Research report

Fundamental deficits of auditory perception in Wernicke’s aphasia

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Abstract

Objective: This work investigates the nature of the comprehension impairment in Wernicke’s aphasia (WA), by examining the relationship between deficits in auditory processing of fundamental, non-verbal acoustic stimuli and auditory comprehension. WA, a condition resulting in severely disrupted auditory comprehension, primarily occurs following a cerebrovascular accident (CVA) to the left temporo-parietal cortex. Whilst damage to posterior superior temporal areas is associated with auditory linguistic comprehension impairments, functional-imaging indicates that these areas may not be specific to speech processing but part of a network for generic auditory analysis.

Methods: We examined analysis of basic acoustic stimuli in WA participants (n = 10) using auditory stimuli reflective of theories of cortical auditory processing and of speech cues. Auditory spectral, temporal and spectro-temporal analysis was assessed using pure-tone frequency discrimination, frequency modulation (FM) detection and the detection of dynamic modulation (DM) in “moving ripple” stimuli. All tasks used criterion-free, adaptive measures of threshold to ensure reliable results at the individual level.

Results: Participants with WA showed normal frequency discrimination but significant impairments in FM and DM detection, relative to age- and hearing-matched controls at the group level (n = 10). At the individual level, there was considerable variation in performance, and thresholds for both FM and DM detection correlated significantly with auditory comprehension abilities in the WA participants.

Conclusion: These results demonstrate the co-occurrence of a deficit in fundamental auditory processing of temporal and spectro-temporal non-verbal stimuli in WA, which may have a causal contribution to the auditory language comprehension impairment. Results are discussed in the context of traditional neuropsychology and current models of cortical auditory processing.

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1 Contributions by Manon Grube are of sufficient magnitude to warrant joint first authorship.
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1. Introduction

Wernicke’s aphasia (WA) is an acquired language impairment characterised by severely impaired single-word comprehension and repetition with fluent but disordered speech. WA most commonly results from a cerebrovascular accident (CVA) to the left posterior tempo-parietal cortex, affecting areas involved in semantic, phonological and auditory processing. The close proximity of these posterior temporal lobe language-related cognitive systems often results in lesions to this region impacting multiple systems. As a result, WA is a behaviourally and cognitively heterogeneous disorder. The presence of semantic and phonological impairments have been documented in WA (Baker et al., 1981; Blumstein et al., 1977; De Renzi et al., 1972; Ogar et al., 2011; Robson et al., 2012b). In contrast, while auditory processing deficits have been suggested in WA (Auerbach et al., 1982; Kirshner et al., 1981; Polster and Rose, 1998), they have been little explored experimentally. This study investigated fundamental, non-linguistic auditory processing in WA in relation to current models of cortical auditory processing and explored the relationship with auditory language comprehension.

Whilst WA has been shown to be globally cognitively heterogeneous, the classical view suggested an instability in phonological word-form representations as the cause of the comprehension deficit (Luria, 1976; Luria and Hutton, 1977). This view is consistent with recent behavioural findings that suggest a phonological impairment is a critical cognitive component of WA (Robson et al., 2012b) and the classical lesion distribution in WA, which overlaps with phonological-processing regions in the left superior temporal lobe (Price et al., 2005). The current study investigated participants who could be described as having classical WA, i.e., individuals with core phonological deficits. Two pieces of evidence, however, support previous proposals that phonological deficits in WA may be associated with a more fundamental impairment in auditory analysis. Firstly, behavioural work has shown that individuals with WA can have deficits in discriminating phonemes with very different acoustic structures, for instance in distinguishing a /b/ from an /f/ (Robson et al., 2012a). If only damage to more abstract phonological representations had occurred, one might expect that early auditory processing would still allow detection of a difference between the stimuli based on their considerably different acoustic structure. Secondly, lesions in WA frequently include primary and non-primary auditory regions in the left-hemisphere (Bogen and Bogen, 1976; Ogar et al., 2011). These regions respond to both generic and speech-related acoustic stimuli: noise (Binder et al., 2000), pure tones (Binder et al., 2000; Hall et al., 2000), modulated tones (Binder et al., 2000; Hall et al., 2000), frequency sweeps (Husain et al., 2004), harmonic sounds (Menon et al., 2002), and phonological stimuli (e.g., Benson et al., 2001; Binder et al., 2000; Price, 2010; Scott et al., 2006). These neural activation patterns imply that speech and non-speech perception systems may be subserved by the same, or highly overlapping, cortical network.

Neural activations in response to verbal and non-verbal sounds (in contrast to rest) are strongly bilateral. However, contrasts between different types of acoustic stimuli reveal differential response patterns, reflecting a hierarchical and in part lateralized organisation within the network. The auditory cortices display a functional architecture similar to the homologous organisation intensively studied in the macaque brain (Chelvan et al., 2011; Petkov et al., 2006). Primary auditory regions appear maximally responsive to auditory stimuli with the most simple acoustic structure; with the surrounding secondary and tertiary association auditory cortices responding preferentially to increasingly complex auditory stimuli (Rauschecker and Tian, 2004; Tian and Rauschecker, 2004). In addition, functional asymmetries between the left and right-hemisphere have been proposed, whereby the left and right auditory cortices display differential sensitivity to acoustic properties. Specifically, the right-hemisphere has been suggested to process spectral information (how energy is distributed across the frequency spectrum) (Schonwiesner et al., 2005a,b; Zatorre and Belin, 2001) and of changes in the spectrum over longer time windows of several hundreds of milliseconds (Boemio et al., 2005), while the left-hemisphere has been proposed to preferentially respond to rapid changes over shorter time windows of less than 50 msec (Boemio et al., 2005).

The lesion distribution in WA corresponds to left-hemisphere regions implicated in both speech and non-speech auditory analysis, but leaves the possibility that intact right-hemisphere auditory structures could be able to support non-verbal auditory analysis. However, current neuropsychological evidence indicates that unilateral brain lesions can cause fundamental auditory processing impairments, which are, for the most part, consistent with the neuroimaging literature and theories of auditory network organisation. Non-verbal auditory processing deficits have been identified in a range of unilateral lesions with mixed aetiology including CVA (Biederman et al., 2008; Bungert-Kahl et al., 2004; Divenyi and Robinson, 1989; Fink et al., 2006; Robin et al., 1990), temporal or frontal lobectomy following epilepsy (Samson and Zatorre, 1988; Samson et al., 2002) and tumour (von Steinbuechel et al., 1999). Such studies have demonstrated dissociations between groups of individuals with right and left-hemisphere pathology. Individuals with right-hemisphere lesions showed more frequency and more severe impairments for spectrally based judgement tasks (such as frequency discrimination, pitch matching and timbre analysis), whilst individuals with left-hemisphere lesions show more frequent and severe impairments in temporal judgement tasks (including gap detection, pattern judgements and click fusion) (Divenyi and Robinson, 1989; Robin et al., 1990; Samson and Zatorre, 1988; Samson et al., 2002). In particular, auditory temporal processing impairments have been associated with (pure) word deafness; a condition resulting in an isolated speech perception deficit with intact speech production, typically resulting from bilateral lesions (Albert and Bear, 1974; Auerbach et al., 1982; Griffiths et al., 2010; Otsuki et al., 1998; Pinard et al., 2002; Wang et al., 2000), and in approximately 30% from unilateral lesions to the left superior temporal lobe (Poeppel, 2001). Such individuals show impairments in discriminating verbal and non-verbal stimuli containing rapid temporal modulations (Albert and Bear, 1974; Slevc et al., 2011; Stefanatos et al., 2005). This impairment is thought to disproportionately affect speech
perception due to the rapid acoustic modulations contained in phonetic stimuli. In the majority of cases of word deafness secondary to bilateral superior temporal lesions (Poeppel, 2001), additional deficits in spectral analysis might be expected. This is consistent with reports of word deafness being rarely “pure” and most cases displaying additional deficits in environmental sound and music perception (Griffiths et al., 2010; Phillips and Farmer, 1990), where spectral analysis may be more critical, especially in the case of music (de Cheveigne, 2005). Of interest for the current study, word deafness frequently evolves from or to WA (Saffran, 2000; Yaqub et al., 1988), and the conditions have been considered to form a spectrum of impairments to WA (Saffran, 2000; Yaqub et al., 1988), and the conditions have been considered to form a spectrum of impairments to WA (Saffran, 2000; Yaqub et al., 1988). This implies that the comprehension elements (but not the production elements) of WA may partly involve similar fundamental auditory deficits.

In sum, existing neuropsychological and functional-imaging evidence implies that the condition of WA might be associated with a fundamental deficit in auditory processing. In this study, robust criterion-free measures were used to assess spectral, temporal and spectro-temporal elements of auditory processing in WA. Acoustic stimuli were designed to reflect auditory cues relevant to speech perception and to mirror theories of the functional organisation of the auditory cortices.

2. Methods

2.1. Participants

Ethical approval was granted by the North-West Multi-Centre Research Ethics Committee. Ten participants with WA and 10 age- and hearing-matched controls were recruited. T-tests showed no significant difference in age or hearing thresholds between the WA and control groups (Table 2).

2.1.1. WA participants

WA participants were recruited from speech and language therapy services in the north of England. For background information see Table 1.

<table>
<thead>
<tr>
<th>Participant</th>
<th>Age</th>
<th>Sex</th>
<th>Time post-onset at testing</th>
<th>BDAE comp. (%)</th>
<th>BDAE fluency (%)</th>
<th>BDAE word repetition (%)</th>
<th>sWPM</th>
<th>Phon. discrimination</th>
<th>RCPM (percentile)</th>
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<td>DL</td>
<td>73</td>
<td>M</td>
<td>6 months</td>
<td>3</td>
<td>63</td>
<td>&lt;1</td>
<td>8</td>
<td>10.5</td>
<td>25</td>
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<tr>
<td>LS</td>
<td>84</td>
<td>M</td>
<td>2.5 years</td>
<td>8.5</td>
<td>77</td>
<td>10</td>
<td>19</td>
<td>12.5</td>
<td>75</td>
</tr>
<tr>
<td>CB</td>
<td>59</td>
<td>M</td>
<td>14 months</td>
<td>10</td>
<td>38</td>
<td>10</td>
<td>30</td>
<td>13</td>
<td>50</td>
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<tr>
<td>MR</td>
<td>64</td>
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<td>10</td>
<td>68</td>
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<tr>
<td>RD</td>
<td>86</td>
<td>M</td>
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<td>10</td>
<td>80</td>
<td>10</td>
<td>47</td>
<td>9.5</td>
<td>75</td>
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<tr>
<td>EL</td>
<td>61</td>
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<tr>
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<td>53</td>
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<td>3 years</td>
<td>15</td>
<td>68</td>
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<tr>
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<td>= 90</td>
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<tr>
<td>CH</td>
<td>77</td>
<td>M</td>
<td>2 years</td>
<td>40</td>
<td>90</td>
<td>5</td>
<td>53</td>
<td>3.5</td>
<td>95</td>
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<td>100</td>
<td>15</td>
<td>51</td>
<td>1</td>
<td>90</td>
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</table>

images were acquired on a 3T Philips Achieva scanner with an eight-element SENSE head coil with a sense factor of 2.5. An inversion recovery sequence produced a $256 \times 256$ matrix of 128 transverse slices with 1 mm$^3$ voxels. Automated abnormality identification was carried out on the T1w images as described in Seghier et al. (2008). This algorithm enhances lesion identification by including an extra tissue class to the unified segmentation algorithm representing abnormality/lesion (Ashburner and Friston, 2005). Following segmentation, grey and white matter images were smoothed using an 8 mm full-width at half maximum Gaussian kernel. Binary outlier images were then produced based on the degree of abnormality on a voxel-by-voxel basis by comparing WA participant images to 13 elderly healthy control participants; voxels with a degree of abnormality greater than .5 identified as abnormal/lesion. The outlier images were overlaid to produce a lesion overlap map across all participants (Fig. 2). Consistent with traditional accounts of WA, maximal lesion overlap was seen in the temporo-parietal junction extending into inferior parietal, middle temporal and anterior temporal regions. Inspection of MR and CT images indicated left-hemisphere Heschl's gyrus (HG) lesions in seven out of the nine participants, five of whom showed extension into medial HG, i.e., the anatomical correlate of primary auditory cortex (Hackett et al., 2001) to various extents (MR, RD, EL, AC, CH). The two WA participants who did not show any HG involvement (NM, CW) had lesions affecting non-primary auditory areas anterior and posterior to HG. Images of lesions in relation to primary auditory cortex are displayed in the supplementary materials (Figure S1).

2.2. Auditory assessments

2.2.1. Stimulus design

This study assessed auditory processing of purely spectral cues and well as of changes in spectrum over time. The acoustic parameters selected for the auditory assessments
were reflective of acoustic cues used in speech perception and mirrored theories of cortical hierarchical organisation and hemispheric temporal processing asymmetry in auditory processing. While speech contains multiple spectral and temporal cues, these do not typically occur in isolation but in combination; therefore, stimuli with spectral changes (modulations) over time may correspond better to acoustic components of phonemes and phoneme transitions (Langers et al., 2003) than stimuli based on one type of cue.

Basic spectral processing was measured using pure-tone discrimination centred around the frequency value of 500 Hz, chosen with respect to the relevant frequency range of speech. Frequency modulation (FM) detection was used to test the processing of basic changes in frequency over time. This was assessed at two different time windows by the use of two modulation rates: 2 Hz and 40 Hz, aiming to reflect the analysis of slow, prosodic variations (2 Hz) and fast phonemic variations (40 Hz) (Griffiths et al., 2001; Witton et al., 2002, 1998). The processing of more complex changes in spectrum over time were assessed using dynamic modulation (DM) detection based on spectro-temporal “moving ripple” stimuli with regular, sinusoidal modulations in the spectral and the temporal domain. This study used spectral modulation rates (or, densities) and temporal modulation rates (or, velocities) known to be common to speech and relevant to speech perception (Chi et al., 1999; Elliott and Theunissen, 2009) and to activate auditory cortices (Langers et al., 2003; Schonwiesner and Zatorre, 2009).

2.2.2. Auditory tasks
Graphic representations of example stimuli are provided in Fig. 3, audio examples are included in the supplementary materials.

Supplementary audio related to this article can be found at http://dx.doi.org/10.1016/j.cortex.2012.11.012.

2.2.2.1. Frequency discrimination. This task required one target pure tone to be discriminated against two reference tones based on a difference in frequency. The two reference tones were presented with a frequency of 500 Hz ± 3 semitones, the target tone could be higher or lower. Both the reference frequency and direction of difference were pseudo-randomized across trials in a fixed order. The starting difference between the reference and target tones was five semitones for all participants which was then adaptively changed throughout the test.

2.2.2.2. FM detection. The FM detection tasks required the discrimination of one sinusoidally frequency-modulated pure tone target against two unmodulated reference tones, using a carrier frequency of 500 Hz. FM rates of 2 Hz and 40 Hz were used, and an adaptively varied modulation index for the target. Starting value for the control participants (with the exception of TT and PD, see Supplementary materials) was 3.5 for the 2 Hz FM and .16 for the 40 Hz. For the WA participants, initial testing established that starting modulation indices of up to 20 at 2 Hz and four at 40 Hz were required.

2.2.2.3. DM detection. The DM detection tasks required the discrimination of one modulated target stimulus against two unmodulated reference stimuli. DM detection was tested for three combinations of spectral (cycles/octave, cpo) and temporal (cycles/sec, cps) rates in the WA and control groups (low, 1cpo & 4cps; intermediate, 2cpo & 8cps; high, 4cpo & 16cps) and for two additional combination of rates in the
WA group (1cpo & –16cps, and 4cpo & –4cps). All stimuli had an upward drift in the spectral peaks, as indicated by the negative values for temporal rates (Chi et al., 1999), chosen to be more pleasant than a downward drift. The stimuli consisted of 400 components, logarithmically spaced across four octaves from 250 to 4000 Hz. The starting modulation depth of the target stimulus was .65 for the control participants, and between .65 and 1 for the WA participants. Dynamic modulations in the target stimuli may result in perceived differences in loudness compared with unmodulated reference stimuli and therefore stimulus intensities were pseudorandomly varied to prevent this as an extraneous cue.

2.2.3. Adaptive-tracking procedure and threshold estimation

The tasks were implemented in Matlab (version 7.2.0 Mathworks, 2006). All tasks used a three-interval, two-alternative forced-choice adaptive design with an AXB paradigm, minimising executive demands and memory load (Bishop et al., 2005). The participants were instructed that they would hear three sounds and then be asked to decide whether the first (A) or the last (B) sound was the “odd one out”. The middle sound (X) was a reference stimulus against which the other two could be compared. Participants were asked to respond non-verbally by indicating their decision on a piece of paper showing three black rectangles in a row, reflecting the AXB trial structure. This avoided potential confounding difficulties arising from the significant speech distortions and perseverations in the WA participants. There were 50 trials per task; each trial comprised three stimuli (one target, two reference) and two inter-stimulus-intervals (ISI) of 750 msec each, equalling a total trial duration of 3750 msec. Executive task requirements were thus kept constant across tasks, in order to avoid possible effects on performance accuracy in the aphasic participants (Jefferies and Lambon Ralph, 2006; Noonan et al., 2010). For each task, the initial difference to detect was at a supra-threshold level, which was fixed for controls and selected individually for each WA participant during a training period prior to the start of the task. This approach ensured that each participant was able to perceive the difference reliably at the start. The adaptive procedure used a two-down, one-up algorithm: the difference between the target and reference stimuli was decreased after two consecutive correct responses and increased after one incorrect response. A larger step size was used up to the fourth reversal and a smaller one thereafter, with their magnitudes depending on the starting difference in order to give all participants the opportunity to reach the same
threshold. Thresholds were calculated as the mean of the values at the final six reversals (change between decrease and increase), estimating the 70.9%-correct point of the psychometric function (Levitt, 1971). Sound intensity was set individually to a comfortable level, reported in the supplementary materials (Figure S2). Average intensity levels were 86 dB SPL for the frequency discrimination, 86 dB SPL for FM and 81 dB SPL for DM detection.

3. Results

Auditory processing thresholds for the WA participants, control group and group differences (independent samples \( t \)-test) are presented in Table 3, individual adaptive tracks and individual impairment profiles for WA participants in the supplementary material (Figures S3–S10). For the three types of stimuli, the thresholds indicate respectively the difference in frequency in semitones, the FM modulation index and DM modulation depth required for the participants to reliably detect the difference between target and reference stimuli.

3.1. Threshold reliability

An advantage of the two-down, one-up adaptive-tracking method is that it allows qualitative assessment of whether participants understood task requirements. A normal “staircase” pattern of adaptive tracking is unlikely to be observed by chance (i.e., if the participant is guessing due to lack of understanding). The individual tracks of the WA and the control participants document consistent response patterns and support the assumption that the measured values were realistic estimations in almost all cases (Supplementary materials: Figures S3–S9). Convincing staircases were obtained for all WA participants for the frequency discrimination task, the 2 Hz and 40 Hz FM detection tasks, as well as for the DM tasks at 1cpo &/\( C_0 \) 4cps, 1cpo &/\( C_0 \) 16cps, and 4cpo &/\( C_0 \) 4cps. Two out of the 10 WA participants (MR and RD) produced unreliable tracks at 2cpo &/\( C_0 \) 8cps DM, and half of the group (DL, LS, MR, RD and CH) did so at 4cpo &/\( C_0 \) 16cps (Supplementary materials: Figure S10), despite setting the starting level to maximum modulation depth (\( A = 1 \)). Therefore, although all WA participants were able to do the task, not all modulations could be perceived by the whole group and further analyses on the thresholds for 4cpo &/\( C_0 \) 16cps are interpreted with caution. One control participant (GP) produced an unreliable result at 2 Hz FM.

3.2. Auditory processing impairment

We hypothesised deficits in all of the auditory tasks in the WA participants, based on the fact that the parameters for these tasks were selected specifically with respect to the acoustic structure of speech (see above). Accordingly, one-tailed, independent sample \( t \)-tests were conducted for each auditory measure using an uncorrected alpha of \( p < .05 \), and Bonferroni

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<tr>
<th>Participant</th>
<th>Freq</th>
<th>2 Hz</th>
<th>40 Hz</th>
<th>1cpo &amp; &amp; -4cps</th>
<th>1cpo &amp; &amp; -16cps</th>
<th>2cpo &amp; &amp; -8cps</th>
<th>4cpo &amp; &amp; -4cps</th>
<th>4cpo &amp; &amp; -16cps</th>
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<td>.87</td>
<td>.58</td>
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<td>.79</td>
<td>.7</td>
<td>.95</td>
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<td>.78</td>
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<td>.66</td>
<td>.7</td>
<td>.91</td>
<td>.95</td>
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<td>.67</td>
<td>.31</td>
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<td>.38</td>
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<td></td>
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<tr>
<td>p</td>
<td>.017</td>
<td>.005</td>
<td>&lt;.001</td>
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</table>

Freq = frequency discrimination; ns = non-significant at the level of \( p < .05 \); p values marked in bold = surviving Bonferroni correction; individual threshold in bold = significantly elevated based on Crawford and Garthwaite, 2007).

Borderline outside normal limits \( p = .06 \) two-tailed; individual thresholds marked in italics = unreliable threshold value.
correction for multiple comparisons ($n = 6$), after testing for normal distribution of the data: all the control samples displayed a normal distribution and only one sample of the WA group showed a minor deviation (2 Hz FM, $p = .0356$; Lilliefors-version of the Kolmogorov–Smirnoff Test for Composite Normality). In addition, thresholds were analysed at the individual level using Bayesian inferential methods to identify those amongst the WA participants that differed significantly from the controls, based on uncorrected, two-tailed significance level of $p \leq .05$ (Crawford and Garthwaite, 2007). For the frequency discrimination task, the WA and control participants did not significantly differ in their thresholds at the group level (Table 3; Fig. 4). At the individual level, none of the WA participants had a significantly elevated threshold, although two of them were close to significance (DL, CB) (Table 3; Supplementary materials, Figure S10). Group differences were observed for all other auditory tasks; the WA displayed significantly elevated thresholds for the 2 Hz and 40 Hz FM tasks as well as the three DM tasks administered in both groups (1cpo & $-4$cps, 2cpo & $-8$cps and 4cpo & $-16$cps) (Table 3; Fig. 4; independent samples t-tests). These are moderate-to-large effects (Cohen et al., 1980), and the group was significantly different from the controls for all tasks except for the frequency discrimination task.

Fig. 4 – Auditory task thresholds for WA and control participants: group data. Boxplots display interquartile ranges (boxes) and max. to min. range excluding outliers (whiskers) for each of the tasks. There was no group difference found for the frequency discrimination task (A) but for both 2 and 40 Hz FM (B) and all three DM (C) detection tasks undertaken in both groups, i.e., for low rates (sparse and slow: 1cpo & $-4$cps), intermediate (2cpo & $-8$cps), and high rates combination (dense and fast: 4cpo & $-16$cps).
differences remain significant also after Bonferroni correction (n = 6). Impairments at the individual level were found for six WA participants on 2 Hz FM, five on 40 Hz FM, all 10 on DM 1cpo & –4cps, four on DM 2cpo & –8cps, and nine on DM 4cpo & –16cps (Fig. 5). Inspection of individual data (Table 3; Supplementary materials, Figure S11) showed that all WA participants had at least one other elevated thresholds in addition to DM 1cpo & –4cps.

For the DM 4cpo & –16cps, six of the WA participants were unable to reliably perceive the modulation even at maximum modulation depth (A = 1). In order to investigate whether this was primarily due to the spectral or temporal complexity of the stimuli, two additional combinations of rates were assessed in the WA participants: low spectral & fast temporal (1cpo & –16cps), and high spectral & slow temporal (4cpo & –4cps). If temporal analysis was primarily impaired then modulation detection at 1cpo & –16cps should be more affected than modulation detection at 4cpo & –4cps, whilst if spectral aspects were of particular difficulty then the opposite pattern should be observed. Neither of these patterns was observed: there was no significant difference between DM at 1cpo & –16cps and 4cpo & –4cps. All of the participants who had not been able to perceive the modulation at 4cpo and –16cps were able to perform the two additional DM tasks.

3.3 Relationship with peripheral hearing loss

Almost all participants, WA and controls, displayed some degree of age-related hearing loss. To examine whether impairments on the auditory tasks could be explained by peripheral hearing loss, an overall "hearing loss score" was computed using principal component analysis based on the pure-tone audiometry thresholds, obtained from either ear at 500 Hz, 1 kHz, 2 kHz and 4 kHz (Table 2). The control participants showed significant positive correlations between hearing score and 40 Hz FM detection (Spearman’s rho = .87, p < .001), DM detection at 1cpo & –4cps (Spearman’s rho = .73, p = .018), DM at 4cpo & –16cps (Spearman’s rho = .87, p < .001), and a borderline significant correlation with DM detection at 2cpo & –8cps (Spearman’s rho = .57, p = .083). The WA participants, however, showed no such correlations, further supporting the hypothesis that their deficits are part of a neurological impairment.

3.4 Correlations with comprehension

In order to examine the hypothesized relationship between auditory impairment in FM and DM detection and speech-comprehension deficits in WA participants, correlations were assessed between the auditory detection thresholds and the three linguistic measures (BDAE global comprehension percentile, sWPM score and phonological discrimination threshold). For the BDAE comprehension percentile scores, a significant relationship was found for FM detection at 2 Hz (Spearman’s ρ = −.64, p = .022) but not for 40 Hz. Amongst the DM detection measures, a highly significant correlation was found for 1cpo & –4cps (Spearman’s ρ = −.93, p < .001) and 1cpo & –16cps (Spearman’s ρ = −.74, p = .007) (Table 4). The correlations with both DM detection tasks survived Bonferroni correction (for n = 6). For the sWPM task, significant correlations were found for FM detection at 2 Hz (Spearman’s ρ = −.74, p = .007) and DM detection at 1cpo & –4cps (Spearman’s ρ = −.77, p = .0043) and 1cpo & –16cps (Spearman’s ρ = −.65, p = .020) (Table 4); those for 2 Hz FM and DM 1cpo –4cps survived Bonferroni correction. For the phonological discrimination thresholds, significant correlations were found for 40 Hz FM detection (Spearman’s ρ = .55, p = .05), and for DM detection at 1cpo & –4cps (Spearman’s ρ = −.74, p = .007), 1cpo & –16cps (Spearman’s ρ = −.64, p = .022) and 2cpo & –8cps (Spearman’s ρ = −.55, p = .048); only the correlation with DM at 1cpo & –4cps survived Bonferroni correction (Table 4). The Spearman’s ρ values of the significant correlations for FM and DM at the lower and intermediate modulation rates ranged from .55 to .93 for the BDAE, up to .77 for the sWPM, and up to .74 for the phonological discrimination; these are considered to be large statistical effects (Cohen, 1988). The correlations were strongest for DM detection at 1cpo & –4cps (Fig. 6): this combination of low rates yielded the highest Spearman’s ρ values for all three linguistic measures; all three were highly significant and survived Bonferroni correction. With increasing spectral and temporal rates, correlation strength decreased, whereby the low spectral rate, i.e., the sparseness of spectral peaks appears most relevant. Nevertheless, the additional borderline significant correlations seen between 2 Hz FM and comprehension measures and between 40 Hz FM and phonological discrimination should not be overlooked. Finally, no significant correlations were found between linguistic measures and frequency discrimination or peripheral hearing loss.

Bonferroni correction for n = 6 based on the two FM tasks and DM at low and intermediate spectral and temporal rates, 4cpo & –16cps was excluded due to the large number of participants outside normal limits.
3.5. Results summary

The WA participants were significantly impaired compared to the controls in FM detection at both fast and slow rates tasks and the three DM tasks using low, intermediate and high temporal and spectral rates. The WA participants’ thresholds for modulation detection correlated significantly with their speech-comprehension and phonological scores, with the strongest relationship found for DM detection at low rates.

4. Discussion

Individuals with WA have severe and long-lasting auditory comprehension impairments. Traditional accounts emphasise a disruption to phonological analysis as the cause of the comprehension impairment. However, the close relationship between word deafness and WA as well as the congruency between typical lesion location and functional neuroimaging results implicate a more fundamental auditory processing disorder. By measuring sensitivity to basic acoustic stimuli comprising spectral, temporal and spectro-temporal features relevant to speech perception, this study found evidence that individuals with WA exhibited a core auditory processing disorder, the severity of which correlated significantly with the degree of their comprehension impairment.

Basic, purely spectral analysis, as measured by pure-tone frequency discrimination, was unimpaired in the WA participants. This result replicated previous findings that individuals with left-hemisphere lesions are able to perform this task (Biedermann et al., 2008; Bungert-Kahl et al., 2004). Consistent with this, the mismatch negativity component of electroencephalography (EEG) recordings (indicating the processing of stimulus change) in response to pure-tone changes in frequency has been found to be normal in individuals with aphasia (Csepe et al., 2001). Whilst our participants with WA were unimpaired in the detection of simple changes in the static spectral feature of pure-tone frequency, deficits were found in the ability to detect temporal modulations of pure-tone frequency in the form of sinusoidal FM. Further, a more severe impairment was observed for the detection of modulation occurring simultaneously along the spectral and temporal dimension (DM in “moving ripple” stimuli). The successful performance on frequency discrimination indicated that the WA participants understood and were able to carry out the executive and memory requirements for all the auditory tasks used here, as those were kept as constant as possible throughout. It is unlikely that any executive component contributed significantly to the impairments observed.

### Table 4 – Correlations between auditory FM and DM thresholds and linguistic measures in WA participants.

<table>
<thead>
<tr>
<th></th>
<th>2 Hz FM</th>
<th>40 Hz FM</th>
<th>1cpo &amp; –4cps</th>
<th>1cpo &amp; –16cps</th>
<th>2cpo &amp; –8cps</th>
<th>4cpo &amp; –4cps</th>
<th>4cpo &amp; –16cps</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDAE comprehension</td>
<td>ρ = –.64</td>
<td>–.40</td>
<td>–.93</td>
<td>–.74</td>
<td>–.61</td>
<td>–.40</td>
<td>–.41</td>
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<tr>
<td>p</td>
<td>.022</td>
<td>ns</td>
<td>&lt;.001</td>
<td>.007</td>
<td>.031</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>sWPM</td>
<td>ρ = –.74</td>
<td>–.36</td>
<td>–.77</td>
<td>–.65</td>
<td>–.26</td>
<td>–.21</td>
<td>–.08</td>
</tr>
<tr>
<td>p</td>
<td>.007</td>
<td>ns</td>
<td>.004</td>
<td>.020</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Phonological discrimination</td>
<td>ρ = .51</td>
<td>.55</td>
<td>.74</td>
<td>.64</td>
<td>.55</td>
<td>.43</td>
<td>.44</td>
</tr>
<tr>
<td>p</td>
<td>ns</td>
<td>.051</td>
<td>.007</td>
<td>.022</td>
<td>.048</td>
<td>ns</td>
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</table>

BDAE (Goodglass et al., 2001) auditory comprehension percentile. sWPM (Bozeat et al., 2000). Phonological discrimination = phonological discrimination threshold (Robson et al., 2012a). Spearman’s ρ correlation coefficients and p values from one-tailed tests. In italics are those that are significant at the level of p ≤ .05 (including borderline p = .051), and in bold those that survive Bonferroni correction (n = 7).

![Fig. 6](image) – Scatter plots for significant correlations between the three linguistic measures and DM detection thresholds in WA participants. Correlations are depicted for DM detection thresholds for the low rate combination (1cpo & –4cps) as those yielded the strongest correlations with all three linguistic measures: BDAE comprehension percentiles (Spearman’s ρ = –.93, p < .001) (A), sWPM scores (Spearman’s ρ = –.4, p = .001) (B), and phonological discrimination thresholds (C).
and the correlations with the WA participants’ level of verbal comprehension. Another requirement that might be suspected to play a role here is peripheral hearing sensitivity, i.e., the ability to perceive the presented stimuli. The results from the auditory tasks in the control group showed a significant relationship with pure-tone audiometry hearing thresholds. No such relationship was observed in the WA group. This was taken as further evidence that the auditory processing deficits observed in the WA group were primarily neurological in nature. However, this does not exclude the possibility of an additional contribution from hearing loss which may, in individual cases, compound neurologically-based impairments in WA; for example, while CW performed well on auditory tasks overall, he displayed a considerable peripheral hearing loss which is likely to compound his comprehension impairment.

4.1. Co-occurrence and association of auditory deficits with comprehension and phonological-processing impairments

There was a significant impairment in DM detection in WA participants that was found to show a significant relationship with their BDAE comprehension scores, sWPM and their phonological discrimination thresholds—an ability that has been classically associated with comprehension impairment in WA (Luria, 1976; Luria and Hutton, 1977). The correlations with the linguistic measures were strongest for low modulation rates. Dynamic modulations are present in speech (Chi et al., 1999) and have been suggested to be of major importance to speech processing (Elliott and Theunissen, 2009; Langers et al., 2003). In fact, any speech (or non-speech) sound can be constructed from linear combinations of DM components using linear signal processing. The most relevant DM range for speech perception, based on the frequency of occurrence of spectral and temporal modulation rates in speech, lies between 25 and 4cpo, and 4 and 9cps, respectively (Chi et al., 1999; Schonwiesner and Zatorre, 2009). The strong correlations with the DM thresholds at 1cpo & –4cps are consistent with these modulation rates corresponding to the centre of the range found most frequently in speech (Chi et al., 1999; Schonwiesner and Zatorre, 2009). Therefore the strength of this correlation may indeed reflect the critical relevance of these parameters to speech perception.

Compared with DM thresholds, there was a less striking relationship found between 2 Hz FM thresholds and both comprehension measures (BDAE and sWPM), but no relationship between 2 Hz FM and phonological discrimination thresholds. The FM stimuli are less speech-like in their fine acoustic structure than DM as they are based on variation of only one dimension and consist of one pure tone. However, the correlation between 2 Hz FM and word and sentence-level comprehension is consistent with proposals that this slow modulation rate corresponds to prosodic changes in speech. Impairments in 2 Hz FM detection have additionally been found in developmental dyslexia and developmental language impairment (Witton et al., 2002, 1998). In this study, there was a lack of correlation between 2 Hz FM detection and phonological discrimination. This is consistent with phonological discrimination depending on the detection of single-phoneme differences, which are realised over more rapid time scales than that captured in 2 Hz FM. In contrast, a borderline significant correlation was demonstrated between phonological discrimination and 40 Hz FM detection. These FM detection findings are consistent with the idea that the processing of 2 Hz FM and 40 Hz FM corresponds to the processes needed for the analysis of slow prosodic and fast phoneme-related changes, respectively. However, the relative weakness of the 40 Hz FM correlations require further investigation, given that the left-hemisphere is thought to play a particular role in analysing such fast modulations and that this rate of modulation is proposed to be related to phoneme-level information (Boemio et al., 2005; Drullman, 1995; Shannon et al., 1995).

Whilst this study indicates that the comprehension impairment in WA may be causally related to the capacity to resolve spectro-temporal acoustic cues, it is important to note that there are alternative explanations or common third factors that cannot be dismissed. The extent of damage might be suspected as a major factor in determining the severity of effect; however, in the current group, visual inspection of lesion maps did not reveal regular patterns between auditory cortex lesion extent and severity of auditory and linguistic impairment: see Section 4.3. However, lesion mapping is clearly not trivial; and neither remote nor plasticity effects can be known. Furthermore, disruption to additional cognitive systems contributes to the overall comprehension deficit in WA. Multiple investigations have established a semantic level impairment in a large proportion of individuals with WA, as lesions extend into semantic processing regions in middle temporal and inferior parietal regions (Ogar et al., 2011; Robson et al., 2012b). Additionally, auditory comprehension, particularly sentence and discourse comprehension, is likely to be affected by auditory short-term memory, the neural substrate of which has been localised to left-hemisphere superior temporal regions (Jeff et al., 2009). However, the extent to which auditory short-term memory and phonological deficits in WA are separable from auditory processing proper, rather than an emergent property, remains to be established.

At the individual level, therefore, multiple factors must be accounted for to fully describe an individual’s comprehension impairment. Further, individuals may also be non-separable on single measures but have differences in the effective connectivity between cognitive systems. Two WA participants in the current group (CH & CW) displayed considerably better comprehension than the other participants. While these participants did show better auditory thresholds than many other of the more impaired participants, the difference in acoustic processing scores did not appear to be as great as the difference in comprehension scores. This may indicate that these two participants had greater overall network efficiency or that the relationship between auditory processing impairment and auditory comprehension is not linear, due to high redundancy in the speech stream. Overall however, the current group of WA participants were recruited to be highly homogeneous in nature, reflecting “classical” WA and the correlations found in the current data set were likely a product of this high homogeneity in linguistic and auditory processing profiles but variation in severity over the case series. The
contribution of additional cognitive systems and peripheral hearing is likely to be even more important with individuals who display a Wernicke’s-type aphasia that is less classical in nature e.g., those who additionally produce semantic jargon.

4.2. Spectral and temporal hemispheric asymmetries

Theories of laterality in auditory processing suggest that the right-hemisphere responds preferentially to spectral cues and the left-hemisphere to temporal cues (Zatorre and Belin, 2001). Laterality theories have been further elaborated into models of asymmetric temporal sampling, which suggest that the right-hemisphere processes modulations, including spectral changes, which occur over time windows of up to several hundred milliseconds, while the left-hemisphere responds preferentially to rapid modulations over short temporal windows of up to 50 msec (Boemio et al., 2005). Neuropsychological reports have been broadly consistent with a hemispheric lateralization of function, in that individuals with right-hemisphere lesions show a disproportionate impairment on spectral tasks and individuals with left-hemisphere lesions show a disproportionate impairment on spectral tasks requiring the analysis of rapid temporal modulations (e.g., 40 Hz FM and 8–16cps DM). Consistent with the postulated hemispheric asymmetry, the WA participants were unimpaired at basic analysis of changes in a static spectral cue (frequency discrimination for pure tones) but impaired at detecting temporal modulations of frequency changing over time (FM detection) and of spectral peaks moving in time (DM detection), and in some cases unable to detect fast modulations at all (DM detection at 4cpo & –16cps). However, inconsistent with predictions of the window-length model (Boemio et al., 2005), the WA participants were impaired at detecting not only fast modulations (40 Hz FM), but also slower modulations (2 Hz FM). Neither did the systematic manipulation of spectral and temporal parameters in the DM tasks reveal a disproportionate impairment with increasing temporal rate over increasing spectral density; both spectral and temporal complexity affected the capacity to detect DM. These results are consistent with a functional-imaging study in which the activation patterns elicited by dynamic ripple presentation did not support a clear hemispheric specialization but only a regional one for high spectral density in the right lateral HG (Schonwiesner and Zatorre, 2009) and a general decrease in preferred temporal rate from primary to secondary auditory cortex. The available data from the current study support the hypothesis that the right-hemisphere is capable of processing spectral information over structurally simple stimuli, however suggests that increasing spectro-temporal complexity requires a greater bilateral contribution.

4.3. Neuroanatomical correlates and neuropsychological context

While this study was not designed to be a neuroanatomical investigation, and limited participant availability prevents such an approach; individual lesion profiles were visually examined to establish whether there was any relationship between the degree of auditory processing impairment and auditory cortex lesion. No systematic patterns could be detected over the whole group. However, the participants with the most severe auditory impairment, for whom scanning data were available, (DL & CB) displayed greater involvement of anterior as well as posterior cortical fields, and the three participants with the least severe auditory impairment (EL, NM & CW: see mean percentile score of Supplementary Figure S11) had no lesion involvement of the left transverse temporal gyri. These two observations are confounded, however, by the two most severe participants also having the largest lesions and the most severe participant (DL) also sparing almost the entire left transverse temporal gyri. At the group level, the lesion distribution was relatively consistent, in that all seven participants [for whom magnetic resonance imaging (MRI) scans were available] displayed lesion in the white matter underlying the left mid–to-posterior superior temporal gyrus and auditory cortices and a further six participants had involvement of the left grey matter of the primary auditory cortex and mid-to-anterior superior temporal gyrus. Inspection of 2/3 remaining participants’ CT scans showed involvement of left HG for two further participants. The extent to which such unilateral lesions are capable of causing disruption of auditory processing for speech perception has been questioned. For example, left-hemisphere intracarotid sodium amobarbital injection has not been shown to significantly disrupt phonological discrimination (Boatman et al., 1998) or lead to disproportionately greater phonological errors in sWPM (Hickok et al., 2008). In addition, word deafness, a perceptually based comprehension impairment, results from bilateral lesions to the superior temporal cortex in the majority of cases. Indeed, it has been hypothesised that only bilateral cases of word deafness arise from an apperceptive, pre-phonemic processing impairment, and unilateral word deafness cases arise from an associative deficit in recognising perceptual input (Auerbach et al., 1982); although behavioural evidence showing pre-phonemic auditory deficits in unilateral word deafness (Slevc et al., 2011; Stefanatos et al., 2005; Wang et al., 2000) may appear inconsistent with this hypothesis. However, unilateral word deafness cases are often reported to include sub-cortical, white matter regions underlying the superior temporal gyrus, implicating both hemispheres through deafferenting the left posterior auditory association cortices from both the left and right primary auditory cortices (Poeppe, 2001; Praamstra et al., 1991; Takahashi et al., 1992) or impoverishing the capacity for integrative processing between the right and left auditory cortices. Thus, the lesion distribution in the current group of WA participants is consistent with reports from cases
of unilateral word deafness, in that the greatest lesion overlap was observed in the white matter underlying the left mid-posterior superior temporal lobe. In addition, behavioural results from the current study accord with those from studies of word deafness which have identified impairments in non-verbal auditory temporal analysis: e.g., raised click fusion and gap detection thresholds reduced capacity to discriminate stimuli containing rapid modulations (Albert and Bear, 1974; Otsuki et al., 1998; Slevc et al., 2011; Stefanatos et al., 2005; Wang et al., 2000). In fact, temporal processing impairment has been considered to be causally related to the speech perception deficit in word deafness, although no statistical relationship has been observed due to the rarity of the condition preventing cases-series investigations. Overall, these behavioural profiles and lesion patterns in the current study are consistent with the hypothesis that word deafness and WA are part of a spectrum of impairments (Auerbach et al., 1982). This is further supported by reports that unilateral word deafness cases frequently resolve from or to WA (Yaqub et al., 1988). However, the extent to which WA and unilateral word deafness truly implicate both auditory cortices through structural and functional disconnection cannot be established with the current data. Future structural and functional neuroimaging evidence may be able to answer this clinically and theoretically important question; see Slevc et al. (2011) for an initial diffusion tensor imaging exploration in a case of word deafness. Although word deafness and WA appear to overlap in their combined auditory comprehension and auditory processing impairment, there are a number of aspects in which they differ. Word deafness is a relatively specific disorder, both behaviourally and cognitively. WA is more heterogeneous, in that the comprehension impairment has additional contributions from phonological and semantic level impairments (Ogar et al., 2011; Robson et al., 2012b). Additionally, individuals with WA suffer severely distorted language production, which is not the case in word deafness. There has been renewed interest in the contribution of the speech production system to speech perception (Liberman and Mattingly, 1985). In a recent review of the literature, Devlin and Aydelott (2009) conclude that the motor components of the speech production system have an influence on speech perception in conditions of degraded auditory input. This is an interesting possibility given that both individuals with word deafness and WA suffer from pathologically degraded speech perception systems, but only individuals with WA suffer from additional speech production difficulties. If motor elements were to contribute to speech perception, it could be hypothesised that individuals with word deafness would be better able to use their residual speech perception resources by employing top-down, constraining influences from the intact speech production network. In contrast, individuals with WA would lack this additional resource leading to more significant behavioural consequences for a similar degree of auditory processing impairment.

4.4. Conclusions

This work demonstrates a significant impairment in the analysis of fundamental acoustic cues in individuals with WA. An impairment was found in the spectro-temporal analysis of dynamic cues relevant to speech but not for the analysis of basic differences in frequency. Furthermore, the significant correlation found between the auditory processing and auditory comprehension impairments may indicate a causal contribution to the overall language profile, alongside traditionally implicated cognitive impairments such as semantic processing.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.cortex.2012.11.012.

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