The inability to repeat others' speech is a common impairment among patients with aphasia. Naturally, this impairment varies considerably based on aphasia type and severity. Although impaired repetition is found in several of the different aphasia types, it is the primary impairment in conduction aphasia. In 1874 Wernicke predicted that severing the connection between the speech production and comprehension modules included in the Wernicke-Lichtheim (Lichtheim, 1885; Wernicke, 1874) model would result in a disorder of repetition where speech fluency and comprehension remained intact. Although Wernicke had never seen such a patient at the time of his prediction, a patient with this condition was later described by Lichtheim (1885). Today, the definition of conduction aphasia is largely unchanged: Impaired repetition with relatively spared speech fluency and auditory comprehension. Conduction aphasia has been classically viewed as a result of acquired brain damage involving the left arcuate fasciculus where, true to the Wernicke-Lichtheim model, the connection between the posterior comprehension areas in the temporal lobe are disconnected from the anterior speech production region in the posterior-inferior frontal lobe; hence, conduction aphasia is commonly referred to as a disconnection syndrome.

Several cases of conduction aphasia and its accompanying brain damage have been described in the literature (e.g. Damasio & Damasio, 1980; Demeurisse & Capon, 1991; Poncet, Habib, & Robillard, 1987). Most of these studies suggest that, indeed, damage to the left arcuate fasciculus results in conduction aphasia. However, several recent papers have challenged this claim suggesting that damage to cortical gray matter in the left inferior parietal lobe is sufficient to elicit conduction aphasia (Bartha & Benke, 2003; Geldmacher, Quigg, & Elias, 2007; Hickok et al., 2000; Quigg, Geldmacher, & Elias, 2006). Nevertheless, other contemporary studies maintain the claim that conduction aphasia is caused by damage to the arcuate fasciculus in the presence of an intact left parietal lobe (Geldmacher et al., 2007).

The purpose of this study was to examine the critical lesion location associated with impaired repetition – the primary symptom of conduction aphasia. Patients with acute stroke to the left hemisphere were examined at bed-side utilizing a short aphasia battery which included a section for testing oral repetition. In addition, all patients underwent MRI examination which was used to demarcate lesion locations on case-by-case basis. Then, a lesion-behavior analysis was performed to understand which lesion location is most likely to impair the ability to repeat.

Method

Participants

The participants included in this study were 51 consecutive stroke patients admitted to the Landspitali – University Hospital in Reykjavik, Iceland. All participants had incurred a single event ischemic stroke to the left hemisphere and gave an informed consent for study inclusion. Patients were excluded from the study sample based on the following criteria: 1) non-native speaker of Icelandic; 2) evidence of a prior infarct (as per report from Radiology); 3) history of dementia or psychiatric illness; and 4) contraindication for MRI examination. Out of 51 patients, three were unable to complete the neuropsychological battery or MRI examination and four more were excluded based on severe auditory comprehension impairment. Therefore, data from a total of 44 patients (18 female) were included in the final statistical analyses described below. The mean patient age was 63 (plus-minus 11 years), with a range of 34-85 years. For each participant, behavioral and MRI examination was completed within two days of hospital

admission. Behavioral and MRI examinations were always completed with no more than three hours separating the two.

Behavioral testing

All participants were administered a neuropsychological workup which included the Bedside Evaluation Screening Test, 2nd edition (BEST-2; West, Sands, & Ross-Swain, 1998). The Repetition sub-test of the BEST-2 was utilized to quantify the severity of repetition impairment. This section includes five items where the level of presentation of each item is titrated based on patients' success with the previous item. Each of the five items includes: 1) A complete sentence; 2) A phrase; 3) A single word. Based on the BEST-2 overall aphasia severity scale, 15 patients had moderate or severe language impairment while the remaining 29 presented with either mild or no language impairment.

Neuroimaging data

All participants underwent a 1.5T MRI workup (using a Siemens scanner) that included T1-weighted imaging (T1-MRI), diffusion-weighted imaging (DWI), and FLAIR. Only those who had an infarct seen on the FLAIR or DWI were included in the final data sample. Images were converted from DICOM to NIfTI format using dcm2nii (www.mricro.com), which preserves spatial coordinates (yielding a good starting estimate for the subsequent co-registration of the T1 image to the T2 scan).

Brain lesions were demarcated on DWI images by a trained neurologist with extensive experience with lesion-symptom mapping, using FLAIR and T1 images to help guide lesion boundaries. Spatial processing was conducted using SPM5. Initially, DWI images were co-registered to the individuals T1 scan. This transform was applied to the lesion map. Then, the T1-scan was coregistered to the MNI T1 template image provided with SPM5 (offering an accurate starting estimate for the subsequent normalization). Finally, the T1 image was warped to standard MNI space using SPM5's unified segmentation and normalization algorithm, which has proved robust even in the case of large lesions (Crinion et al., 2007). At this stage, the T1-MRI scans and lesion maps for each patient were resliced to an isotropic 2mm in standard MNI space, allowing voxel wise analysis across individuals.

Voxel wise lesion-behavior mapping (VLBM) was carried out using NPM (non-parametric mapping; Rorden, Karnath, & Bonilha, 2007), a software package available from www.mricro.com. For every voxel a t-test was computed contrasting behavioral performance in patients with a lesion at that location to those without a lesion (Bates et al., 2003). The resulting statistical map was corrected for multiple comparisons using a 5% family-wise error threshold as determined using 1000 resampling permutations (Rorden, Fridriksson, & Karnath, 2008).

Results and Discussion

The VLBM analysis revealed that damage to the posterior portion of the arcuate fasciculus is a strong predictor of impaired repetition in stroke patients with left hemisphere damage (Figure 1). The results were corrected for multiple comparisons suggesting that patients with damage to this area are highly likely to have difficulty with oral repetition – the hallmark impairment in conduction aphasia. Thus, the present findings would strongly support the

classical view suggesting that conduction aphasia is caused by disconnection between the anterior and posterior speech areas (Geschwind, 1965).
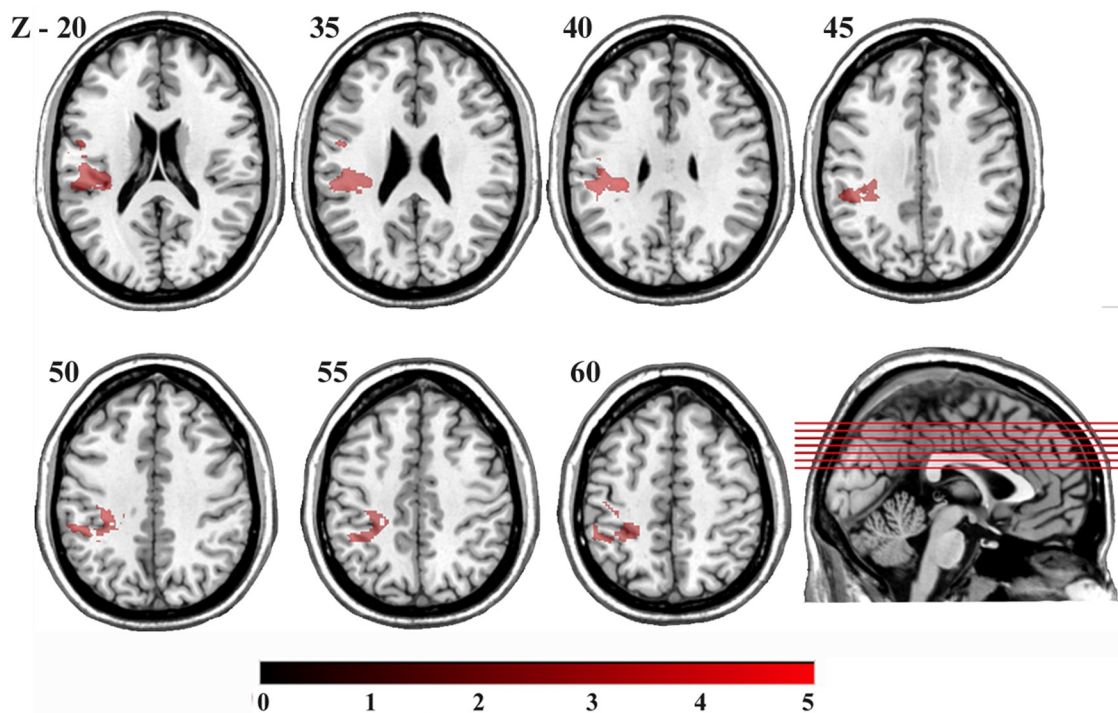

Figure 1. The critical lesion location (red) associated with impaired repetition in stroke patients with left hemisphere damage. The results are rendered on a standard brain template and MNI coordinates are shown on the top left of each slice. The color scale represents Z-scores.

The present study did not examine the direct relationship between conduction aphasia and brain damage. Patients with apraxia of speech and/or non-fluent aphasia were not removed form the study sample. Thus, the study sample included some patients who had difficulty repeating due to a motor-speech disorder rather than the primary repetition impairment seen in conduction aphasia. Nevertheless, the VLBM analysis did not reveal anterior damage as a predictor of impaired repetition suggesting that motor speech impairment may have "washed out" in the analysis.

Finally, it is important to note that all of the patients in this study were administered a perfusion weighted MRI (PWI) allowing for the examination the relationship between repetition impairment and hypoperfusion beyond the frank lesion. At the time of this submission, the analysis of these data had not been completed. However, if accepted for presentation, the PWI data will be discussed.

References

Bartha, L., & Benke, T. (2003). Acute conduction aphasia: an analysis of 20 cases. *Brain and Language, 85*(1), 93-108.

Bates, E., Wilson, S., Saygin, A., Dick, F., Sereno, M., Knight, R., Dronkers, N. (2003). Voxel-based lesion-symptom mapping. *Nature Neuroscience, 6*(5), 448-450.

Crinion, J., Ashburner, J., Leff, A., Brett, M., Price, C., Friston, K. (2007). Spatial normalization of lesioned brains: performance evaluation and impact on fMRI analyses. *Neuroimage, 37*(3), 866-875.

Damasio, H., Damasio, A. (1980). The anatomical basis of conduction aphasia. *Brain*, *103*(2), 337-350.

Demeurisse, G., & Capon, A. (1991). Brain activation during a linguistic task in conduction aphasia. *Cortex, 27*(2), 285-294.

Geldmacher, D., Quigg, M., Elias, W., Yamada, K., Nagakane, Y., Mizuno, T., et al. (2007). MR tractography depicting damage to the arcuate fasciculus in a patient with conduction aphasia. *Neurology, 69*(3), 321-322.

Geschwind, N. (1965). Disconnexion syndromes in animals and man. *Brain, 88*(3), 585-644.

Hickok, G.*,* Erhard, P., Kassubek, J., Helms-Tillery, A., Naeve-Velguth, S., Strupp, J., Strick, P., Ugurbil, K. (2000). A functional magnetic resonance imaging study of the role of left posterior superior temporal gyrus in speech production: implications for the explanation of conduction aphasia. *Neuroscience Letters, 287*(2), 156-160.

Lichtheim, L. (1885). On aphasia. *Brain, 7*, 433-484.

Poncet, M., Habib, M., Robillard, A. (1987). Deep left parietal lobe syndrome: conduction aphasia and other neurobehavioural disorders due to a small subcortical lesion. *Journal of Neurology, Neurosurgery and Psychiatry, 50*(6), 709-713.

Quigg, M., Geldmacher, D., & Elias, W. (2006). Conduction aphasia as a function of the dominant posterior perisylvian cortex. Report of two cases. *Journal of Neurosurgery, 104*(5), 845-848.

Rorden, C., Fridriksson, J., Karnath, H. (2008). An evaluation of traditional and novel tools for lesion behavior mapping. *Neuroimage, 44*(4), 1355-1362.

Rorden, C., Karnath, H., Bonilha, L. (2007). Improving lesion-symptom mapping. *Journal of Cognitive Neuroscience, 19*(7), 1081-1088.

Wernicke, C. 1874. *Der aphasische symptomencomplex.* Breslau, Germany: Cohn and Weigert.

West, J., Sands, E., Ross-Swain, D. (1998). Bedside Evaluation Screening Test, 2nd ed. Austin, TX: Pro-Ed.