 2013). Consequently, this false-positive activity is then regarded

1 Uncertainty exists in perception regardless of impairment of not. Our sensory systems are not made to process 100% of the input the world provides.
as a real stimulus and results in a non-existing perception, better known as a hallucination (see the bottom part of Figure 3 for a simple depiction of auditory deafferentation). This theory however is mainly theoretical as of now. To test whether this theory is in line with the actual activity underlying hallucinations I will review the current literature describing auditory and visual deafferentation, as well as assess the role of spontaneous brain activity in individuals experiencing auditory deafferentation hallucinations.

**Figure 3**: Simple depiction of perception (top) and deafferentation (bottom) on the example of hearing. Perception: Sound (i.e., a stimulus) enters the ear. It is then processed in the primary auditory cortex. In a feedback loop with higher order cortices the inner representation of the stimulus is created by combining the information from the sensory cortex (bottom-up) and experience/memory from the higher order cortices (top-down). Deafferentation: Generally, the information stream is similar to perception, but less input is received from the sensory organ. This may lead to more spontaneous activity being misinterpreted from the bottom-up stream and/or more reliance on the top-down stream.
Hearing-impairment and hallucinations

Most people know of tinnitus\(^2\), the perception of a simple sound often associated with hearing-impairment. However, people seem less aware of the occurrence of complex hallucinations, such as voices or music, in people with hearing-impairment. Yet, such hallucinations are quite common, with a prevalence of 16.2% of people with hearing-impairment experiencing deafferentation hallucinations (Linszen et al., 2019) and approximately 430 million people worldwide having some form of hearing impairment (World Health Organization, 2021). It is as of yet unclear why this type of hallucination is largely unrecognized but may be related to a combination of several factors. Among these are stigma surrounding hallucinations, a bias in the literature towards describing deafferentation hallucinations as music (therefore not recognizing other forms), the way auditory assessment addresses the occurrence of non-existing sounds, and just general awareness of deafferentation in the public as well as among clinicians. Even though they are sometimes referred to as musical hallucinations, deafferentation can actually occur in many forms. In fact, a recent study showed that people most frequently perceive voices (Linszen et al., 2019). This indicates that auditory deafferentation can take quite complex forms and show similarities with auditory verbal hallucinations experienced by other patient groups. Whether the seeming lack of knowledge about deafferentation affects clinical settings will be assessed in this thesis.

This type of hallucination seems to be rather unique, as it has a clear causal relationship between the sensory impairment and the hallucination (hallucinations can be induced by depriving individuals from sensory input over a longer period of time). In line with this it is possible to alleviate auditory deafferentation hallucinations by restoring the sensory abilities, for example, with a hearing-aid, which seems to be more effective than anti-psychotic medication (Coebergh et al., 2015). Additionally, people who experience deafferentation hallucinations tend to have preserved insight into the unreal nature of the hallucination (David and Fernandez, 2000; Moseley et al., 2018; Pasquini and Cole, 1997), which is less often the case in other patient groups (Lera et al., 2011; van Ommen et al., 2019). Yet, there is some reason to assume at least partly common underlying mechanisms between auditory deafferentation and more commonly studied auditory hallucinations, such as auditory verbal hallucinations in schizophrenia spectrum disorders.

\(\text{2 Whether tinnitus should be considered a hallucination is a debatable topic and goes beyond the scope of this thesis}\)
First of all, it has been suggested that hearing impairment can increase the risk of experiencing psychotic symptoms, specifically hallucinations, in patients with schizophrenia spectrum disorders (Linszen et al., 2016; Sommer et al., 2014a). Sensory impairment is generally considered a risk factor for hallucinations (Johns et al., 2002; Kimhy et al., 2007; Waters et al., 2014a). Additionally, the phenomenology of deafferentation hallucinations has just recently been confirmed to be more similar to auditory verbal hallucinations than initially thought (Linszen et al., 2019). Interestingly, there have also been some reports suggesting that not all hearing-impaired have preserved insight into the hallucinations (Linszen et al., 2016; Sommer et al., 2014b). These commonalities make it specifically difficult to distinguish deafferentation hallucinations from psychosis unless hearing abilities have been assessed. Further, the deafferentation theory also parallels strikingly with some established theories of hallucinations in psychosis, suggesting an unbalanced top-down and bottom-up processing as an underlying cause (Aleman et al., 2003; Behrendt, 1998; Hugdahl, 2009).

Deafferentation seems to not only be limited to sensory input but may also extend to social interactions. Hoffman (2007) has coined the social deafferentation theory, which suggests that social isolation may induce hallucinations to compensate for human's innate need for socialization. Especially in the context of sensory impairment social deafferentation may play a role, as the impairment can impact a person's ability for social interaction. Indeed, hallucinations in hearing-impairment have been shown to be associated with loneliness and a problem with social functioning (Linszen, 2021; Shoham et al., 2019).
Hallucinations in the general population

Hallucinations beyond clinical disorders

Most people consider hallucinations to be a symptom of specific disorders, yet they can occur in the general population in the absence of any clinical condition. Based on data from the World Health Organization World Mental Health Surveys, approximately 5% of people experience hallucinations throughout their lifetime (McGrath et al., 2015) and prevalence levels seem to decrease with age (Larøi et al., 2019; Yates et al., 2021). However, lifetime prevalence levels differ between studies depending on the way they are assessed, ranging from 5% to 15% (Blom, 2013; Linscott and van Os, 2013; Maijer et al., 2018). One study using a much broader definition of hallucinations based on the Questionnaire for Psychotic Experiences (QPE) (Rossell et al., 2019) reported that 80.1% of the 10,448 participants had experienced at least one hallucination during their lifetime (Linszen et al., 2022).

Generally, visual hallucinations seem to have a higher lifetime prevalence than auditory hallucinations (Khaled et al., 2020; McGrath et al., 2015). Hallucinations can be infrequent. McGrath et al. (2015) reported that the majority of individuals who hallucinate experience them fewer than 10 times throughout their lives. Even though there is no underlying diagnosis related to the hallucinations, these experiences may relate to mental health issues that are not typically associated with hallucinations. Higher rates of mental disorders, such as anxiety and depression have been highlighted in this subpopulation (Yates et al., 2021). Increased suicide ideation and lifetime suicide attempts have also been reported (Yates et al., 2021). A large-scale cross-sectional study has shown that these associations show variations over the lifespan and are more pronounced in early adulthood and middle age and lessen with increasing age (Yates et al., 2021). Other studies reported similar variability throughout the lifespan (Larøi et al., 2019; Maijer et al., 2018). Larøi et al. (2019) suggested that different levels of anxiety and depression throughout life may contribute to this effect. Additionally, having gone through traumatic experiences may contribute to the occurrence of hallucinations (Begemann et al., 2017, 2016; McGrath et al., 2017). This may be due to an increased disposition for psychotic experiences caused by trauma in general (Liu et al., 2017; McCrory et al., 2011; McLaughlin et al., 2010).
Introduction

Healthy voice-hearers

While the occasional experience of hallucinations described above is rather common, a small group of individuals exists who perceive a specific type of hallucinations, namely voices, on a regular basis. Approximately 2% of the general population fall into this category (Johns et al., 2002; Kråkvik et al., 2015). These individuals are sometimes referred to as non-clinical voice-hearers or healthy voice hearers. The auditory verbal hallucinations perceived by this group show strong similarities to those experienced by people with a schizophrenia spectrum disorder (Baumeister et al., 2017; Daalman et al., 2011a). Especially regarding the perceptual features of the hallucinations, there is much overlap, such as comparable levels of loudness or the location of the voices (Daalman et al., 2013, 2012, 2011a; Diederent et al., 2010; Hill et al., 2012; Honig et al., 1998).

In spite of these perceptual similarities, the hallucinations experienced by healthy voice hearers are usually of a more positive content and not considered bothersome (de Boer et al., 2021; Honig et al., 1998; Sommer et al., 2010). Besides that, non-clinical voice hearers tend to have more control over their hallucinations (Daalman et al., 2011a, 2011b; Hill et al., 2012). Generally, they may show some symptoms related to psychosis, however not on a clinically relevant level (Hill et al., 2012; Howes et al., 2013b, 2013a; Sommer et al., 2010; Sommer et al., 2010; van Lutterveld et al., 2014). Individuals who have these experiences therefore do not meet the criteria to be diagnosed with psychosis or other suchlike disorders usually associated with hallucinations. In fact, these healthy voice hearers are often described to be functioning on a normal level. Nonetheless, there has been some evidence that these individuals are rather situated between clinical samples and healthy controls with regard to cognitive biases and global functioning (Daalman et al., 2011b; Diederent et al., 2010; Jagsen et al., 2019; Sommer et al., 2010; van Lutterveld et al., 2014). Interestingly, when Daalman et al. (2016) followed up on a group of healthy voice hearers, they found that 39.5% of their sample developed mental health issues. This proportion was significantly higher than in their control groups (12.2%).

Non-clinical voice hearers offer a different view on hallucinations, as they allow us to study this phenomenon free from the influence of medication or comorbid symptoms such as delusions.
Continuum theory

With the existence of healthy voice hearers, the idea that hallucinations are a symptom of disease is not as straightforward as long assumed. In the past, auditory verbal hallucinations were thought of as a hallmark of schizophrenia and classically used as an identifying symptom for that diagnosis (Schneider, 1959). This categorial way of approaching auditory hallucinations has been criticized (Bentall, 2006; Kaymaz and van Os, 2010; Linscott and van Os, 2010; van Os et al., 2009) as hallucinations can affect individuals differently and not necessarily reflect a need for care (Baumeister et al., 2017; Johns et al., 2014; Peters et al., 2016). As an alternative, the idea of a continuum of hallucinations (and similar psychotic experiences) has been put forward (Baumeister et al., 2017; Claridge, 1994; Linscott and van Os, 2013, 2010; van Os et al., 2009) with healthy non-voice hearing individuals on one end and psychosis on the other. In the first descriptions of the continuum theory, hallucinations were assumed to be related to disease severity, with non-clinical voice hearers representing a sub-clinical form of psychosis (Claridge, 1994; Claridge and Beech, 2010). More nuanced ways of looking at the continuum theory suggest, however, that hallucinations may exist regardless of diagnosis or risk thereof. Here, the continuum is rather related to the impact hallucinations have on an individual’s daily functioning and may correspond to the negative appraisal (Claridge, 1994; Johns et al., 2014; Waters and Fernyhough, 2019).
In accordance with this theory, there may be considerable overlap in the neurobiological mechanisms involved in hallucinations in clinical as well as non-clinical populations. Whether this is indeed the case will be studied in this thesis. Still, this theory leaves room to explain differences. Nonetheless, there has been some criticism as this theory does not provide a profound view on psychosis (David, 2010; Kaymaz and van Os, 2010; Linscott and van Os, 2010). Linscott and van Os (2010), for example, argue that this model does not reflect the non-continuous risk for schizophrenia. Additionally, factors moderating clinical outcomes, such as epidemiological and genetic influences are neglected in a continuum (Kaymaz and van Os, 2010).
Potential benefits of going off the beaten path

Investigating hallucinations either in lesser studied populations or as a transdiagnostic symptom can provide several benefits for our understanding of hallucinations. These benefits include, but are not limited to, better understanding of the neurobiological mechanisms, increased awareness, better treatment, and reduced stigma.

Transdiagnostic approach

The need for a different approach in studying hallucinations has been voiced more frequently over the last years (Ford et al., 2014; Pienkos et al., 2019; Waters et al., 2014b; Waters and Fernyhough, 2017), in particular since the focus on psychiatric disorders classified by the ICD/DSM diagnoses has been questioned (Cuthbert and Insel, 2013; Hyman, 2007; Insel et al., 2010; Sanislow et al., 2010). To address the issue of heterogeneity within the DSM diagnoses, the US National Institute for Mental Health has proposed the Research Domain Criteria (RDoC; Cuthbert & Insel, 2013; Insel et al., 2010; Morris et al., 2022), which can serve as an example for hallucination research (Ford et al., 2014). Instead of using symptoms as a cut off score, this approach takes the larger picture into account. This is done by quantifying normative neurobehavioral processes across several domains, like cognitive processes and arousal, to gain insight into their full range of variation. Based on this information, mental disorders can be described in an integrative multi-dimensional manner. As such it is, for example, proposed that symptoms not only lay on a continuum ranging from health to illness, but should also be studied across diagnostic labels.

Hallucination research can benefit from such an approach as the aforementioned heterogeneity seen in both the experience of hallucinations but also the people who encounter hallucinations bears problems similar to those addressed by the RDoC. In fact, predating the RDoC it has been proposed that hallucinations should not be seen as a dichotomy (i.e., either you experience them or not) but rather a continuum (Claridge, 1994; Linscott and van Os, 2013). A hallucination continuum seems to accommodate the fact that healthy voice-hearers experience hallucinations without any burden (while a dichotomous view of hallucinations does not).
Subtyping hallucinations and improved models

The idea that there must be some similarity among hallucinations is reflected in the classical way of using them for diagnostic classification. However, building upon the idea of a transdiagnostic approach of hallucinations, the characteristics of hallucinations may not infer diagnoses, but instead relate to subtypes of hallucinations regardless of diagnosis. Similar phenomenology among this otherwise heterogeneous experience has been suggested to exist in auditory verbal hallucinations (Jones, 2010; McCarthy-Jones et al., 2014; McCarthy-Jones et al., 2014; Sommer et al., 2018) and several studies have tried to identify subtypes either based on the content or phenomenology (McCarthy-Jones et al., 2014; Scott et al., 2020; Stephane et al., 2003), the linguistic features (Corona-Hernández et al., 2022), or the mechanisms involved (Dodgson and Gordon, 2009; Garwood et al., 2015). This way of investigating hallucinations may be useful, as it can increase our understanding of the neurobiological processes underlying these experiences, our ability to differentiate between the different subtypes, and allow us to help optimize treatment.

A plethora of models have been proposed to explain the neurobiological mechanisms of hallucinations. Some examples are the inner speech model (Allen et al., 2007; Frith and Done, 1988), reality monitoring deficit theory (Diederich et al., 2005; Garrison et al., 2017; Muller et al., 2014), intrusive memory hypothesis (Hoffman, 1986; Waters et al., 2006), and the abnormal salience monitoring hypothesis (Palaniyappan and Liddle, 2012). Generally speaking, these models and theories suggest a misinterpretation or mismatch between internally generated information and the external world. As such the inner speech model and the intrusive memory hypothesis suggest that specific internally generated stimuli, such as inner speech or memories may be perceived as coming from the external world and therefore considered hallucinations (Allen et al., 2007; Frith & Done, 1988; Hoffman, 1986; F. A. V. Waters et al., 2006). In a similar vein the reality monitoring deficit theory and salience monitoring hypothesis propose an inability to differentiate between internal and external stimuli as the cause of hallucinations, which may be related to dysfunction in the medial anterior prefrontal cortex (Garrison et al., 2017) or the salience network respectively (Palaniyappan and Liddle, 2012).

Considering the possibility that there may be several subgroups of hallucinations, these models do not need to be exclusive but rather explain certain aspects that relate to particular types of hallucinations. Sommer et al. (2018) for instance
suggested that the phenomenology of a hallucination may be related to the neurotransmitters responsible for the experience, which can lead to differences in the treatment outcome. As a result, being able to determine whether a patient experiences hallucinations related to dopamine synthesis or cholinergic deprivation should increase the success of the treatment provided. Similarly, the association between impaired hearing and a heightened tendency for psychotic symptoms in patients with schizophrenia (Linszen et al., 2016; Sommer et al., 2014a), may point towards an intersection between psychosis and deafferentation, and in turn offer a different way to alleviate hallucinations, such as improvement of the hearing abilities.

**Personalized approach**

A thorough understanding of the mechanisms involved in hallucinations and the phenomenological variation they can exhibit, may also lead to advances in the clinical setting (Fernyhough, 2019). As such it may be possible that a more personalized approach to diagnosis and therapy can lead to better long-term outcomes for individuals in need of treatment. The idea of acknowledging personal differences is not new and advocates of this approach have proposed a detailed, individualized assessment. Consequently, a more selective treatment to address neurobiological deviations on the individual level could be provided (Sommer et al., 2018).
Overview and aims:

The first part of this thesis is dedicated to hallucinations in hearing impairment. This group is often overlooked when discussing hallucinations and the research devoted to examining complex hallucinations in this population is sparse.

The aims of part I are:

- providing an overview of the current knowledge of deafferentation hallucinations
- assessing awareness of auditory deafferentations among clinicians
- testing mechanisms put forward by the deafferentation theory

Chapter 2 provides an overview of the most recent literature describing the association between hallucinations and sensory loss with a focus on vision and hearing impairment. Here, the deafferentation theory is explained as a possible neurobiological mechanism underlying the occurrence of hallucinations in sensory impairment, and studies investigating this theory with a variety of neuroimaging techniques are reviewed.

The rather limited number of studies describing auditory deafferentation made me wonder if the lack of information available may also be reflected in clinical settings. Chapter 3 describes the results of a survey among 125 clinicians who frequently encounter hearing impaired individuals in their clinics. The aim of this survey is to learn more about clinicians’ awareness and opinions regarding auditory deafferentation hallucinations.

The first part of this thesis finishes with an investigation of the deafferentation theory in hearing impaired individuals experiencing hallucinations. Chapter 4 describes a neuroimaging study, which assessed the role of spontaneous activity in hallucinations in hearing impairment. By comparing a measure called amplitude of low frequency fluctuation in hearing-impaired individuals with auditory hallucinations to that in individuals with normal hearing abilities, I identified brain areas which may be responsible for the manifestation of deafferentation hallucinations.

The second half of this thesis focuses on a wider range of disorders associated with hallucinations, again, with an emphasis on hallucinations outside the context of psychosis.
Chapter 1

The aims of part II are:

- assessing the phenomenology and subtypes of hallucinations across disorders
- assessing the phenomenology and subtypes of hallucinations in the general population
- studying the dynamic changes in brain activity during auditory verbal hallucinations in clinical and non-clinical individuals

Hallucinations occur as a symptom of a variety of psychiatric, neurological, and medical disorders. To examine whether the experience of hallucinations is disorder-specific or rather occurs in certain subtypes across disorders, a phenomenological comparison of hallucinations and delusions across a wide range of disorders was performed. Chapter 5 describes the findings of this study.

Chapter 6 aims to identify whether certain types of hallucinations tend to co-occur in specific subgroups. This was done by performing hierarchical density-based clustering on a large dataset describing hallucinations in the general Dutch population. Differences between the subgroups were assessed regarding their demographic characteristics as well as their tendency for delusions.

Auditory verbal hallucinations in non-clinical individuals, so called healthy voice hearers, are a curious phenomenon. While these hallucinations are very similar to those experienced by people with schizophrenia spectrum disorders, the similarity of the neurobiological mechanisms underlying the hallucinations in these groups is still under debate. Chapter 7 uses a dynamic functional connectivity method to assess the brain activity underlying auditory verbal hallucinations in a clinical and non-clinical sample. This analysis allowed me to test whether the characteristics of the networks involved in AVH differ between these two groups.

Finally, in Chapter 8 the results of this thesis are summarized, and a general discussion of the findings considering previous literature and existing theories is provided.
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PART 1:

Hallucinations in hearing impairment