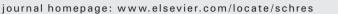
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Auditory verbal hallucinations and cognitive functioning in healthy individuals

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ABSTRACT

Auditory verbal hallucinations (AVH) are a characteristic symptom in schizophrenia, and also occur in the general, non-clinical population. In schizophrenia patients, several specific cognitive deficits, such as in speech processing, working memory, source memory, attention, inhibition, episodic memory and self-monitoring have been associated with auditory verbal hallucinations. Such associations are interesting, as they may identify specific cognitive traits that constitute a predisposition for AVH. However, it is difficult to disentangle a specific relation with AVH in patients with schizophrenia, as so many other factors can affect the performance on cognitive tests. Examining the cognitive profile of healthy individuals experiencing AVH may reveal a more direct association between AVH and aberrant cognitive functioning in a specific domain.

For the current study, performance in executive functioning, memory (both short- and long-term), processing speed, spatial ability, lexical access, abstract reasoning, language and intelligence performance was compared between 101 healthy individuals with AVH and 101 healthy controls, matched for gender, age, handedness and education.

Although performance of both groups was within the normal range, not clinically impaired, significant differences between the groups were found in the verbal domain as well as in executive functioning. Performance on all other cognitive domains was similar in both groups. The predisposition to experience AVH is associated with lower performance in executive functioning and aberrant language performance. This association might be related to difficulties in the inhibition of irrelevant verbal information.

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1. Introduction

Auditory verbal hallucinations (AVH) are a characteristic symptom of schizophrenia but have also been described in the general population (Tien, 1991; Verdoux and Van Os, 2002). Thus far, the pathophysiology of AVH is still largely unknown. Many theories concerning the origin of AVH have been postulated of which several have implicated specific cognitive dysfunctions as the core abnormality to cause AVH. For example, Frith and Done (1988) hypothesized a failure in self-monitoring as the basic deficit in AVH whereas Verkammen et al. (2008) stated that increased top-down processing plays an important role in the vulnerability to experience AVH. In support of such cognitive deficits or traits, hypothesized to underlie AVH, a number of studies found prominent impairments in several

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cognitive functions such as speech processing (Hoffman et al., 1999), working memory (Hoffman et al., 1999), episodic memory (Berenbaum et al., 2008), source memory (Brébion et al., 2007), attention (Berman et al., 1997), inhibition (Waters et al., 2003) and self-monitoring (Seal et al., 2004; Waters et al., 2010). However, patients with schizophrenia suffer from various other symptoms besides AVH, among which avolition, lack of motivation and a general decline in cognitive functioning. Therefore, decreased performance on specific tests is not necessarily a reflection of their tendency to hallucinate. A more specific reflection of AVH may be provided by cognitive differences that occur in non-psychotic individuals with AVH, who are free of negative symptoms and have only sub-clinical levels of positive symptoms (Sommer et al., 2010a,b). The fact that these healthy individuals with AVH function at a normal level, were able to finish their education, are medication naïve and have no history of admission to hospital is an additional advantage. Although differences in AVH have been found between healthy individuals and psychotic patients, regarding for instance frequency and emotional content, several similarities remain: no differences were found between location of AVH, loudness, number of voices and personification (Daalman et al., 2011). Based on these results one cannot conclude that both types of AVH are different. Furthermore, Diederen et al.

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(2011) found no significant differences in brain activation during the experience of AVH between healthy individuals with AVH and patients.

In order to measure cognitive functioning in non-psychotic individuals with AVH, a group of 101 persons with AVH who were screened for axis I or II pathology was compared to a matched control group with a battery of neuropsychological tests. These tests focus primarily on cognitive domains that were previously found to be affected in patients with a psychotic disorder experiencing AVH. The most important cognitive domains in that perspective were included: memory, language, executive functioning, processing speed, spatial ability, verbal and nonverbal reasoning.

The aim of the present study was to establish a cognitive profile of healthy individuals with AVH. Compared to healthy individuals without AVH, this group might show deviant cognitive performance. These cognitive differences will then provide clues for a potential cognitive mechanism that could underlie AVH since these individuals are otherwise healthy.

2. Method

2.1. Participants

A total of 101 healthy individuals with AVH were compared to 101 healthy individuals without AVH. Hallucinating individuals that were free of a DSM-IV diagnosis, as assessed by an independent psychiatrist using the Comprehensive Assessment of Symptoms and History (CASH) interview (Andreasen et al., 1992) and the Structured Clinical Interview for Personality Disorder (SCID-II, First et al., 1995), were included. Depressive disorder in complete remission was not an exclusionary criterion. Urine samples were used to screen for cannabis, amphetamine, cocaine, methadone or heroine abuse, which was an exclusion criterion. Additional exclusion criteria for both groups were alcohol abuse and IQ below 80.

For the healthy individuals with AVH, the minimum frequency to experience AVH was once every three months and the minimum duration since onset of AVH was one year.

Both healthy controls and healthy individuals with AVH were recruited with the help of a Dutch website called 'explore your mind' (www.verkenuwgeest.nl). For more details about selection and assessment procedure see previous studies by our group (Sommer et al., 2010a, b; Daalman et al., 2011). The control group was matched for gender, age, handedness and education and did not differ significantly on these variables, as shown in Table 1. All participants had four Dutch grandparents. The study was approved by the Humans Ethics Committee of the University Medical Center Utrecht. After complete description of the study to the participants, written informed consent was obtained.

2.1.1. Phenomenology of AVH in healthy individuals

To establish the phenomenological characteristics of AVH, the PSYRATS Auditory Hallucination Rating Scale (AHRS, Haddock et al., 1999) was administered. This questionnaire describes 11 characteristics of AVH. Each item of this scale is evaluated on a 5-point Likert Scale

Table 1

Demographic characteristics of the participants: healthy individuals with AVH and healthy controls.

Group	Individuals with AVH	Controls	Difference (significance)
n Male (%) Right handed (%) Mean age (s.d.) Mean years of education (s.d.)	101 33.7 78.2 43.78 (12.50) 13.39 (2.18)	101 29.7 84.2 43.30 (14.23) 13.76 (2.40)	$\begin{array}{l} \chi^2 = .366 \ (P = 0.545) \\ \chi^2 = 1.167 \ (P = 0.280) \\ t = .257 \ (P = 0.797) \\ t = -1.17 \ (P = 0.245) \end{array}$

ranging from 0 to 4. For the use of this questionnaire in healthy individuals, the range of the frequency scale is extended to 0–6 (also covering options 'at least once every month' and 'at least once every three months' since AVH are experienced less often than once a week (the original minimum score of this item). This questionnaire was administered by trained psychologists.

Due to high correlations between several of these items, two new variables were computed (see also Daalman et al., 2011). The variable 'emotional valence of content' was operationalized as the sum of three items from the AHRS: 'amount of negative content of voices', 'degree of negative content' and 'amount of distress'; i.e. an ordinal variable expressing overall burden of voices with negative content. The variable 'total distress' was operationalized as the sum of two items from the AHRS: 'intensity of distress', and 'disruption to life caused by voices'. As a result, the following items were used in this study: frequency, duration, location, loudness, beliefs re-origin of voices, controllability, emotional valence of content and total distress.

2.2. Measures

2.2.1. Neuropsychological assessments

The neuropsychological tests used in this study cover the domains in which impaired functioning in psychotic patients with AVH is found, and are thus candidates for examining the relationship between AVH in healthy individuals and cognitive functioning (Table 2).

Tests were administered in a fixed order and all examiners were extensively trained and supervised in the use of the tests. To rule out language deficits (aphasia, language expression and comprehension difficulties), the Boston naming task (Kaplan et al., 1983) and Tokentest (De Renzi and Vignolo, 1962) was administered. Participants who showed impaired language functioning, as measured by these tasks, were excluded.

2.3. Statistical analyses

Between-group comparison on the above described cognitive measures was achieved through multivariate analysis of variance (MANOVA), applying a General Linear Model. The independent variable was group (experiencing AVH or not i.e. controls) and the dependent variables were the raw scores on the fourteen cognitive tasks as described above. The Step-Up Hochberg correction was used to adjust P-values because of multiple testing (Westfall and Young, 1993; Benjamini and Hochberg, 1995). All data were analyzed with the Statistical package for the Social Sciences (SPSS, 2006).

3. Results

Table 3 describes how often AVH were experienced in the healthy individuals. Table 4 provides more information about the phenomenology of AVH in this group.

As expected, individuals of both groups performed the tests within the normal range, when compared to the norm reference scores of each test. There was a statistically significant difference between the groups on the combined dependent variables: F(14,187) = 3.65, P < 0.001; Pillai's Trace 0.22. When the results for the dependent variables were considered separately (Table 5), the individuals experiencing AVH were more sensitive to distraction as reflected in lower performance on the Stroop interference measure, had a lower verbal working memory capacity (reflected in lower Digit-span backward performance), underperformed, compared to controls, on a task for vocabulary (Vocabulary test, WAIS III subtask) and for judging verbal similarities (Similarities test, WAIS III subtask). In addition the individuals with AVH performed slightly lower on the NART, an estimate of verbal intelligence. No differences were found on tasks tapping verbal and nonverbal memory, attention span, nor on

Table 2

Description of neuropsychological tests and measured domains.

Task	Measured domain
Stroop Color-Word Task (Stroop, 1935)	Executive functioning: response inhibition and
Card 1: Subject is asked to read names of colors	selective attention (time card 3-time card 2)
Card 2: Subject is asked to name color of ink	Processing speed (time card 1, time card 2)
Card 3: Subject is asked to name color of ink while written word states different color	
Backward digit span-task, WAIS III subtask (Wechsler, 1997)	Verbal working memory
Numbers are presented and subject has to repeat them backwards. Sequence of	Executive functioning and verbal working memory,
numbers increases after two trials	requiring executive manipulation of verbal presented stimuli
Forward digit span, WAIS III subtask (Wechsler, 1997)	Attention span
Numbers are presented and subject has to repeat them in same order. Sequence of	
numbers increases after two trials	
California Verbal Learning Test (CVLT, Delis et al., 1987) (Dutch version: VLGT, Mulder et al., 1996)	Long-term verbal memory
Recall of list of words after 25 min. Words can be grouped into categories	
Complex figure of Rey-Osterrieth (Rey-O, Knight and Kaplan, 2003)	Spatial ability
Subject has to copy a complex figure. After 25 min, subject is asked to draw this figure again from memory	Non-verbal long-term memory (recall after 25 min)
Vocabulary test, WAIS III subtask (Wechsler, 1997)	Lexical access
Subject is asked to give the definition of words	
Similarities test, WAIS III subtask (Wechsler, 1997)	(Verbal) abstract reasoning
Subject is asked to state the similarity between two concepts	
Dutch version of the controlled oral word association test, COWAT (Lezak et al., 2004)	Executive functioning
Subject is asked to name as many words within 1 min, starting with a specific letter	Phonemic fluency (letters N and A, each 1 min), verbal retrieval
	and recall,
	self-monitoring, self-initiation
Semantic fluency (Lezak et al., 2004)	Semantic memory
Subject is asked to name as many items from a category within 2 min	Categorical fluency (animals and occupations, each 2 min).
	Verbal retrieval and recall, self monitoring, Semantic associations
	in the lexicon
National Reading Test for Adults (NART, Crawford et al., 1989; Blair and Spreen, 1989).:	Verbal IQ
Dutch adaptation NLV, Schmand et al., 1992)	
Subject is asked to read aloud a list of words with irregular pronunciation	
Raven's Advanced progressive Matrices (Raven et al., 1998)	Non-verbal IQ and abstract reasoning
Subject has to choose which pattern is missing from the overall matrix on the page.	
With increasing difficulty after each item	

verbal fluencies. The level of nonverbal reasoning and non-verbal IQ was also similar in both groups.

4. Discussion

We compared cognitive functioning in various domains between 101 non-psychotic individuals with auditory verbal hallucinations (AVH) and 101 healthy controls matched for age, gender, handedness and education. As expected, task performance of both groups was within the non-pathological range, both groups scored within the top 50% to 25% on all the tests.

The cognitive profile of healthy individuals experiencing AVH was largely similar to that of healthy controls without AVH. However, they underperformed on several domains compared to the controls. Healthy individuals with AVH showed poorer performance on verbal distractibility, inhibition (Stroop interferences), verbal working memory and on tasks tapping lexical access and reasoning (WAIS backward digit-span, vocabulary and similarities, respectively). Thus, it appears that a specific combination of decreased executive functioning, consisting of verbal inhibition, distractibility and verbal working memory in particular, and

Table 3	
Frequency	of AVH.

Frequency of AVH	Percentage	Frequency (N = 101)
At least once every 3 months	3.0	6
At least once a month	11.4	23
At least once a week	17.3	35
At least daily	11.4	23
At least once per hour	4.5	9
Continuous	2.5	5

a reduced level of verbal intellectual performance is associated with the tendency to hallucinate in the auditory verbal domain.

Although the groups were matched for total years of education and also had similar levels of nonverbal abstract reasoning (nonverbal intelligence estimate), individuals with AVH had significantly lower scores on a verbal estimate for level of intellectual functioning (NART). Lower scores in the AVH group on the vocabulary test and the similarities test may be related to this lower verbal intelligence, since the NART scores correlate highly with WAIS-R Verbal-IQ as well as with WAIS-R Vocabulary scores (Carswell et al., 1997; Uttl, 2002). Interestingly, no difference between both groups was found on phonological and semantic verbal fluency tasks. However, these tasks also assess the ability to generate concepts and to associate which is, apparently, similar in both groups.

Characteristics of AVH in the healthy individuals.

Characteristic of auditory verbal hallucinations	Mean (s.d.)	Description of closest anchor
Age at onset	14.5 (14.3)	Mean age of onset voices is 14.5 years old
Frequency (0–6)	3.31 (1.2)	At least once a week
Duration (0–4)	1.47 (0.65)	A few seconds
Location (0–4)	2.41 (1.18)	Voices outside the head. Inside the head may also be present
Loudness (0-4)	1.91 (0.60)	About same loudness as own voice
Beliefs of re-origin (0–4)	3.04 (1.09)	Holds \geq 50% conviction (but <100%) that voices originate from external causes
Controllability (0–4)	2.00 (1.6)	Some control over their voices, approximately half of the time
Emotional valence (0-12)	1.25 (2.53)	Hardly any negative content
Total distress (0–8)	0.51 (1.38)	No distress due to voices

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Comparison of cognitive measures in healthy individuals experiencing AVH and controls.

Measures	AVH $(n = 101)$	Controls $(n = 101)$	F(1,200),
	Mean (s.d.)	Mean (s.d.)	P-value
Executive function and			
working memory			
Stroop interference	35.42 (19.66)	28.98 (12.95)	$7.55 (0.007^{a})$
Digit-span backward	6.35 (2.06)	7.13 (2.01)	7.46 (0.007 ^a)
Attention			(,
Digit-span forward	8.75 (1.67)	9.17 (1.88)	2.77 (0.098)
Memory			(
CVLT delayed recall	12.45 (2.82)	12.31 (2.56)	0.13 (0.715)
Rey-O delayed recall	19.72 (6.73)	19.41 (6.32)	0.12 (0.731)
Processing speed			
Stroop card 1	46.41 (7.75)	44.96 (7.79)	1.75 (0.188)
Stroop card 2	57.96 (10.66)	56.54 (10.60)	0.90 (0.345)
Spatial ability			
Rey–O copy	32.71 (3.46)	32.74 (2.89)	0.00 (0.947)
Lexical access and			
abstract reasoning			
Vocabulary test	47.43 (10.83)	53.75 (6.52)	25.29 (<0.0005 ^a)
Similarities test	26.28 (4.33)	28.01 (3.66)	9.44 (0.002 ^a)
Verbal fluency			
Letter fluency total	28.87 (9.02)	28.77 (8.58)	0.01 (0.936)
Semantic fluency total	71.72 (16.43)	68.99 (14.91)	1.53 (0.217)
Intelligence correlates			
Raven's matrices	9.14 (2.14)	9.27 (2.18)	0.18 (0.673)
National adult reading	84.12 (10.07)	89.37 (7.36)	17.87 (<0.0005 ^a)
test			

^a Significant after Step-Up Hochberg correction for multiple testing.

Speculating, this reduced inhibition and increased distractibility in the verbal domain could render individuals less apt to inhibit irrelevant verbal information. Decreased inhibition could prevent them from focusing on the appropriate information, resulting in reduced performance on executive tasks within the verbal domain. In support of this hypothesis, healthy individuals with AVH were found to have increased levels of positive formal thought disorder as compared to controls without AVH, including peculiar word and sentence usage and peculiar logic (Sommer et al., 2010a,b). Possibly, irrelevant verbal associations which are not adequately inhibited may not be recognized as selfgenerated and, as such, be attributed to an external source, resulting in an auditory verbal hallucination.

To our knowledge, this is the only study assessing cognitive performance in healthy individuals with AVH. However, other groups have assessed cognitive functioning in related groups, such as healthy individuals with an increased tendency to experience hallucinations, healthy siblings of patients with schizophrenia, individuals at increased genetic risk to develop psychosis and individuals with schizotypal traits. Individuals with high scores on the Launay Slade Hallucination Scale, and thus with a high predisposition to hallucinate were found to have poorer intentional inhibition of memories (Paulik et al., 2007). This is in line with our finding that the presence of AVH is associated with aberrant inhibition. As these individuals were not extensively screened to investigate their hallucinations, it remains unclear whether their experience can be truly classified as, for example, an AVH and whether they have experienced this once or more frequently. Sibling studies show deficits in most cognitive domains, including executive functions, attention, (working) memory, spatial ability, language and performance speed (Snitz et al., 2006; Kuha et al., 2007). For individuals at high genetic risk for psychosis this profile is somewhat similar albeit less extensive: poorer performance on executive function, on global intellectual function, on learning and memory (Byrne et al., 2003). These observed cognitive deficits in siblings and high-risk individuals can be related to the genetic predisposition for schizophrenia in general, rather than to AVH specifically, since there were no differences in spatial ability, processing speed and (working) memory in our sample. Healthy individuals with AVH have significantly higher scores on the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) (Sommer et al., 2010a,b)), situating them on a continuum somewhere between healthy controls on one end and individuals with schizotypal personality disorder at the other. While they did experience perceptual abnormalities and some degree of suspicion, their social abilities were generally good and they functioned both socially and professionally within the normal range. Studies on cognitive functioning in individuals with schizotypal traits, as measured by the SPQ, may therefore show partial overlap with our results. With respect to verbal subtasks of the WAIS-R, poorer cognitive performance was found in healthy individuals with high scores on the SPQ (Noguchi et al., 2007). Executive working memory was also found to be lower (Matheson and Landon, 2008) in the subjects with schizotypal traits, but not executive functioning (Noguchi et al., 2007). In the latter study a relationship between schizotypal traits and an inductive reasoning component of IQ was found, whereas in our study, this domain appears unaffected. Decreased 'cognitive inhibition' is also often found in individuals with high schizotypy (Beech et al., 1989; Peters et al., 1994; Moritz and Mass, 1997). The fact that our healthy individuals with AVH show cognitive deviations that partly fit these findings of individuals with high schizotypal traits comes as no surprise since these two groups show considerable overlap in features of perceptual abnormalities and the tendency to suspicion.

Our results should be interpreted with caution as they provide no information with respect to causality. It could be hypothesized that aberrant verbal and executive functioning underlies the predisposition to hallucinate, but alternatively the experience of AVH may lower performance on these specific tasks. As most participants did not experience AVH during cognitive testing, the first explanation appears stronger, although the second cannot be ruled out. Another limitation is that the individuals that participated in this study are a highly selected group as only participants who were willing to visit us, and in the case of the healthy individuals with AVH, who were willing to talk openly about their AVH, could be included. This might also be the reason for the overrepresentation of women in the sample, although auditory hallucinations are more prevalent in women than in men (Rector and Seeman, 1992).

In conclusion, while their cognitive performance is within the normal range and thus not clinically impaired, healthy individuals experiencing AVH do show reduced levels of executive functioning and verbal (intellectual) performance. This deviation compared to individuals without AVH suggests that experiencing AVH is directly associated with difficulties in the inhibition of irrelevant verbal information.

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Contributors

Authors FB and MvZ designed the study. Author KD contributed to the design of the study, collected the subjects, organized the acquisition of data, analyzed the data and wrote the manuscript. All authors contributed to interpretation of the results and have contributed to and approved the final manuscript.

Conflict of interest

The authors report no conflicts of interest.

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