## Introduction

This functional neuroimaging study examined cortical up- and down regulation patterns in six agrammatic aphasic speakers subsequent to treatment-induced language improvement. FMRI scans were obtained prior to and following application of treatment-of-underlying-forms (TUF), a linguistically-based method for improving sentence production and comprehension (Thompson et al., 2003). Participants were trained on complex WH-movement structures (object relatives), while generalization was tested to less complex WH-movement forms, including object clefts and object wh-questions. Based on the Complexity Account of Treatment Efficacy (CATE: Thompson et al. 2003) as well as the results of previous studies (see Thompson & Shapiro 2007), we predicted improvements on both trained and untrained forms reflecting acquisition of phrase structure building ability. We further hypothesized that behavioral changes would coincide with modifications in the neural network that normally subserve sentence processing. Based on a recent review of the literature concerned with the neurobiology of language recovery (Thompson & Den Ouden, 2008), we hypothesized recruitment of both right and left (perilseional) tissue, as well as that outside the normal network for sentence processing, but nevertheless predisposed for this function. Activation patterns found in healthy controls were used to evaluate pre- to post-treatment changes in the aphasic participants.

## Methods

*Subjects*

Participants were twelve healthy (7 females; mean age 54 (32-79)) and six aphasic speakers/listeners (1 female; mean age 54 (38-66); 6-146 months post onset of thromboembolic stroke). All were right-handed, monolinguial English speakers with no prior history of neurological, psychiatric, speech, language or learning disorders. One aphasic participant (A1) evinced a crossed aphasia, while the others suffered a single LH stroke. Extensive pre-experimental language testing, using the Western Aphasia Battery (Kertesz 1982), Northwestern Assessment of Verbs and Sentences (NAVS; Thompson, in preparation) and narrative speech analysis showed language profiles consistent with agrammatism – participants showed grammatically impoverished sentence production as well as difficulty comprehending complex, noncanonical sentences.

*Procedures*

Participants were trained to produce object relative (OR) sentences, until a criterion of 80% correct production/comprhension was achieved on computerized probes administered before each training session. These probes tested both trained and untrained structures as in 1a – 1c, below, such that both acquisition and generalization could be observed.

1. a. Pete saw the groom that the bride carried. (OR)
   b. It was the groom that the bride carried (OC)
   c. Who did the bride carry? (OWH)

An auditory verification task was selected to obtain the functional neuroimaging data. Participants, presented with auditory sentences and concomitant visual scenes, indicated by button-press (yes/no) whether or not the two matched.. Sentence types were object clefts (OC), which have a similar syntactic complexity as the trained OR structures, subject clefts (SC), and simple past tense actives (ACT), matched for sentence length in syllables (see 21- 2c). Forty trials per condition were pseudorandomaly distributed over 4 runs. Control subjects were scanned once, whereas pre-post treatment fMRI scans were obtained for the aphasic participants.

2. a. It was the groom that the bride carried. (OC)
   b. It was the bride that carried the groom. (SC)
   c. Yesterday, the bride carried the groom. (ACT)

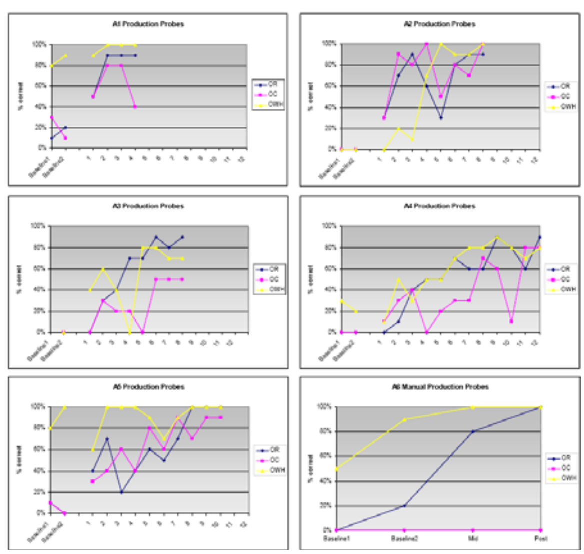
Functional MRIs with BOLD contrast were obtained with a 3T scanner. Data preprocessing and statistical analysis was performed with SPM5. Functional volumes were spatially normalized and smoothed (FWHM 6mm) and effects of global signal removed from the time-series.

After first-level analysis, the data for the healthy controls were entered into a second-level 3x2 ANOVA, with the factors sentence type and sentence-picture matching. The contrast of interest was that between OC and SC conditions, reflecting the syntactic construct on which the aphasic speakers were trained.

Data derived from each of the agrammatic subjects' fMRI sessions were preprocessed together and statistically analyzed in one model. A long-trial task was used to measure the individuals' true hrf in spared tissue in 16 regions of interest (Bonakdarpour et al. 2007). These regions were based on the control group results (see below) and the literature on neural correlates of syntactic processing: Brodmann's Areas 7, 9, 21, 22, 39, 40, 44, 45, bilaterally. Hemodynamic response patterns were fed as weights to the relevant FIR-modeled post-event time bins in the statistical model. Specific contrasts were calculated by giving positive and negative values to these weights.

**Results**

After reaching criterion for OR structures, all agrammatic participants showed generalization to OC and OWH structures, except subject A6, who showed no improvement on OCs (figure 1). Improvement on the WAB AQ, NAVS comprehension scores and MLU was variable, while all subjects showed nominal improvement on the NAVS production scores.




<u>Figure 1</u> *Improvement and generalization patterns for the six agrammatic participants, during training of object-relative (OR, blue) sentence structures. Generalization to object-clefts (OC, purple) and object-extracted WH-questions (OWH, yellow) is present in all subjects, except A6 (bottom right), who remained at floor level on OC structures.*

For control subjects, the contrast OC>SC revealed an activation network including the middle and inferior frontal gyri, precentral gyrus, middle and superior temporal gyri, and insula (figure 2). Despite individual variation in activation differences between scanning sessions in the agrammatic subjects, main-effects analyses revealed a general shift from LH superior temporal activation (BA 22) to more posterior temporoparietal areas, bilaterally (LH BA39; RH BA7 and BA40; figure 3).

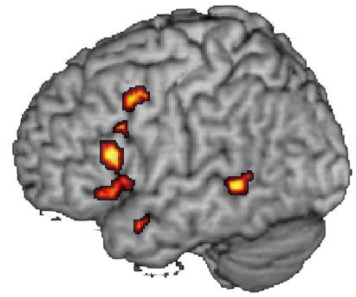


Figure 2. *Activation for the contrast of object-cleft sentence processing versus subject-cleft sentence processing in healthy control subjects (N=12; FDR corrected, p<.05, k>3).*

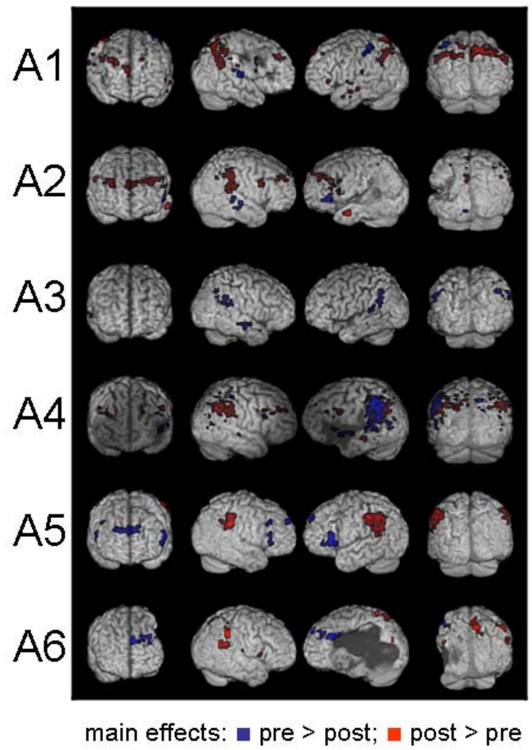



Figure 3. *Individual subjects' activation differences in main effects for auditory verification of object cleft, subject cleft and simple active sentences, between pre-training (blue) and post-training (red) fMRI scans (FDR corrected, p<.05, k>3). Except for A3, all subjects show right-hemisphere activation increase in posterior temporoparietal cortex, while four out the six subjects show a similar pattern in the left hemisphere.*

**Conclusions**

The control data replicated studies examining the neural correlates of syntactic processing, showing activation of the classic language network. Parts of this network were lesioned in the agrammatic participants. However, their pre-post neuroimaging data showed a general shift in activation to more posterior areas, outside of the network primarily activated by healthy controls, indicating the potential for tissue in this region to be recruited for syntactic processing. These neuroplasticity data suggest that training based on CATE stimulates the recruitment of alternative cortical areas for processing complex syntactic material.

## References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