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# Verbal working memory deficits predict levels of auditory hallucination in first-episode psychosis ☆

Jens Gisselgård [a,*], Liss Gøril Anda [a], Kolbjørn Brønnick [a,b], Johannes Langeveld [a], Wenche ten Velden Hegelstad [a], Inge Joa [a,b], Jan Olav Johannessen [a,b], Tor Ketil Larsen [a]

[a] Stavanger University Hospital, TIPS, Regional Centre for Clinical Research in Psychosis, Stavanger, Norway
[b] Network for Medical Sciences, University of Stavanger, 4036 Stavanger, Norway

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ABSTRACT

*Background:* Auditory verbal hallucinations are a characteristic symptom in schizophrenia. Recent causal models of auditory verbal hallucinations propose that cognitive mechanisms involving verbal working memory are involved in the genesis of auditory verbal hallucinations. Thus, in the present study, we investigate the hypothesis that verbal working memory is a specific factor behind auditory verbal hallucinations.
*Methods:* In the present study, we investigated the association between verbal working memory manipulation (Backward Digit Span and Letter–Number Sequencing) and auditory verbal hallucinations in a population study (N = 52) of first episode psychosis. The degree of auditory verbal hallucination as reported in the P3-subscale of the PANSS interview was included as dependent variable using sequential multiple regression, while controlling for age, psychosis symptom severity, executive cognitive functions and simple auditory working memory span.
*Results:* Multiple sequential regression analyses revealed verbal working memory manipulation to be the only significant predictor of verbal hallucination severity.
*Conclusions:* Consistent with cognitive data from auditory verbal hallucinations in healthy individuals, the present results suggest a specific association between auditory verbal hallucinations, and cognitive processes involving the manipulation of phonological representations during a verbal working memory task.


## 1. Introduction

Auditory verbal hallucinations (AVHs) are a core characteristic of schizophrenia. They occur in 70–80% of patients with schizophrenia, and often cause distress and functional disability (Aleman, 2008). Yet, the mechanisms behind this phenomenon remain largely unknown. There are at least two dominant explanations for AVHs. The first school of thought argues that such hallucinations are a product of inner speech (McGuire et al., 1995), while a competing theory advocates that they are caused by resurfacing, often traumatic, memories (Waters et al., 2006).

However, recently a third view of AVHs suggests that they, rather than being a phenomenon associated with speech production or memory retrieval, are better explained in part as a perceptual phenomenon (for a review, see Waters et al., 2012). Perceptual-inhibitory failure models of AVHs assume that speech is spontaneously generated by an over-active primary auditory cortex and that this activity, possibly due to lack of inhibition, is able to propagate to higher levels of processing (Hunter et al., 2006; Northoff and Qin, 2011). There are several previous studies relating auditory hallucinations in schizophrenia to left temporal–parietal deficits during working memory (Wible et al., 2009) and dichotic listening tests (Bruder et al., 1995, 1999). Hugdahl (2009) suggests that AVHs arise when spontaneous perceptual "noise" generated by the temporal lobe is misinterpreted as real voices due to a failure of top-down executive control processes. A model proposed by Allen et al. (2008), based on their review of neuroimaging studies focusing on AVHs, similarly suggests that over-activation of the secondary auditory cortex (left posterior supra-temporal gyrus) creates sensory perceptions in the absence of stimuli. Coupled with dysfunction of a top-down network including the ventral ACC and PFC, this creates a sense of "externality and non-volition" in relation to AVHs. They point to findings of abnormal connectivity between sensory and frontal cortices as a further potential underlying factor underlying dysregulation. In order to examine the potential involvement of executive control processes in AVHs, the present study compared neuropsychological test results from a population study of first episode psychosis (FEP) patients, to their reported degree of AVHs. In accordance with a perceptual-disinhibition model of AVHs, we expected the degree of auditory hallucinations in these patients to be predicted by reduced performance in cognitive tasks that load on executive function and working memory. In particular, we were interested in whether a performance

☆ Department where research was conducted: TIPS — Regional Centre for Clinical Research in Psychosis, Stavanger University Hospital, Stavanger, Norway.

* Corresponding author at: Stavanger University Hospital, Psychiatric Division, TIPS, Armauer Hansensvei 20, N-4011 Stavanger, Norway. Tel.: +47 51515676.
*E-mail address:* jens.petter.gisselgard@sus.no (J. Gisselgård).

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reduction would be specific to verbal processing or associated with a general executive dysfunction.

## 2. Methods

### 2.1. Participants

Data presented in this paper stem from a sample of 52 FEP patients having undergone a comprehensive neuropsychological examination between 2008 and 2012. The sample is part of TIPS2 (early Treatment and Intervention in PSychosis), a naturalistic follow-along first episode psychosis (FEP) study in south Rogaland, Norway. Its catchment area consists of the South sector of Rogaland County, with a total population (all ages) of about 310,000, mainly in urban and suburban areas. Recruitment for the study continued consecutively from January 1, 2002 to November 30, 2010. Inclusion criteria were 1) living in the catchment area; 2) age 15–65 years old; 3) having a first episode of schizophrenia, schizophreniform psychosis, schizoaffective psychosis, delusional disorder, brief psychosis, affective disorder with mood incongruent delusions, or psychosis not otherwise specified, and also from August 1, 2008 substance induced psychosis, according to the DSM-IV; 4) being actively psychotic, as measured by a score of four or higher on at least one of the following items of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) (P1 (delusions), P3 (hallucinations), P5 (grandiose thinking), P6 (suspiciousness) and A9 (unusual thought content); 5) no previous adequate treatment for psychosis (defined as antipsychotic medication of 3.5 mg/day haloperidol equivalents for 12 weeks or until remission of the psychotic symptoms); 6) no neurological or endocrine disorders with relationship to the psychosis; 7) no contraindications to antipsychotic medication; 8) understands/speaks Norwegian; 9) IQ over 70 measured by the Wechsler Adult Intelligence Scale (WAIS-III); and 10) willing and able to give informed consent.

The patients entered the study through the TIPS2 early detection system, described in further detail elsewhere (Joa et al., 2008). All patients were clinically assessed within the first week of contact and assigned to a defined standard treatment program.

The study was approved by the Regional Committee for Medical Research Ethics Health Region West (015.03). Written informed consent was obtained from all study participants. Parents or legal guardians gave informed consent for patients younger than 18 years of age.

### 2.2. Clinical assessments

Clinical interviews were conducted by trained psychologists, psychiatric residents or psychiatrists. Diagnoses were reached using the Structured Clinical Interview for the DSM (SCID). Reliability of SCID in the TIPS study was satisfactory at kappa = .76 at baseline 1997–2000 (Joa et al., 2008), and at kappa = .9 in 2012 (Weibell et al., in press). Regular reliability trainings are undertaken to avoid drift.

The P3 subscale ('hallucinatory symptoms') of the PANSS interview was used to assess the presence and severity of hallucinations at the start of treatment. For the purposes of this study, only auditory hallucinations were included in the P3 score while hallucinations of other modalities were omitted. Patient files and reports from PANSS and SCID interviews were used to ensure that the PANSS P3 score concerned auditory, and no other, hallucinations. Patients reporting only non-auditory hallucinations were scored with a P3 value of 1 (hallucinations absent).

### 2.3. Neuropsychological tests

Participants were assessed using a neuropsychological test battery including performance measures of executive functioning. Tests used were: Block Design, Forward and Backward Digit Span tasks, Letter–Number Sequencing and Vocabulary (all from WAIS-III), Trail Making Test (TMT) trials A and B, Verbal Letter Fluency (FAS), the California Verbal Learning Test II (CVLT-II) and Wisconsin Card Sorting Test (WCST), administered in a set order by a trained examiner. The neuropsychological baseline evaluation was carried out after inclusion (median = 15 weeks after the PANSS interview), when positive psychotic symptoms had remitted as to allow cognitive assessment.

### 2.4. Data analysis

Frequency histograms were used to inspect data distributions for normality, and parametric statistics were deemed suitable for use throughout. Trail Making B scores were corrected to normality using a logarithmic transformation. A composite measure for auditory working memory manipulation was constructed by standardizing raw scores of the Backward Digit Span and Letter–Number Sequencing variables and calculating their mean z-score.

A sequential multiple linear regression analysis was conducted, consisting of 4 blocks, using the PANSS P3 score (hallucinations) as the dependent variable. In block 1, age and total PANSS score (excluding P3) were entered as control variables. In block 2, Verbal Letter Fluency (FAS) and Trail Making B scores were entered to assess the impact of general executive functions not specific to auditory working memory. In block 3, Forward Digit Span scores were entered to assess simple auditory working memory span and finally, in block 4, the composite auditory working memory manipulation variable was entered. Regression diagnostics were done, checking for multicollinearity using a recommended approach (Belsley et al., 2005) and by normal-probability plots. All analyses were carried out using the SPSS 20 software.

## 3. Results

The sample included 38.5% females (n = 20). Demographic and clinical characteristics of the sample are presented in Table 1.

In the sample, 63% (n = 33) of participants reported experiencing auditory hallucinations (P3 validated with regard to auditory hallucinations >2). In Table 2, means and standard deviations of raw scores for the neuropsychological tests are presented, alongside Pearson correlation coefficients with PANSS P3 scores and PANSS total score minus P3 scores.

Only Letter–Number Sequencing correlated significantly with P3 hallucination scores at the application of a Bonferroni corrected alpha level ($p < .005$). As seen in Table 3, the three first blocks of the sequential multiple linear regression analysis were non-significant, showing that age, total PANSS score (excluding P3 auditory hallucinations), executive functions (Trail Making B and Verbal Letter Fluency) and simple auditory span were not independent predictors of auditory hallucinations. However, adding the final block of the analysis resulted in a significant $R^2$ change ($R^2 = .32$, $R^2\Delta = .18$, $p = .001$), and the composite verbal working memory variable (Letter–Number Sequencing and Backward Number Span) was a highly significant independent predictor of auditory hallucinations (beta = −.61, $p < .001$).

**Table 1**
Clinical and demographical data.

| Measures | n | Mean (SD) |
|---|---|---|
| Age | 52 | 25.6 (9.44) |
| Years of education | 51 | 12.2 (2.15) |
| GAF symptoms | 48 | 34.1 (6.45) |
| GAF social functioning | 48 | 45.6 (13.02) |
| PANSS total score | 52 | 64.7 (14.17) |
| PANSS general subscale | 52 | 33.7 (8.16) |
| PANSS positive subscale | 52 | 17.3 (5.41) |
| PANSS negative subscale | 52 | 13.4 (5.44) |
| PANSS hallucinations | 52 | 3.1 (3.77) |