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Auditory verbal hallucinations in schizophrenia as aberrant lateralized speech perception: Evidence from dichotic listening

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ABSTRACT

We report evidence that auditory verbal hallucinations (AVH) in schizophrenia patients are perceptual distortions lateralized to the left hemisphere. We used a dichotic listening task with repeated presentations of consonant–vowel syllables, a different syllable in the right and left ear. This task produces more correct reports for the right ear syllable in healthy individuals, indicative of left hemisphere speech processing focus. If AVHs are lateralized to the left hemisphere language receptive areas, then this should interfere with correct right ear reports in the dichotic task, which would result in significant negative correlations with severity of AVHs. We correlated the right and left ear correct reports with the PANSS hallucination symptom, and a randomly selected negative symptom, in addition to the sum total of the positive and negative symptoms, in 160 patients with schizophrenia. The results confirmed the predictions with significant negative correlations for the right ear scores with the PANSS hallucination item, and for the sum total of positive symptoms, while all other correlations were close to zero. The results are unambiguous evidence for AVHs as aberrant speech perceptions originating in the left hemisphere.

1. Introduction

Auditory verbal hallucinations (AVHs) are a key symptom in schizophrenia (Wing et al., 1974; David, 1999) which directs attention inwards towards the "voice", with consequences for social interaction and reality orientation. It is estimated that about 70% of diagnosed patients experience auditory hallucinations (Wing et al., 1974; Shergill et al., 1998). Auditory verbal hallucinations are the subjective experience and conviction of someone speaking to the patient despite the absence of an acoustic signal (Hugdahl et al., 2009). The "voices" are commonly characterized as having an out-of-head origin, often having a negative and commanding emotional valence, and not possible to cognitively control and to avoid for the patient. Patients also often struggle with complying with the demands and requirements imposed by the "voices" (cf. Daalman et al., 2011). There is an ongoing discussion in the literature regarding the underlying mechanisms for AVH, and whether these can best be described as inner speech (e.g. Blakemore et al., 1998; Allen et al., 2007), traumatic memory (e.g. Badcock et al., 2005; Waters et al., 2006), or as aberrant speech perceptions (e.g. Fiszdon et al., 2005; Spencer et al., 2009, see also Jones, 2010 for a thorough review and discussion of existing theoretical models for AVH). What is lacking, however, are hypothesis-driven empirical tests of the different models. In this study we aimed at an empirical test of a speech perception model, with the hypothesis that if AVHs are aberrant speech perceptions, then they should implicate the left hemisphere receptive language areas (Binder et al., 1996; van den Noort et al., 2008), and interfere with the processing of an external speech sound, that is processed in the same brain areas. Such a hypothesis is derived from previous functional neuroimaging studies showing that the language regions in the brain are in a hyper-excited state during AVHs (Spencer et al., 2009), and that neuronal activation in the left speech perception area is correlated negatively with frequency and severity of AVHs (Plaze et al., 2006). Such a prediction would also follow from the findings by Woodruff et al. (1997) that patients with severe hallucinations showed reduced left temporal cortex response sensitivity to external speech sounds. Adding to this, Aleman and Vercammen (2012) concluded after a review of the existing activation literature that "if auditory hallucinations share a processing system with auditory sense perception, one would not expect an increase in activity upon external auditory stimulation in the auditory areas of patients actively experiencing AVH" (p. 272). A disadvantage with imaging data is however that it is not clear whether an implicated brain region is necessary and sufficient for

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the function in question, this would require experimental behavioral data. A behavioral task that is a valid indicator of lateralization of speech perception, and has been shown to unequivocally probe left hemisphere function is the consonant–vowel (CV) syllables dichotic listening (DL) task (Studdert-Kennedy and Shankweiler, 1970; Hugdahl and Andersson, 1984; Bryden, 1988; van den Noort et al., 2008). The CV-syllables DL task produces a very robust right-ear advantage (REA) in the general population, with about 85–90% reliability (Hugdahl and Hammar, 1997), meaning that subjects correctly report the right ear syllable of the dichotic pair more frequently than the left ear syllable. Since the right ear report is a measure of lateralization of speech perception to the left hemisphere, a negative correlation with severity of AVHs, and a non-significant correlation for the left ear stimulus, will be direct evidence in support of a speech perceptual model. The reasoning is that the more frequent and severe AVHs are, the more should such experiences interfere with perception of an external speech sound, revealed as significant negative correlations between AVH scores and DL scores for the right, but not the left, ear stimulus. To test a perceptual hypothesis with a dichotic listening experimental paradigm, we examined a large sample of patients with schizophrenia diagnosis, and calculated the correlation between the patients' hallucination score on the Positive and Negative Symptom Scale (PANSS) (Kay et al., 1987), and correct reports for the right and left ear stimulus in the DL task, respectively. To examine whether the relationship between DL performance and PANSS score is specific for hallucinations, we also correlated the right and left ear DL correct reports with a negative symptom, randomly chosen among the PANSS negative symptoms. The hypothesis was that a negative symptom should not correlate with DL reports, neither right nor left ear reports, since they should be unrelated to any perceptual disturbances. We have previously reported on the overall structure of relationships between DL performance and the full range of symptom scores in a non-hypothesis driven approach (Hugdahl et al., 2008), we therefore now chose to focus on key symptoms where we would have a priori directed hypotheses.

2. Experimental/materials and methods

2.1. Subjects

The subjects were 160 patients with a DSM-IV or ICD-10 diagnosis of schizophrenia. The data were collected from different sub-samples, from three different countries, Norway (n = 120), USA (n = 28) and Turkey (n = 12), which differ in their culture and social norms. This was done in order to avoid any idiosyncrasies in diagnostic procedures and principles in different samples, countries and cultures, which would limit the generalizability of our findings. The differences in sample size precluded however any meaningful statistical comparison between the sub-samples, the trend of the findings was however similar at all the sites. Patients were interviewed for symptoms using the PANSS scale. The subjects in the USA sample underwent the Brief Psychiatric Rating Scale (BPRS) interview (Ventura et al., 1993), in which case the scores were correspondingly converted to PANSS scores, since these scales are highly positively correlated (Nicholson et al., 1995). All patients were on medication, with either typical or atypical antipsychotic medication. The patients' age was between 18 and 72 years, and with 116 males and 44 females in the sample (a separate analysis on the 44 females showed that the direction and magnitude of the correlations were similar as for the entire sample and for the males). There were 16 left-handers in the sample, who were included since data from our laboratory on a large database sample of 1782 healthy subjects have shown that handedness per se is not a modulatory factor in DL (see also Hugdahl, 2003). The distribution of the 160 patients across the range of PANSS scores for the P3 and N2 symptoms is seen in Table 1.

Table 1
Distribution of subjects across the PANSS positive and negative symptom scores.

PANSS score→ PANSS symptom↓	1	2	3	4	5	6	7
P3 hallucinations	52	9	19	27	32	10	11
N2 emotional withdrawal	42	25	33	37	18	5	0

2.2. The dichotic listening task

The DL task consisted of the presentation of CV-syllables via headphones to the patients. The stimuli were paired presentations of the six stop-consonants /b,d,g,p,t,k/ together with the vowel /a/ to form dichotic CV-syllable pairs of the type /ba–ga/, /ta–ka/ etc. The syllables were paired with each other for all possible combinations, thus yielding 36 dichotic pairs, including the homonymic pairs. The DL task, thus, consists of presenting two different CV-syllables, e.g. /ba/ and /ga/, at the same time but in different ears, such that one syllable is presented to the right and the other simultaneously to the left ear. To avoid confounding the eligibility of the CV-syllables for the different samples, all syllables were spoken in the respective languages, Norwegian, English and Turkish, but with the similar procedure being followed at all three sites. The homonymic pairs were not included in the statistical analysis. The maximum number of correct reports was thus 30 for each ear. The REA is caused by the crossing of the auditory pathways across the brain midline, the contralateral pathways being more preponderant than the ipsilateral pathways (Kimura, 1967; Pollmann et al., 2002). The right ear signal will thus have direct access to the speech processing centres in the speech dominant left hemisphere, which as a consequence will result in more correct reports for the right ear stimulus (see Hugdahl et al., 2009 for further details). The syllables were read by a male voice with constant intonation and intensity. Mean duration was 350–400 ms and the inter-trial interval was 4 s. The syllables were read through a microphone and digitized for later computer editing on a standard PC using state-of-the-art audio editing software (SWELL, Goldwave, CoolEdit). The syllables were recorded with a sampling rate of 44,000 Hz and an amplitude resolution of 16 bit. After digitization, each CV-pair was displayed on the PC screen and synchronized for simultaneous onset at the first identifiable energy release in the consonant segment between the right and left channels. The stimuli were played to the subject using a digital play-back equipment, connected to high-performance headphones, with an intensity between 70 and 75 dB. The subject was told that he/she would hear repeated presentations of the six CV-syllables (ba, da, ga, pa, ta, ka), and that he/she should report which one he/she heard from the six possible syllables after each trial. The subjects were furthermore told that "on some occasions there seems to be two sounds coming simultaneously". They should ignore this and just report the syllable they heard first, or best. They were shown a cardboard sheet with all six syllables written before the experiment started (because of slight differences in the procedure between labs, the cardboard was not always shown). The subject was explicitly instructed to orally report *one* item on each trial irrespective of whether he/she perceived one or both items. This procedure was originally introduced by Bryden (1988) in order to reduce working memory loading as when the subject has to provide two responses, or as in the original Kimura (1961) studies when the subject had to withhold his/her response until four stimulus pairs had been presented, and then perform a recognition procedure. The subjects were tested with either a PC or a cassette player version of the DL test, using the same CV-syllables stimulus set-up and instructions.

2.3. Statistical analysis

Percentage correct reports, separate for the right and left ears, were correlated with PANSS scores for the P3 and N2 items, as well as with the sum total score for positive and negative symptoms. Due to the ordinal scale of the PANSS scores (min 1–max 7), Spearman rank-order correlations (two-tailed) were computed. In order to get an estimate of the effects, we calculated 95% confidence intervals (CI) around each significant correlation that is reported.

Randomly picking a single negative symptom, as mentioned in the Introduction, rather than correlating all negative symptoms would protect against obtaining spurious correlations just by chance because of the large number of correlations. On the other hand, selecting just one negative symptom might lead to a spurious effect of being "lucky-by-chance". Therefore, we included the sum total of negative symptoms that were also correlated with DL correct reports, separate for the right and left ear reports, to provide an overall measure of the relationship between DL performance and negative symptoms, thus avoiding both the “multiple testing” and the "lucky-by-chance" problem.

3. Results

3.1. Main correlations

The left-hand panels of Fig. 1 show scatter plots for the correlations between the right and left ear DL scores and the scores for the PANSS P3 item, hallucination. There was a significant negative correlation for right ear DL score ($r = -.304$, $p = .00009$, CI95%: $-.280$ to $-.537$), with a non-significant (n.s.) correlation for the left ear score ($r = -.135$, $p = .088$, n.s.). The right-hand panels of Fig. 1 show the corresponding correlations for the PANSS N2 item, emotional withdrawal. Here, both correlations were non-significant and close to zero ($r = .061$, $p = .443$, n.s. and .026, $p = .744$, n.s. for the right and left ear correlations, respectively).

Fig. 2 shows the correlations for the right and left ear DL scores with the sum total of PANSS positive symptoms, and with the sum total of

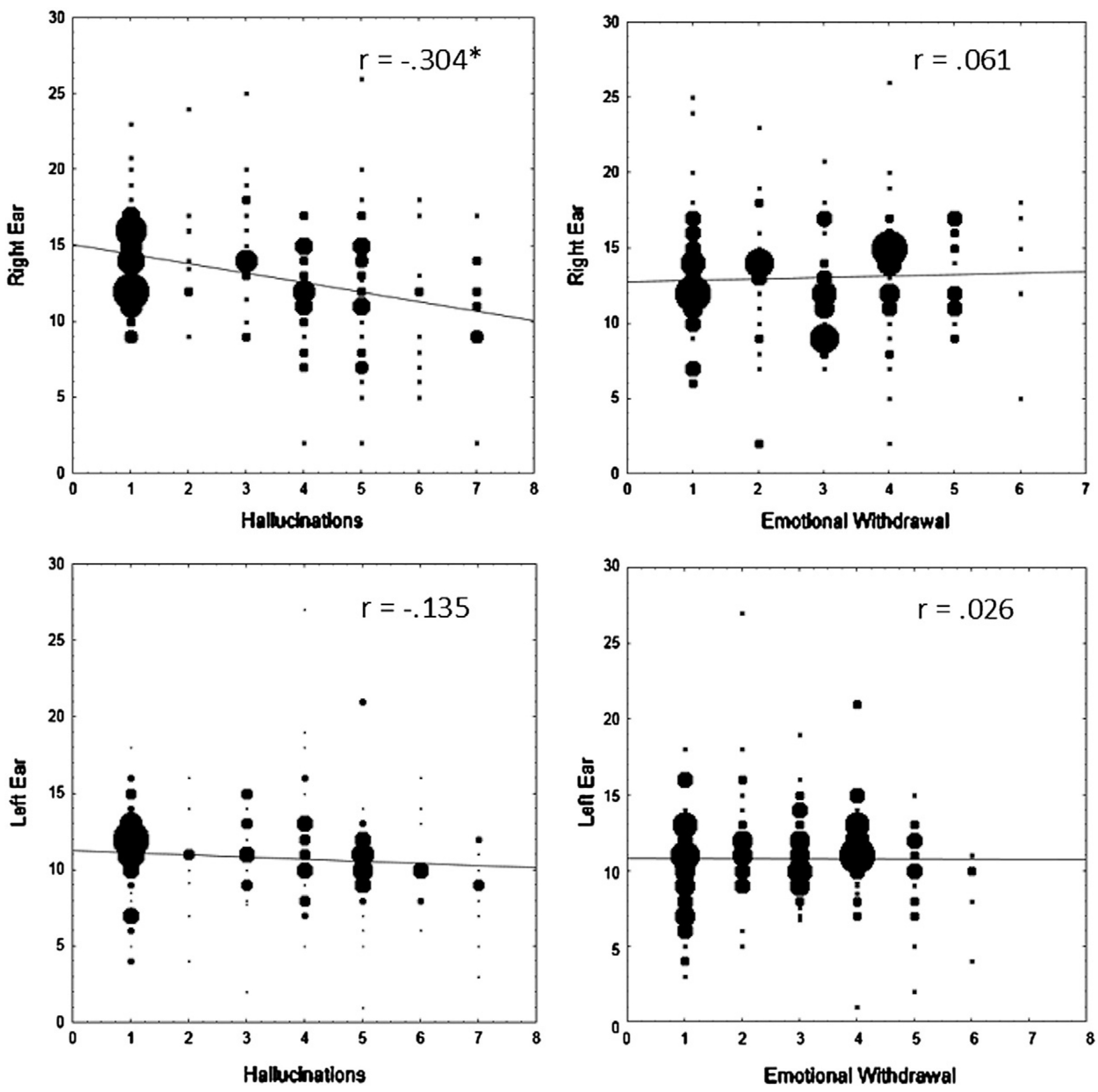

Fig. 1. Scatter-plots of the correlations between the right- and left-ear scores (min 0–max 30) in the DL task and scores on the hallucinations (P3) symptom scores (min 1–max 7) in the two upper panels, and the corresponding scatters for the emotional withdrawal (N2) negative symptom in the two lower panels. The size of the "blobs" in the scatter plots corresponds to the number of subjects having the same xy-scores.

negative symptoms. The left-hand panels show a significant negative correlation for the sum total of positive symptoms and the right ear scores (r = −.327, p = .00002, CI95%: −.136 to −.438), and a non-significant correlation for the left ear scores (r = −.119, p = .134, n.s.). The left-hand panels show the correlations for the PANSS sum total of negative symptoms. Here, both correlations with DL scores were non-significant and close to zero (r = .063, p = .429, n.s. and .002, p = .980, n.s. for the right and left ear scores, respectively).

3.2. Additional correlations

Correlations between positive and negative symptoms were non-significant (r = .093, p = .242, n.s., for the correlation of the P3 with the N2 item, and r = .136, p = .086, n.s., for the correlation of sum positive symptoms with sum negative symptoms). The P3 symptom showed an expected significant positive correlation with the sum positive symptoms (r = .883, p = .000002, CI95%: .801 to .901), and a non-significant correlation with the sum negative symptoms score (r = .153, p = .053, n.s). The N2 symptom showed a significant correlation with sum negative symptoms score (r = .858, p = .0000001, CI95%: .853 to .913), and a corresponding non-significant correlation for the N2 symptom with the sum positive symptoms score (r = .108, p = .174, n.s.). Finally, the dichotic listening right and left ear scores were correlated, which showed a significant negative correlation (r = −.233, p = .003, CI95%: .081 to .375). This indicates an expected reduced left ear score as the right ear score increased. Finally, a separate analysis showed that in addition to "hallucinations", in particular "delusions" contributed to the overall correlation between the right ear percentage correct reports and sum total positive symptoms (r = −.280, p = .003, CI95%: .078 to .372, for the P1 Delusions item and right ear correct reports).

4. Discussion

The goal of the present study was to examine whether AVHs have a left hemisphere origin by correlating the severity of AVHs with performance on a dichotic listening speech perception task, which is a marker of left hemisphere speech function. The results showed that more frequency and severe AVHs interfered with perception of speech sounds and, in particular left-hemisphere speech processing. Positive symptoms

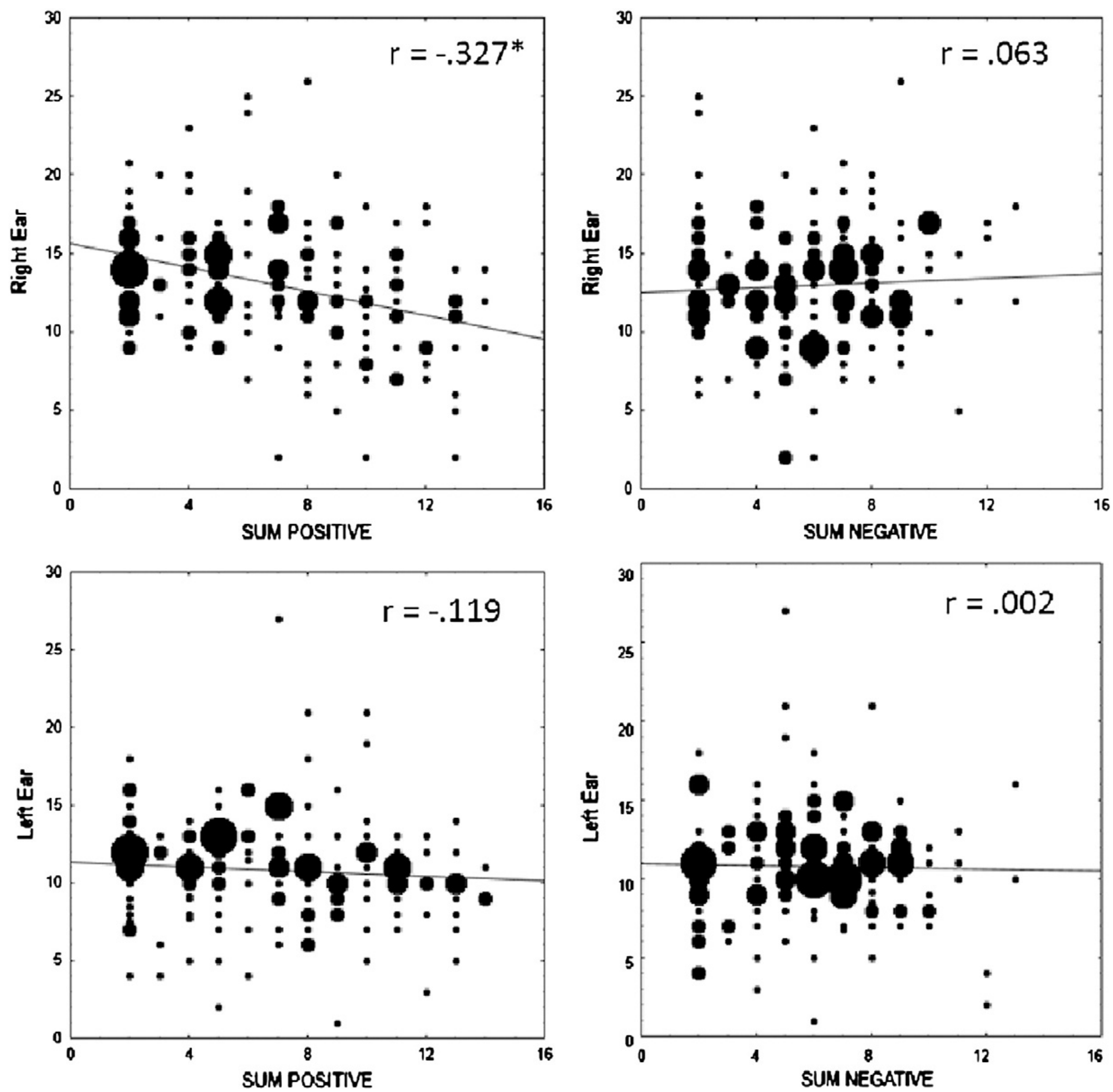

Fig. 2. Scatter-plots of the correlations between right- and left-ear scores (min 0–max 30) in the DL task and sum total scores for positive symptoms (1–49) in the two upper panels, and the corresponding scatters for the sum total scores for negative symptoms in the two lower panels. The size of the "blobs" in the scatter plots corresponds to the number of subjects having the same xy-scores.

in general also showed this effect. These results were in contrast to the relationships for the left ear scores and severity of hallucinations and sum of positive symptoms, where correlations approached zero. The results for severity of AVHs and correct right ear reports were also in contrast to the correlation with a negative symptom for both the right and left ear dichotic reports, where correlations approached zero. The same was true for the correlations with the sum total of the negative symptoms, with zero correlations.

Considering the explicitly directed hypothesis for a predicted difference in the direction and magnitude of the correlation for the right and left ear scores in the DL task and the P3 and N2 symptoms, respectively, it is not unreasonable to conclude that the results show evidence that AVHs have speech perceptual qualities. This conclusion is further supported by the fact that the DL task is the most frequently used and agreed on behavioral measure of left temporal lobe speech perception (see Brancucci et al., 2004; Hugdahl, 2011 and Pollmann et al., 2002 for overviews).

The significant negative correlation for right ear reports and sum total score for positive symptoms in addition shows that the correlation for the AVH symptom is shared with other positive symptoms. As mentioned in the Results section, the correlation with other positive symptoms, e.g. "delusions" contributed to the overall correlation between the right ear percentage correct reports and sum total positive symptoms. This is to be expected since delusional beliefs and hallucinations are closely related and inter-correlated (Lewinsohn, 1970; Lin et al., 1998), and are part of the same positive symptoms factor in the five-factor-structure of psychotic symptoms reported by Emsley et al. (2003). Moreover, these two symptoms are often related in clinical contexts (as a matter of fact, the "person" speaking to the patient in an AVH is often a delusional belief about communications from outer space, or through electronic devices, and the like).

Hugdahl et al. (2008) found negative correlations for DL performance and the positive symptoms "hallucinations", "unusual thought content", and "conceptual disorganization", and essentially zero correlations for all the negative symptoms, using a laterality index statistic based on the difference ratio of the DL right and left ear scores. Correlations based on a laterality index measure can however not tell if the effect was for the right-, left- or both ears, since an index measure statistically speaking confounds the relative contribution of the two signals. Moreover, the study of Hugdahl et al. (2008) was also based on only 87 patients, i.e. about half the sample size in the present study, and the data were analyzed in an analysis of variance, with the aim of finding significant differences between the factors rather than correlations. The present results thus reveal that the effects reported by Hugdahl et al. (2008) are unique for the right ear stimulus and for left hemisphere functioning, de-emphasizing the role of the right hemisphere in AVHs (cf. Sommer et al., 2010). However, as suggested by Badcock and Hugdahl (2012) different views on the roles of the left and right hemispheres in AVHs may not be in conflict since right hemisphere intrusive emotions related to the experience of AVHs may be more easily elicited from the right hemisphere after weakening of the left hemisphere inhibitory functions caused by AVHs.

The present results fit a theoretical model that sees AVHs as causing spontaneous hyper-activation of the receptive language areas in the left temporal lobe, as also suggested by (Spencer et al., 2009); see also (Hubl et al., 2007), and which causes interference, and shut-down of the perceptual system for an external auditory stimulus (as also suggested by Fiszdon et al., 2005; Hugdahl et al., 2009; Jardri et al., 2011; Kompus et al., 2011). Hubl et al. (2007) suggested "competition for available cognitive resources" in the left hemisphere receptive language areas between the internally generated AVH and the externally presented auditory stimulus. The interference this causes could either be a central auditory processing deficit or a sensory gating failure. Schizophrenia patients have been shown to fail to filter out irrelevant sensory input (Clementz et al., 1998; Boutros et al., 2004), which may have the consequence of information overflow for available processing capacity in the presence of AVHs. The present experimental design and data cannot answer this question, since it would need the inclusion of low-level acoustic stimuli, like sound clicks, or startle signals typically used in sensory gating studies (which should be the target for a follow-up study). The current results should, however, not be interpreted to mean that perception is the sole factor behind AVH. No existing cognitive or neuronal activation model can fully explain the phenomenology of AVH, at best the different models can explain parts of the phenomenology (Jones, 2010; Badcock and Hugdahl, 2012).

Turning to a discussion of the three theoretical models for AVH, it is true that, at least at a gross surface-view, perceptual, inner speech, and traumatic memory models all engage the left hemisphere. There are however clear differences in anatomical landmarks within the left hemisphere that are important to distinguish when teasing the models apart. Speech perception engages the upper posterior parts of the temporal lobe, including the superior temporal gyrus and sulcus, the Heschl's gyrus and the planum temporale, while memories engage the anterior medial parts of the temporal lobe, mainly the hippocampus. Thus, even though both of these models engage the temporal lobe, they differ in more detailed anatomical landmarks. The same is true for an inner speech model, although both speech perception and speech production (inner speech) is confined to the left hemisphere, an inner speech model would engage areas in the inferior frontal gyrus (Broca's area), while a speech perception model engages areas in the superior temporal gyrus (Wernicke's area).

A possible extension of the DL paradigm to the clinical domain is the use of a dichotic training procedure for improving the ability to ignore or withstand the "voices" when they tend to overwhelm the patient, and to improve other cognitive functions, see Egeland et al. (2003) for discussion of cognitive functions in schizophrenia. This was suggested in a review paper by (Hugdahl et al., 2009) and recent preliminary data from a few patients seems to support such a view.

In summary, the present correlational data support a left hemisphere speech perceptual model for AVHs, which is also supported by fMRI studies (see e.g. Jardri et al., 2011).

A potential limitation of the present study is the modest, although statistically significant, correlation coefficients, explaining about 10% of the common variance for the right ear stimulus. A counter argument is however that the difference between the right and left ear situation is minimal from a procedural point of view, thus, it is highly unlikely that a significant correlation for the right, and a non-significant correlation for the left ear are due to chance alone. It is moreover similarly highly unlikely that a significant negative correlation for the right ear stimulus and the PANSS hallucination item, and a corresponding zero correlation for a randomly chosen negative symptom, is due to chance alone, considering the minimalistic procedural differences between conditions. This is actually a strength of the DL task as compared to standard neuropsychological tests, which all differ between themselves along a number of procedural and cognitive dimensions in addition to the hypothesized difference in any particular study where they are used. This was nicely demonstrated in a recent meta-analysis study of Stroop interference effects in schizophrenia (compared with healthy controls) by Westerhausen et al. (2011) where it was shown that a card-version of the test produces larger effect-sizes than a PC-version (of the same test). Thus, having a minimalistic procedural difference between conditions, as in the DL task, is a great advantage when evaluating subtle experimental effects.

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Contributors

Kenneth Hugdahl designed the study, analyzed the data, and wrote the manuscript.

Else-Marie Løberg contributed to the patient recruitment, collected and scored parts of the data, and read and commented on the manuscript.

Liv E. Falkenberg collected and scored parts of the data, and read and commented on the manuscript.

Erik Johnsen contributed to the patient recruitment, read and commented on the manuscript.

Kristiina Kompus read and commented on the manuscript.

Rune Kroken contributed to the patient recruitment, read and commented on the manuscript.

Merethe Nygård collected and scored parts of the data, and read and commented on the manuscript.

Rene Westerhausen read and commented on the manuscript.

Koksal Alptekin contributed to the patient recruitment, read and commented on the manuscript.

Murat Özgören collected and scored parts of the data, and read and commented on the manuscript.

Conflict of interest

Köksal Alptekin has received grants and honoraria for consulting work, lecturing and research from Lundbeck, Janssen, Pfizer, Schering-Plough, AstraZeneca, Bristol-Myers Squibb, Sanofi-Aventis, Santa Farma Sanovel, Zentiva, Eczacıbaşı, Nobel, Bilim, Abdi İbrahim, and Wyeth.

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Rune Kroken has been reimbursed by Eli Lilly, Janssen Cilag and Bristol-Myers Squibb and Lundbeck for attending conferences.

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Further reading

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