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Prevalence and classification of hallucinations in multiple sensory modalities in schizophrenia spectrum disorders

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ABSTRACT

Background: Auditory hallucinations are experienced by 60–80% of all patients diagnosed with a schizophrenia spectrum disorder. However, in this patient group, the prevalence of hallucinations in multiple sensory modalities, i.e. multimodal hallucinations (MMHs), is unknown.
Aims: To assess the prevalence of MMHs in patients diagnosed with a schizophrenia spectrum disorder, data were analyzed from 750 patients who participated in the Dutch Genetic Risk and Outcome of Psychosis (GROUP) study.
Method: We drew on the section of the CASH (Comprehensive Assessment of Symptoms and History) that probes into the lifetime presence of auditory, visual, somatic/tactile, and olfactory hallucinations.
Results: A lifetime prevalence of 80% was found in this group for hallucinations in any of these modalities. Within the whole group, 27% of the participants reported unimodal hallucinations and 53% MMHs. There were no significant differences in prevalence rate for Dutch versus migrant participants from Morocco, Turkey, Surinam or the (former) Dutch Antilles.
Conclusion: We conclude that MMHs, rather than auditory hallucinations, are the most frequent perceptual symptom of patients diagnosed with a schizophrenia spectrum disorder. Our data also suggest that hallucinations experienced in a single sensory modality (notably auditory ones) stochastically increase the risk for more sensory modalities to join in. We recommend that future studies take into account all 14 sensory modalities in which hallucinations can be experienced. For this we provide a classification of MMHs that allows characterization of their serial versus simultaneous occurrence and their congruent versus incongruent nature.

1. Introduction

Of all patients diagnosed with a schizophrenia spectrum disorder, 60–80% experience auditory hallucinations (Waters et al., 2014) and a smaller proportion visual or other unimodal hallucinations. However, in this patient group, little is known about hallucinations in multiple sensory modalities, also known as multimodal hallucinations (MMHs). Below, we will explain that the term multimodal hallucination is used for both serial and simultaneous hallucinations occurring in different sensory modalities. As noted in a review (Waters et al., 2014) the nature of the relationship between hallucinations of different sensory modalities has hardly been examined. Although this situation is not unique for schizophrenia spectrum disorders (Waters et al., 2014), some studies indicate that the prevalence of multimodal hallucinations may be severely underestimated in this group (Goodwin et al., 1971) while others indicate that the presence of MMHs may be indicative of an underlying

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Table 1
Overview of studies describing multimodal hallucinations in the context of various psychiatric and somatic conditions.

Diagnosis	Study	Sensory modalities	Serially/simultaneously occurring hallucinations
Psychiatric disorders			
Schizophrenia	Goodwin et al. (1971)	Auditory and visual	Serially and simultaneously
Late onset schizophrenia	Hussein et al. (2012)	Not mentioned	Not mentioned
Late onset schizophrenia	Pearlson et al. (1989)	Not mentioned	Not mentioned
Late onset schizophrenia	Eissa et al. (2013)	Not mentioned	Not mentioned
Schizophrenia in Saudi Arabia	Zarroug (1975)	Auditory, visual, tactile	Simultaneously
Schizophrenia in Kenya	Ndetei and Singh (1983)	Not mentioned	Not mentioned
Borderline personality disorder	Yee et al. (2005)	Visual and olfactory	Not mentioned
Neurological disorders			
Temporal lobe epilepsy	Penfield and Perot (1963)	Auditory and visual, sometimes tactile and olfactory	Serially and simultaneously
Narcolepsy	Szűcs et al. (2003)	Hypnagogic hallucinations; tactile and visual	Not mentioned
Right temporo-basal tumor	Güzelcan et al. (2008)	Visual and tactile	Simultaneously
Right thalamic stroke	Mollet et al. (2007)	Auditory and visual	Simultaneously
Cerebrovascular accident presenting with peduncular hallucinosis	Dogan et al. (2013)	Auditory and visual	Simultaneously
Charles Bonnet syndrome	Alroe and McIntyre (1983)	Visual and olfactory	Simultaneously
Delirium tremens	Deahl (1987)	Auditory and visual	Simultaneously
Infectious disease			
Peduncular hallucinosis	Vita et al. (2008)	Auditory and visual	Simultaneously
Neuropsychiatry			
Lewy body disease	Aarsland et al. (2001)	Auditory and visual	Not mentioned
Substance abuse			
Ketamine use	Lim (2003)	Auditory and olfactory	Not mentioned
Alcohol hallucinosis	Bhat et al. (2012)	Auditory, visual, and tactile	Not mentioned
Drug and alcohol abuse	Scher and Neppe (1989)	Auditory, visual, and gustatory	Not mentioned
Iatrogenic cause			
Carbamazepine use	Benatar et al. (2000)	Auditory, visual, and tactile	Auditory and visual simultaneously

organic etiology (Roberts, 1984; Albert, 1987), or, in children and adolescents, of a more severe expression of schizophrenia (David et al., 2011; Jardri et al., 2014; Cachia et al., 2015).

MMHs are also known as polymodal hallucinations, polysensual hallucinations, polysensory hallucinations, polysensorial hallucinations, intersensorial hallucinations, and fantastic hallucinations (Blom, 2010). In the literature these terms tend to be used interchangeably; however, in some cases they refer to hallucinations experienced in various sensory modalities simultaneously, while in others they refer to those experienced serially (Chesterman and Boast, 1994).

Whatever the reason, the literature on MMHs is scarce. The most extensive review to date was published by Chesterman and Boast in 1994 and the most recent review prior to that is a chapter in Specht's 1914 German textbook *Wahrnehmung und Halluzination* (Specht, 1914). During the 80-year intervening period, as well as during the 20 years since the publication of Chesterman and Boast, MMHs have mainly been referenced in case reports (Alroe and McIntyre, 1983; Scher and Neppe, 1989; Benatar et al., 2000; Lim, 2003; Szűcs et al., 2003; Yee et al., 2005; Mollet et al., 2007; Güzelcan et al., 2008; Vita et al., 2008; Bhat et al., 2012; Dogan et al., 2013), in the field of neuropsychiatry (Aarsland et al., 2001), and in studies in the field of transcultural psychiatry (Zarroug, 1975; Al-Issa, 1977; Ndetei and Singh, 1983; Kent and Wahass, 1996; Blom et al., 2010; Johns et al., 2002; Bauer et al., 2011; Hussein et al., 2012; Larøi et al., 2014; Lim et al., 2015; Luhrmann et al., 2015), see Table 1. Even classic authors such as Parish (1894), Bleuler (1911) and Jaspers (1965), who wrote extensively on hallucinations in various sensory modalities, treated the subject only cursorily. Table 1 provides an overview of studies we retrieved on MMHs experienced in the context of psychiatric *and* somatic conditions.

To further our understanding of MMHs and their prevalence rate in patients diagnosed with a schizophrenia spectrum disorder, we drew on data from the *Genetic Risk and Outcome of Psychosis* (GROUP) study, conducted in the Netherlands from 2004 through 2013 (Korver et al., 2012). Below, we present data from this study on hallucinations in various sensory modalities, address various conceptual issues pertaining to MMHs, and propose a classification of this neglected group of phenomena to serve both clinical and research purposes.

2. Method

2.1. Study design

A longitudinal cohort study on gene-environment vulnerability and resilience in patients diagnosed with a schizophrenia spectrum disorder (DSM IV classification), their unaffected family members, and non-related controls, was performed by the GROUP project. Individuals were recruited to elucidate etiological and pathogenetic factors influencing the onset and course of psychotic disorders. The study was conducted in the Netherlands within a consortium of four university psychiatric centers and 30 of their affiliated mental healthcare institutions (Korver et al., 2012). One of the instruments used was the CASH (*Comprehensive Assessment of Symptoms and History*) (Andreasen et al., 1992) which contains sections on the lifetime presence and the present state (i.e., past month) of hallucinations experienced in the auditory, visual, somatic/tactile, and olfactory modalities.

2.2. Subjects

Ethnicity was determined in the GROUP project by country of birth of grandfather and grandmother on the fathers' and mothers' sides. Thus, a subject was considered to be of Dutch ethnicity when three or more grandparents were born in the Netherlands. Mutatis mutandis, this rule applied to all ethnicities. Whenever less than three grandparents were born in the same country, the subject was said to have a mixed ethnicity. We selected all patients who had completed the study's baseline measurements and excluded those whose data were incomplete. Outcome measures were (1) the number of patients who had ever experienced any of the aforementioned types of hallucination, (2) the types of hallucination, and (3) their distribution.

2.3. Data analysis

Analyses comprised a calculation of odds ratios (ORs) from cross tabulations and multivariate logistic regression. A confidence interval (CI) of 95% was considered to indicate statistical significance for the ORs. Akaike's Information Criterion (AIC) (Akaike, 1974) was used for model-selection purposes regarding the logistic regression. For the statistical analyses, SPSS version 23 and Excel 2010 were used.

3. Results

For the present study, complete data on hallucinations in patients diagnosed with a schizophrenia spectrum disorder were available from 750 patients who had participated in the GROUP study. Their mean age was 27 (range 15–57, SD 7.424) years, and 77.3% were men. Of all these patients, 603 (80%) had experienced one or more types of hallucination throughout their lives. Hallucinations in a single sensory modality were reported by 204 of them, yielding a lifetime prevalence for unimodal hallucinations of 27%, whereas hallucinations in two or more sensory modalities were reported by 399 patients, yielding a lifetime prevalence for MMHs of 53% in the total group. Twenty-nine percent of the patients experienced hallucinations in two sensory modalities, 17% experienced them in three sensory modalities, and 8% experienced hallucinations in four sensory modalities. Table 2 shows that auditory hallucinations were the most prevalent type of hallucination in the unimodal-hallucination group (68%) as well as in the MMH group (88%), followed by visual, somatic/tactile, and olfactory hallucinations. Fig. 1 presents the distribution of the various types of hallucination.

Present-state scores on hallucinations showed that 285 patients (38%) experienced one or more hallucinations during the month preceding the CASH interview. Hallucinations in a single sensory modality during the last month were reported by 162 patients (22%), whereas hallucinations in two or more sensory modalities were reported by 123 patients, yielding a present-state (i.e., one-month) prevalence for MMHs of 16% (Table 2). Fig. 2 displays the distribution of the present-state hallucinations. The lifetime ORs for MMHs in two sensory modalities for patients who already experienced unimodal hallucinations were, respectively, 2.312 [1.454–3.676; from auditory]; 11.320 [7.121–17.997; from visual]; 4.311 [2.447–7.594; from somatic/tactile]; and 3.664 [1.759–7.632; from olfactory]. The ORs for MMHs in three sensory modalities in patients who already experienced bimodal hallucinations were also increased, respectively 2.715 [1.640–4.494; from auditory-visual]; 7.013 [4.275–11.507; from auditory-somatic]; 11.111 [5.83167–21.170; from auditory-olfactory]; 15.911 [8.579–29.507; from visual-somatic]; 9.590 [4.934–18.640; from visual-olfactory]; and 7.905 [3.330–18.769; from somatic-olfactory].

We also calculated ORs for the lifetime prevalence of MMHs in Dutch patients versus the combined groups of patients from Morocco (n = 23), Turkey (n = 15), Surinam (n = 18), and the (former) Dutch Antilles (n = 4), but found no significant differences (OR 0.768, [0.433–1.363]) between these latter groups and the Dutch group.

4. Discussion

Our findings indicate that the lifetime prevalence of MMHs in patients diagnosed with a schizophrenia spectrum disorder is almost twice as high as that of all unimodal hallucinations taken together (53% vs. 27%). As unimodal auditory hallucinations (notably of the verbal type) are traditionally considered the most prevalent type of hallucination in this patient group, this raises the question why this high prevalence of MMHs has rarely been reported. Or, to rephrase the question, why studies that did find elevated prevalence rates for MMHs are rarely cited. For example, Table 1 lists several studies that, retrospectively, appear to have anticipated our findings. In the general population, probably the most extensive prevalence study of MMHs is the 19th-century *Census of Hallucinations*, carried out by the Society for

Table 2
Distribution of unimodal and multimodal hallucinations among 750 patients diagnosed with a schizophrenia spectrum disorder.

Number and type of sensory modalities								Patient group (n = 750)
Lifetime								
0								147
1	Auditory	Visual	Somatic/tactile	Olfactory				204
	139	37	18	10				
2	Auditory-visual	Auditory-somatic/tactile	Auditory-olfactory	Visual-somatic/tactile	Visual-olfactory	Somatic/tactile-olfactory		212
	124	40	12	16	13	7		
3	Auditory-visual-somatic/tactile	Auditory-visual-olfactory	Auditory-olfactory-somatic/tactile	Visual-olfactory-somatic/tactile				128
	62	39	17	10				
4	Auditory-visual-somatic/tactile-olfactory							57
	57							
Present state								
0								465
1	Auditory	Visual	Somatic/tactile	Olfactory				162
	127	12	17	6				
2	Auditory-visual	Auditory-somatic/tactile	Auditory-olfactory	Visual-somatic/tactile	Visual-olfactory	Somatic/tactile-olfactory		90
	47	20	11	4	6	2		
3	Auditory-visual-somatic/tactile	Auditory-visual-olfactory	Auditory-olfactory-somatic/tactile	Visual-olfactory-somatic/tactile				26
	11	6	7	2				
4	Auditory-visual-somatic/tactile-olfactory							7
	7							

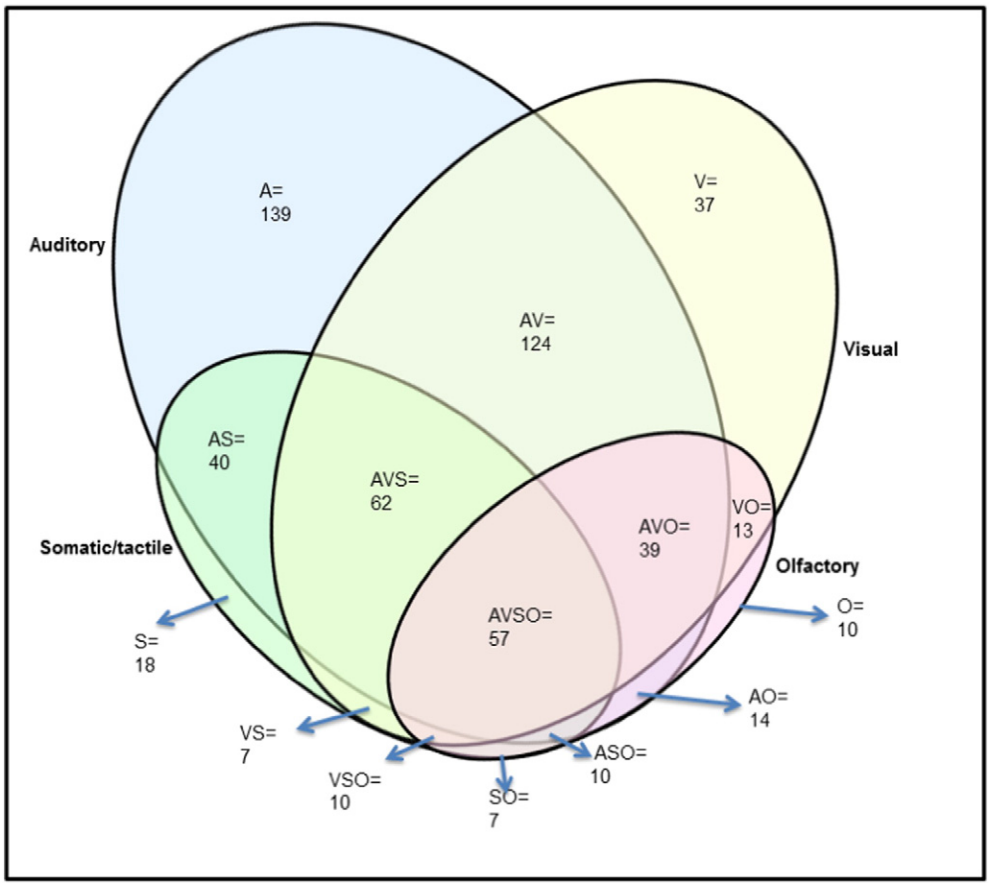

Fig. 1. Schematic diagram showing the lifetime distribution of unimodal and multimodal hallucinations among 603 patients from a total of 750 patients diagnosed with a schizophrenia spectrum disorder.

Psychical Research (SPR). This study aimed to chart the prevalence of death-related visions and, to that end, collected data from 27,329 individuals in the UK, the USA, Germany, and France, among whom 11.96% had experienced one or more hallucinatory episodes (Parish, 1894; Sidgwick et al., 1894). Within the hallucinating group, MMHs in the auditory, visual and tactile modalities were reported by 12.3% of all hallucinating individuals. In a study by Goodwin et al. (1971), among 117 patients diagnosed variously with affective disorder, schizophrenia, alcoholism, organic brain syndrome, and hysteria, about 75% experienced hallucinations in two or more sensory modalities. Among the few prevalence studies of MMHs among patients diagnosed with a schizophrenia spectrum disorder, a relatively large study stands out (Mueser et al., 1990), describing 117 patients with a DSM-III-R diagnosis of schizophrenia or schizoaffective disorder, among whom auditory hallucinations were the most common, followed by visual, and then tactile, olfactory, and gustatory hallucinations. Interestingly, the authors also found that hallucinations in two sensory modalities were experienced more frequently in their group than isolated auditory hallucinations. A retrospective study comparing adults with early-onset schizophrenia and with late-onset schizophrenia, as well as elderly patients with early-onset schizophrenia, found that the number of types of hallucination for the late-onset group was significantly higher than in the early-onset groups (Pearlson et al., 1989). In a smaller study conducted in the Middle East, patients with late-onset schizophrenia experienced MMHs more often than those with early-onset schizophrenia; however, their distribution and prevalence rate were not extensively discussed (Eissa et al., 2013). In another small study from the Middle East, elderly patients with late-onset schizophrenia experienced MMHs more often than psychotic patients who were not diagnosed with schizophrenia (Hussein et al., 2012). Zarroug (1975) examined 69 Saudi-Arabian patients diagnosed with schizophrenia and found that 51% experienced MMHs. In a cross-cultural comparative study, Ndetei and Vadher (1984) found that MMHs in the auditory and visual sensory modalities were more prevalent in African, West-Indian, and Asian patients than in British patients, most of whom experienced unimodal auditory hallucinations.

Our analysis of the GROUP data largely confirms the above-mentioned prevalence data for the various types of unimodal hallucination in patients diagnosed with a schizophrenia spectrum disorder (Goodwin et al., 1971; Mueser et al., 1990). A reason why other studies failed to replicate the findings of these authors may be that they did not broaden their scope to include other types of hallucination (Waters et al., 2014) and that the prevalence of MMHs has therefore been systematically underestimated. Secondly, the presence of hallucinations in other sensory modalities has traditionally led to non-psychiatric diagnoses (Waters et al., 2014) such as organic or neurological ones (Roberts, 1984; Albert, 1987). Another explanation may be that the CASH, apart from providing a systematic screening of hallucinations in four sensory modalities, has the advantage of describing their present-state occurrence as well as their lifetime presence. As verbal auditory hallucinations experienced by psychotic patients are probably more frequent and more persistent than those experienced in any of the other sensory modalities (Goodwin et al., 1971), MMHs may be missed by studies that focus exclusively on their present-state occurrence. This also holds true for clinical practice, in which the focus tends to lie quite exclusively on present-state symptoms. Altogether, these observations may also explain why our analysis failed to replicate the findings from earlier transcultural studies showing that MMHs seem more prevalent in non-Western than in Western patient groups diagnosed with a schizophrenia spectrum disorder.

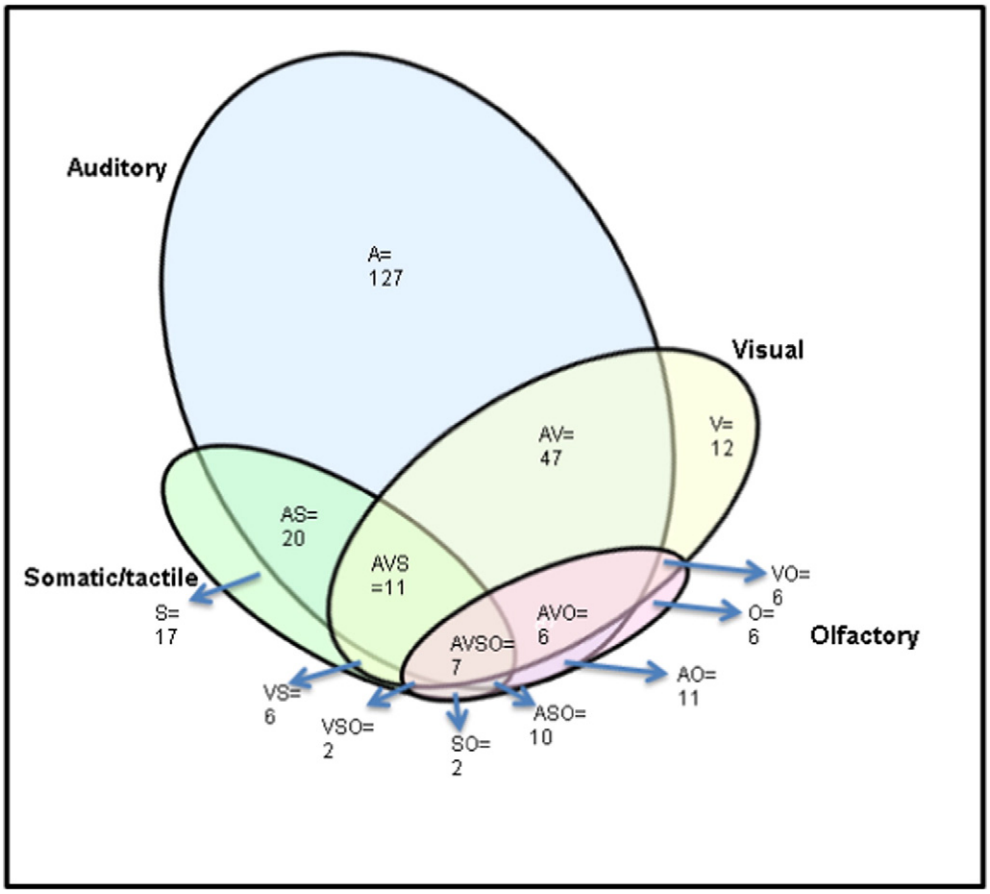

Fig. 2. Schematic diagram showing the one month distribution of unimodal and multimodal hallucinations among 285 patients from 750 patients diagnosed with a schizophrenia spectrum disorder.

4.1. Sensory modalities

The high prevalence rate of MMHs found in our patient group as a whole is all the more remarkable when considering that the CASH allows to chart hallucinations experienced in four sensory modalities (i.e., auditory, visual, olfactory, and somatic/tactile), whereas some classifications distinguish up to 14 sensory modalities (Gibson, 1966; Blom, 2013) and equally many main groups of hallucinations (Table 3). In Table 3, although the category 'somatic/tactile' is split into two separate categories (with tactile hallucinations referring to hallucinations of touch, and somatic ones to hallucinations experienced inside the body), it still leaves nine more types of unimodal hallucination that can be explored. Many of those types have not yet been systematically studied and still have unknown prevalence rates; however, even if these rates prove to be low, the prevalence rate of MMHs found in the present study may be considered a conservative estimate of the actual rate.

Table 3
Sensory modalities and corresponding unimodal types of hallucination.
Adapted from Blom (2013).

Sensory modality	Type of hallucination
1. Visual modality	Visual hallucination
2. Auditory modality	Auditory (acoustic) hallucination
3. Olfactory modality	Olfactory hallucination
4. Gustatory modality	Gustatory hallucination
5. Exteroceptive modality	Tactile (haptic) hallucination
6. Interoceptive modality	Somatic hallucination
7. Proprioceptive modality	Proprioceptive hallucination
8. Kinesthetic modality	Kinesthetic hallucination
9. Vestibular modality	Vestibular hallucination
10. Cenesthetic modality	Cenesthetic hallucination
11. Pain modality	Algesic hallucination (hallucinated pain, central pain)
12. Sexual modality	Sexual hallucination
13. Temperature modality	Thermal (thermic) hallucination
14. Temporal modality	Time distortion

Another important finding from our analysis is that the number of patients reporting MMHs in three or four sensory modalities is relatively high. Although the GROUP data do not allow for a reconstruction of the temporal order in which various unimodal hallucinations add up to MMHs, this suggests that the threshold for developing auditory hallucinations in this group is relatively low (given their high distribution rate) and that, in turn, the presence of auditory hallucinations lowers the threshold for developing any additional types of hallucination, notably visual ones. When hallucinations are present in these two sensory modalities, the chance for even more sensory modalities to become involved seems to increase further. This peculiar stochastic process was noted as early as 1900 by Störring, whose observations prompted him to remark that when one sensory modality is involved in hallucinatory activity, another one may easily join in (Störring, 1900). This process was also mentioned by David et al. (2011), who speak of "an additive progression of hallucination categories in order of descending frequency" to explain the considerable overall overlap between various types of hallucination, and the finding that somatic/tactile and olfactory hallucinations did not appear in their subjects without the appearance of hallucinations in the auditory and visual modalities. We speculate that the networks involved in the mediation of verbal auditory hallucinations may serve as hubs in the perceptual network which promote the recruitment of subsequent sensory modalities to mediate MMHs (Looijestijn et al., 2015).

4.2. Nomenclature and classification

An issue that cannot be solved on the basis of our data, is whether the MMHs, as reported by the participants of the GROUP study, combine to constitute compound hallucinations, or even whether they are experienced serially or simultaneously. In the literature, MMHs are sometimes designated in terms of combinations of the sensory modalities involved, e.g. audiovisual hallucination, audioalgesic hallucination, and so on (Jacome and Gumnit, 1979). Terms such as these have the advantage of describing the sensory modalities involved, but fail to indicate whether the hallucinations in these sensory modalities are experienced simultaneously or serially. As noted previously (Chesterman and Boast, 1994), the literature on MMHs suffers from a lack of information on these phenomenological characteristics, and even from the lack of a precise nomenclature with which to address this problem. A proper nomenclature of MMHs should allow us to identify the exact number *and* nature of the sensory modalities involved, to differentiate between hallucinations in various sensory modalities which are experienced serially or simultaneously, and, in the latter case, to differentiate between incongruent and congruent (i.e., compound) ones. Here, the adjective 'incongruent' refers to phenomena such as a visually hallucinated face experienced simultaneously with the sound of a barking dog, and the adjective 'congruent' refers to a visually hallucinated face that is seen talking, with verbal auditory hallucinations to match. Table 4 presents a classification of MMHs that allows for such a uniform and systematic characterization of MMHs, provided that the sensory modalities involved are also carefully listed.

4.3. Pathophysiology

Apart from its clinical usefulness, a proper nomenclature of MMHs is also a prerequisite for studies on the pathophysiology of MMHs. Systematic studies in this area are lacking, and even case reports are rare. In his 1914 book chapter, Specht posed the cardinal question: whether MMHs are mediated by various sensory brain areas showing separate but simultaneous hallucinatory activity, or by a single higher integrative center (Störring, 1900). As recently indicated by ffytche and Wible (2014), that question has gone unanswered throughout the intervening century and is even more pressing today than it was then. Classical cortical probing experiments, such as those performed by Penfield, suggest that MMHs (notably perceptions that take the form of panoramic hallucinations) may be mediated by circumscript brain areas in relative isolation (Penfield and Perot, 1963), whereas Liddle et al. (2000) consider the left hippocampus, ventral striatum, and various disseminated cortico-striato-thalamic feedback loops to be responsible for their mediation. With the aid of functional magnetic resonance imaging (fMRI) and other imaging techniques it is now possible to test hypotheses such as these, in a way similar to the many studies that helped to chart the neuropathological correlates of verbal auditory hallucinations over the past decade (Blom, 2015). However, the success of studies such as these relies on the adequate coupling of activation maps and phenomenological descriptions as outlined above, including the use of a uniform nomenclature.

Table 4
Classification of unimodal and multimodal hallucinations.

Type of hallucination	Characterization
Unimodal hallucination	Hallucination experienced in a single sensory modality
Multimodal hallucination	Hallucinations experienced in two or more sensory modalities
Serial multimodal hallucination	Hallucinations experienced in two or more sensory modalities at different moments in time
Simultaneous multimodal hallucination	Hallucinations experienced in two or more sensory modalities simultaneously
Incongruent multimodal hallucination	Hallucinations experienced in two or more sensory modalities simultaneously which do not add up to a coherent whole
Congruent multimodal hallucination (compound hallucination)	Hallucinations experienced in two or more sensory modalities simultaneously which add up to a coherent whole

4.4. Limitations

As in previous studies on MMHs, the present study has several limitations. First, the number of sensory modalities under study comprised only four (or five, if we take tactile and somatic as separate sensory modalities) whereas some authors distinguish up to 14 sensory modalities. Secondly, the CASH was designed to probe the (lifetime) presence of hallucinations in these four sensory modalities without attempting to reconstruct the temporal order in which they are experienced, and without addressing the questions whether they are experienced serially or simultaneously and whether they are congruent or incongruent in nature. As a result, these questions remain unanswered in the present study. Thirdly, the GROUP study excluded patients who were insufficiently fluent in Dutch, but whose inclusion might have yielded a larger proportion of migrants and, hence, a shift in the prevalence rates of MMHs as found in our study. Fourth, women with schizophrenia spectrum disorders are underrepresented. Last but not least, our study does not allow to answer the question from previous studies, as to whether MMHs are indicative of any underlying organic etiology. Starting from the general premise that hallucinations are mediated by the perceptual system, their etiology may be considered invariably organic in nature. Nevertheless, whether or not MMHs are more often associated with non-psychiatric etiologies, such as epilepsy or demonstrable intracranial lesions, remains unknown.

4.5. Conclusion and recommendations

Multimodal hallucinations (MMHs) are twice as prevalent in patients diagnosed with a schizophrenia spectrum disorder than unimodal ones. Based on the present study we conclude that MMHs, rather than auditory hallucinations, are a characteristic feature of this patient group and that hallucinations experienced in a single sensory modality stochastically increase the chance of more sensory modalities to join in. Future studies need to assess the full range of sensory modalities in which hallucinations can be experienced; these studies need to carefully reconstruct i) the temporal order in which these modalities become involved, ii) whether the hallucinations are experienced serially or simultaneously, and iii) whether they are congruent or incongruent in nature. Such analyses of the phenomenology together with research on the prognostic value of MMHs may further elucidate these phenomena. To facilitate this process, we recommend the development of dedicated measurement tools that address all three issues mentioned above.

Conflict of interest

All authors declare that they have no conflicts of interest.

Contributors

MD Lim A: conception and design of the study, data interpretation, statistical analysis, primary author of the article.

MD, Professor Hoek HW: data interpretation, participation in the discussion of the design, coauthor of the article.

MSc Deen ML: data interpretation, statistical analysis.

MD, Professor Blom JD: conception and design of the study, data interpretation, overall supervision of the study, coauthor of the article.

GROUP investigators: study design of the GROUP project.

All authors approved the final draft of the manuscript for publication.

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ZonMw had no further role in the study design, in the collection, analysis and interpretation of data, in the writing of the report, and in the decision to submit the paper for publication.

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