CORTEX 69 (2015) 68–75

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Clinical neuroanatomy

Speech entrainment compensates for Broca's area damage

Julius Fridriksson [a,*], *Alexandra Basilakos* [a], *Gregory Hickok* [b], *Leonardo Bonilha* [c] *and Chris Rorden* [d]

[a] *The Aphasia Lab, Department of Communication Sciences & Disorders, University of South Carolina, USA*
[b] *Department of Cognitive Sciences, University of California Irvine, USA*
[c] *Department of Neurosciences, Medical University of South Carolina, USA*
[d] *Department of Psychology, University of South Carolina, USA*

ARTICLE INFO

Article history:
Received 9 November 2014
Reviewed 3 January 2015
Revised 7 January 2015
Accepted 16 April 2015
Action editor Marco Catani
Published online 27 April 2015

Keywords:
Broca's aphasia
Treatment
Non-fluent speech
Speech production
Voxel-based lesion-symptom mapping

ABSTRACT

Speech entrainment (SE), the online mimicking of an audiovisual speech model, has been shown to increase speech fluency in patients with Broca's aphasia. However, not all individuals with aphasia benefit from SE. The purpose of this study was to identify patterns of cortical damage that predict a positive response SE's fluency-inducing effects. Forty-four chronic patients with left hemisphere stroke (15 female) were included in this study. Participants completed two tasks: 1) spontaneous speech production, and 2) audiovisual SE. Number of different words per minute was calculated as a speech output measure for each task, with the difference between SE and spontaneous speech conditions yielding a measure of fluency improvement. Voxel-wise lesion-symptom mapping (VLSM) was used to relate the number of different words per minute for spontaneous speech, SE, and SE-related improvement to patterns of brain damage in order to predict lesion locations associated with the fluency-inducing response to SE. Individuals with Broca's aphasia demonstrated a significant increase in different words per minute during SE versus spontaneous speech. A similar pattern of improvement was not seen in patients with other types of aphasia. VLSM analysis revealed damage to the inferior frontal gyrus predicted this response. Results suggest that SE exerts its fluency-inducing effects by providing a surrogate target for speech production via internal monitoring processes. Clinically, these results add further support for the use of SE to improve speech production and may help select patients for SE treatment.

* *Corresponding author*. Department of Communication Sciences & Disorders, University of South Carolina, Discovery 1, 915 Greene Street, Suite 202A, Columbia, SC 29208, USA.
E-mail address: jfridrik@sc.edu (J. Fridriksson).
http://dx.doi.org/10.1016/j.cortex.2015.04.013

1. Introduction

Recent work from our group has shown that speech entrainment (SE), which involves the real-time mimicking of audiovisually presented speech, may facilitate fluent speech production in individuals with chronic Broca's aphasia (Fridriksson et al., 2012). During SE, patients are provided a speech model that involves hearing speech and seeing the mouth of the speaker. In essence, the patient's speech is entrained, or pulled along, by the audiovisual (AV) speech model. This effect was not demonstrated when participants attempted to mimic an audio only speech model suggesting that the visual component of SE is crucial for improving speech production in patients. Importantly, the necessity of the visual component demonstrated that the effect of SE cannot be attributed to enhanced lexical or syntactic processing, as such effects should also be present when relying on audio only SE. Real-time mimicking is a central feature of SE as the same effect is not realized when a patient attempts to repeat speech that has already been produced. Using functional magnetic resonance imaging (fMRI), we showed that AV SE (compared to spontaneous speech) elicited bilateral activation in the anterior insula, inferior frontal gyrus *pars orbitalis*, posterior inferior temporal cortex, and in the left middle temporal gyrus and left dorsal region of Broca's area (Fridriksson et al., 2012). Although we showed a robust response to SE under AV conditions, not all patients benefitted to the same degree. Accordingly, it is not clear if only a subgroup of Broca's aphasic patients or patients with other types of aphasia benefit from AV SE. Whereas Broca's aphasia is the most frequent type of non-fluent aphasia, non-fluent speech is also a major characteristic of global and transcortical motor aphasia. In addition, some patients with other types of aphasia such as conduction or moderate-severe anomic aphasia often produce speech that is laden with pauses and hesitations even though these patients' speech is typically classified as being 'fluent.' Based thereon, more research is warranted to determine which patients' speech benefits from the aid of SE. In addition, further study of SE's mechanisms may ultimately maximize available treatment strategies by determining how a treatment that incorporates AV stimuli circumvents impairments in the speech production network to improve fluency.

Here, we investigated the brain-behavior basis underlying the fluency-inducing effects of SE in a group of chronic post-stroke individuals by identifying neuroanatomical damage that predicts improved fluency when speaking with the aid of SE. The purposes of this study were twofold: 1) to inform future studies about patients who will benefit from SE by characterizing their response to SE based on patterns of cortical damage, and 2) to develop further the theoretical underpinnings of SE based on models of speech production. Individuals with various aphasia types and severities were included to identify patterns of brain damage that relate to a positive response to SE conditions. Based on previous findings that speech fluency in patients with Broca's aphasia benefits from AV SE (Fridriksson, Baker, et al., 2009; Fridriksson, Moser, et al., 2009; Fridriksson et al., 2012), damage to regions typically associated with Broca's aphasia (Fridriksson, Fillmore, Guo, & Rorden, 2014) were hypothesized to predict improved speech production with the aid of SE.

2. Methods

2.1. Participants

Forty-four participants (15 female, mean age = 60.61 ± 10.9) were recruited as part of a larger stroke study, in which recruitment criteria were based on history of single event left hemisphere stroke ($n = 5$ hemorrhagic; $n = 39$ ischemic). Patients with lacunar strokes were excluded but patients with sub-cortical strokes were included in the study. No participants had history of neurological disease or developmental language abnormalities. All participants were tested at least six months post-stroke (Table 1).

Because the goal for this study was to localize brain damage that predicts the ability to speak with the aid of SE, individuals qualified for this study regardless of aphasia diagnosis. Based on language testing with the Western Aphasia Battery-Revised (WAB-R; Kertesz, 2007), 32 participants received a diagnosis of aphasia and 12 did not classify with aphasia. Nevertheless, it is possible that some of the participants in the group without aphasia presented with mild language difficulty that was not detected on the WAB-R. Consistent with Rorden and Karnath (2004) who recommend that voxel-wise lesion-symptom mapping (VLSM) studies also test patients that do not present with impairment in the dependent factor, patients who did not present with aphasia were not excluded from the current study. Aphasia classification for the participants with aphasia was as follows: Anomic: 12; Broca's: 14; Global: 1; Wernicke's: 1; and conduction: 4. The mean Aphasia Quotient, a measure of aphasia severity, on the WAB-R for all individuals with aphasia was 69.61 ± 20.07, and mean for individuals without aphasia was 97.96 ± 1.71. A lesion overlap map for all participants is presented in Fig. 1 (Panel A). All participants consented to study participation, and research protocols were approved by the Institutional Review Board of the University of South Carolina.

2.2. Procedures

Participants completed two tasks: a) picture description and b) audiovisual SE. The picture description task required

Table 1 – Participant characteristics.

Gender	15 Females, 29 Males
Mean age at time of testing	60.61 (SD = 10.9)
Months post-stroke	63.73 (SD = 58.15)
Aphasia quotient on WAB-R	Individuals with aphasia: 69.61 (20.07) Individuals without aphasia: 97.96 (1.71)
Lesion size	97.4 (SD = 83.1) CM^3
Aphasia types	Anomic: 12 Broca's: 14 Conduction: 4 Global: 1 Wernicke's: 1 None: 12

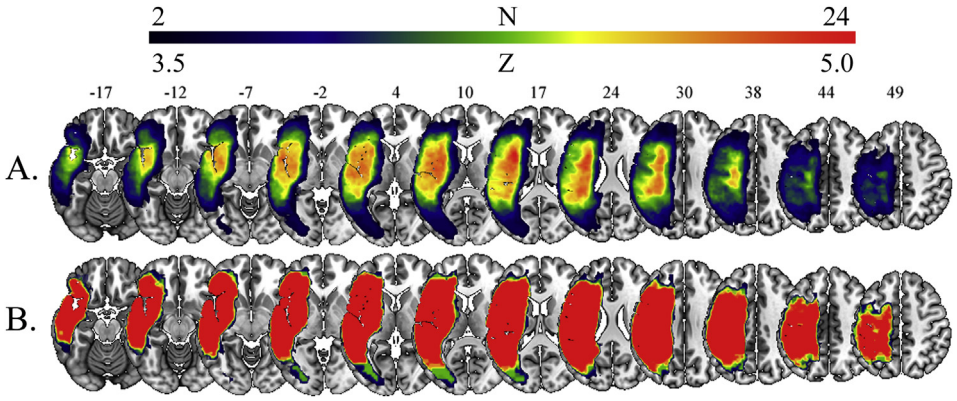

Fig. 1 – Lesion overlap maps for all participants. Panel A shows the lesion distribution for the sample with warmer colors representing more lesion overlap. The greatest lesion overlap occurred in the superior portion of the second frontal gyrus of the insula where 24 patients had damage. Accordingly, the color scale ranges from the least overlap (2 patients) to the greatest overlap (24 patients). Panel B shows a statistical power map for the VLSM analysis. The map is thresholded at Z > 3.5, which means that there is sufficient statistical power in the highlighted regions of this map to detect an effect of Z = 3.5 or greater. The color bar on top pertains to lesion overlap (N = 2–24) and statistical power (Z = 3.5–5.0).

participants to describe three pictures that included visually rich material to obtain measures of spontaneous speech. The three pictures that were used as stimuli were the cookie theft picture from the Boston Diagnostic Aphasia Examination (Goodglass, Kaplan, & Barresi, 2001), the picnic scene picture from the WAB-R, and the circus scene picture from the Apraxia Battery for Adults, second edition (Dabul, 2000). Each picture was shown for 2 min and participants were encouraged to speak in sentences. During SE, participants were instructed to mimic three audiovisual speech models that included a videotaped speaker producing a short script about a generic topic. Only the mouth of the speaker was visible, and participants were instructed to mimic the speaker in real-time. Participants were provided a model for task completion and a brief practice prior to starting the task. SE passages ranged from 50 to 56 words, and were spoken by the model in approximately 40–45 sec, depending on the passage (with an average of 65 WPM over the three passages). Passages were presented on a laptop computer using E-Prime software. Stimuli were presented at a comfortable hearing level, determined by sound test prior to initiation of SE.

Methods for recording and scoring the behavioral tasks were adopted from Fridriksson et al. (2012). All picture description and mimicking of SE passages was video recorded for offline transcription and scoring. For both tasks, 'different words per minute' (DWPM) was used as the primary dependent factor. It should be noted that all words, regardless of erred productions, were included in the DWPM count. Specifically, semantic or phonological errors were not excluded from the word count. If only correct words would have been counted, patients who presented with relatively fluent speech but produced frequent speech errors could have been incorrectly characterized as producing very few words and non-fluent speech. To determine extent of improvement in speech output with the aid of SE in comparison to spontaneous speech (picture description), standard scores were calculated for the dependent factors in both behavioral tasks based on the mean and standard deviation for each task. Z-scores for picture description were then subtracted from Z-scores for SE to make a third dependent factor that represented the difference in DWPM produced in each of the two tasks. This factor was calculated to determine the extent to which SE negatively or positively influences speech fluency, and used in the VLSM analysis to relate SE-induced fluency improvement to anatomy (Fridriksson et al., 2012).

2.2.1. *MRI data acquisition*

MRI data were acquired using a Siemens 3T Trio System with a 12-channel head-coil. All participants underwent scanning that included two MRI sequences: 1. T1-weighted imaging sequence using an MR-RAGE (TFE) sequence with a voxel size = 1 mm^3, FOV = 256 × 256 mm, 192 sagittal slices, 9-degree flip angle, TR = 2250 msec, TI = 925 msec, and TE = 4.15 msec, GRAPPA = 2, 80 reference lines; 2. T2-MRI for the purpose of lesion-demarcation with a 3D SPACE (Sampling Perfection with Application optimized Contrasts by using different flip angle Evolutions) protocol with the following parameters: voxel size = 1 mm^3, FOV = 256 × 256 mm, 160 sagittal slices, variable flip angle, TR = 3200 msec, TE = 352 msec, no slice acceleration. The same slice center and angulation was used as with the T1 sequence.

2.2.2. *Preprocessing of structural images*

The Clinical Toolbox (Rorden, Bonilha, Fridriksson, Bender, & Karnath, 2012) for SPM8 was used for the preprocessing of images. Stroke lesions were demarcated by a neurologist (LB) in MRIcron (Rorden & Brett, 2000) on individual T2-MRIs (in native space). Preprocessing began with the coregistration of the T2-MRI to match the T1-MRIs, aligning the lesions to native T1 space. Lesion cost-function masking (Brett, Leff, Rorden, & Ashburner, 2001) was then utilized for segmentation and normalization (Ashburner & Friston, 2005) to the stroke-control template image included with the Clinical Toolbox. The normalization parameters were used to reslice the lesion into standard space using linear interpolation, with the resulting lesion maps stored at 3 × 3 × 3 mm resolution

and binarized using a 50% threshold (interpolation can lead to fractional probabilities, this step ensures each voxel is categorically either lesioned or unlesioned without biasing overall lesion volume). All normalized images were visually inspected to verify the quality of preprocessing.

2.2.3. *Data analysis*

A VLSM analysis was completed to identify localized brain damage associated with speech fluency (qualified as DWPM) during the SE and spontaneous speech (picture description) tasks. In addition, a VLSM analysis identified damage that predicts improved speech production during SE relative to spontaneous speech. A general linear model was conducted with voxel-based permutation thresholding (20,000 permutations) to correct for multiple comparisons ($p < .005$ controlled for familywise error). The large number of permutations was used to adjust for the relatively conservative p-value threshold. From first principles, voxels that are infrequently damaged will have low statistical power while increasing the number of comparisons conducted. Therefore, only voxels where at least five patients had damage were included in the analysis. A map that shows the distribution of statistical power across different left hemisphere voxels is included in Fig. 1, Panel B. All of the VLSM routines used here are integrated into our NiiStat toolbox for Matlab (http://www.nitrc.org/projects/niistat).

3. Results

3.1. *Neuroimaging data*

A total of 11272 voxels (each 3 mm^3) were included in the VLSM analysis relating structural damage to mean standardized DWPM across SE, spontaneous speech, and improvement (standardized difference between DWPM for SE and spontaneous speech). A total of 826 voxels survived thresholding for spontaneous speech ($z > -4.26$), and 235 voxels survived for improvement ($z > 3.98$). No voxels survived thresholding for SE. Statistical maps for impaired fluency in spontaneous speech (red) and improvement (green) are presented in Fig. 2. Decreases in fluency in spontaneous speech were associated with damage to the posterior superior temporal, inferior parietal, inferior frontal, and insular regions, while brain damage associated with SE related improvement in DWPM was mostly localized within the inferior frontal and middle frontal gyri. For a more detailed list of regions associated with spontaneous speech and SE improvement, see Table 2.

3.2. *Behavioral data*

Out of the 44 patients included in this study, 25 produced a greater number of DWPM during SE compared to picture description (Fig. 3). Among those 25 patients, 13 had Broca's aphasia, 7 had anomic aphasia, 2 had conduction aphasia, 1 had Wernicke's aphasia, and two did not have aphasia. For the purpose of *post hoc* analyzes of the behavioral data, three groups were created with all participants based on speech fluency ratings on the WAB-R. A 'non-fluent group' ($n = 15$) was comprised of individuals whose fluency rating was equal to or less than 4. This group included 14 individuals with Broca's aphasia, and one individual with global aphasia. A 'fluent group' ($n = 17$) included individuals whose fluency rating ranged between 5 and 9. This group was made up of the 12 individuals with anomic aphasia, four individuals with conduction aphasia, and one individual with Wernicke's aphasia. The final group 'no aphasia' was composed of individuals with a fluency rating of 10 ($N = 12$). Mean DWPM (non-standardized) for the picture description and SE tasks are as follows:

3.2.1. *Non-fluent group*

Mean DWPM across the three picture description tasks was 14.86 ± 8.27, whereas mean DWPM across the SE tasks was 34.44 ± 13.96. A paired samples t-test comparing spontaneous speech (picture description tasks) to SE revealed a significant increase in average DWPM produced under SE conditions, $t(14) = 6.29$, $p < .001$. It is worth noting that the only person with global aphasia included in this study did not benefit from SE. Accordingly, the following discussion of improved speech production with the aid of SE in the non-fluent group only pertains to the patients with Broca's aphasia.

3.2.2. *Fluent group*

There was no significant difference in mean DWPM between spontaneous speech and SE conditions for the fluent aphasia group, $t(16) = .4$, $p = .97$. Mean DWPM was nearly identical between both tasks; spontaneous speech: 34.7 ± 14.4; SE: 34.83 ± 17.15.

3.2.3. *No aphasia group*

The individuals without aphasia demonstrated poorer performance during SE than spontaneous speech, $t(12) = -2.58$, $p = .02$: with the mean DWPM for picture description was 53.97 ± 11.18, while the mean DWPM for SE was 44.14 ± 14.42. This group likely produced fewer words due to constraints

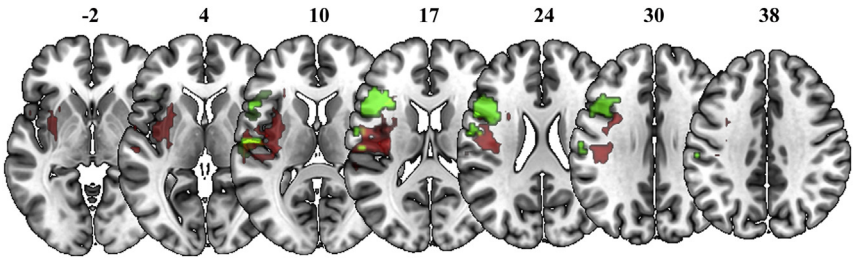

Fig. 2 – Results from lesion-symptom mapping analysis for standardized spontaneous speech scores (red) and improvement in speech fluency (green). These results are thresholded at $p < .005$ using permutation thresholding to control for multiple comparisons.

Table 2 – This table indicates the anatomical regions involved in improved speech production under conditions of SE and spontaneous speech. The percent of the statistical map associated with each cluster is presented (second column), as well as the proportion of each ROI comprised. For example, the inferior frontal gyrus pars opercularis (IFGpo) was the region most associated with SE improvement. The IFGpo comprised 34.24% of the voxels associated with SE improvement, and 26.25% voxels in the IFGpo were associated with SE improvement.

	Percentage of cluster within this region	Percentage of the cluster included in the ROI
Speech entrainment improvement		
Inferior frontal gyrus pars opercularis	34.24	26.25
Inferior frontal gyrus pars triangularis	24.31	15.28
Posterior middle frontal gyrus	10.96	2.67
Postcentral gyrus	9.58	1.99
Precentral gyrus	8.34	1.62
Supramarginal gyrus	7.02	2.18
Superior temporal gyrus	4.98	1.99
Spontaneous speech		
Postcentral gyrus	16.23	11.84
Supramarginal gyrus	13.84	15.1
Precentral gyrus	13.59	9.29
Superior temporal gyrus	12.59	17.66
External capsule (left)	8.47	48.82
Posterior insula	6.62	43.93
Superior longitudinal fasciculus	5.13	14.57
Posterior superior temporal gyrus	4.79	11.35
Putamen	4.19	19.22
Insula	3.95	13.9
Inferior frontal gyrus pars opercularis	3.31	7.1
Middle frontal gyrus	2.48	2.12
Inferior frontal gyrus pars triangularis	1.73	3.92
Superior corona radiata (left)	1.41	3.92

imposed by SE (i.e., a fixed number of words at a fixed rate), in addition to some difficulty with the task.

3.2.4. *Between-groups comparisons*

Results from the paired samples *t*-tests presented above indicate that the individuals with non-fluent aphasia were the only group to demonstrate a significantly increased DWPM during SE conditions relative to spontaneous speech. Between groups differences for each condition were further inspected using a 1(fluency)×3(group) analysis of variance (ANOVA). There was a significant main effect of group on spontaneous speech scores, $F(2, 43) = 35.8$, $p < .001$, with Tukey HSD pairwise comparisons revealing differences between all three groups ($p < .001$ for all). Between groups comparisons for DWPM for SE conditions did not reach statistical significance at alpha = .05 level [$F(2, 43) = 1.5$, $p = .24$], suggesting similar speech output between all three groups during SE conditions. Finally, comparison of standardized improvement scores indicated a significant effect of group [$F(2, 43) = 9.4$, $p < .001$], with Tukey HSD pairwise comparisons revealing the non-fluent group demonstrating greater improvement compared to the fluent ($p = .008$) and no aphasia groups ($p = .001$).

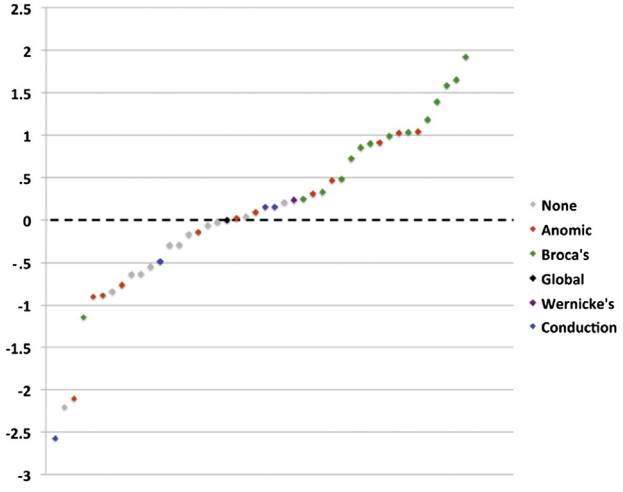

Fig. 3 – Z-transformed scores for improved fluency. Scores greater than 0 indicate increased fluency during SE conditions relative to spontaneous speech. Each participant is plotted along the *x* axis, with colors corresponding to aphasia type.

4. Discussion

4.1. *Summary of findings*

The aim of this study was to understand better the neural mechanism of SE by 1) relating neuroanatomical damage that supports or precludes a positive behavioral response to SE, and 2) providing evidence to inform a theoretical explanation of SE's mechanism of action. The VLSM analysis revealed that participants with damage to a relatively restricted area of the IFGpo and IFGpt benefitted from the fluency inducing effects of SE, while those with damage to other regions of the left hemisphere did not benefit from SE. These findings inform brain-behavior relationships in the response to fluency treatment and indicate that SE compensates for damage to

production mechanisms in the IFG, provided the ventral processing stream, auditory-motor "interface" (Hickok & Poeppel, 2000, 2004, 2007) and cortical motor areas are intact. Individuals with non-fluent aphasia demonstrated significantly fewer DWPM during spontaneous speech production tasks, emphasizing reduced speech fluency in these patients. During conditions of SE, participants with non-fluent aphasia demonstrated significantly greater improvement in DWPM when compared to individuals with fluent aphasias or no aphasia. Interestingly, DWPM scores for the SE tasks were not significantly different between groups, suggesting that during SE, those with non-fluent speech have the capability to demonstrate significantly more fluent speech production comparable to that of more fluent individuals. On the other hand, the non-fluent group showed a numerical trend for slower performance during SE than the control group, and one could speculate that there was some allowable improvement that was not met.

4.2. *Clinical implications*

Here, we demonstrated that individuals with Broca's aphasia reap the most benefit from SE. Following some familiarization with the protocol, SE provides an almost automatic means to increase speech output when production is accompanied by an AV model. This point should be emphasized by the fact that participants in this study completed SE across three short tasks (following clinician instruction), yet still demonstrated significant gains in fluency. As suggested by our previous work, SE training may ultimately provide an efficient and effective treatment for non-fluent individuals, which is especially important when the time and duration of speech/language therapy services for many individuals is often very limited. During SE, non-fluent speech, often intractable to therapeutic gains, appears to respond within a short time frame, with potential for long-term benefit (Fridriksson et al., 2012).

Classical typology of aphasia has been amply criticized for well over a century (Caramazza, 1984; Darley, 1982, 1983; Geschwind, 1965; Goodglass & Kaplan, 1972; see McNeil & Kimelman, 2001 for review; Schwartz, 1984). Nevertheless, most studies of aphasia list aphasia type and several studies suggest that different aphasia types are associated with distinct lesion patterns (Buchsbaum et al., 2011; Damasio & Damasio, 1980; Fridriksson et al., 2014; Kreisler et al., 2000;). Along with our previous study of SE treatment (Fridriksson et al., 2012), the current data suggest that the positive effects of SE on speech production primarily benefit patients with one aphasia type: Broca's aphasia. However, it remains to be demonstrated what specific processes (e.g., motor planning, grammatical processing, lexical retrieval) improve as a result of SE treatment. It is also important to point out that almost half of the patients who spoke more with the aid of SE compared to spontaneous speech did not have Broca's aphasia. Some patients designated as being 'fluent' based on the fluency rating scale (rating >4) on the WAB-R do not necessarily present with normal speech rate. For example, these patients may be rated in the range of 5–7 on the WAB-R. Accordingly, it is possible for patients who are designated as being fluent to improve their speech fluency. Whereas SE may primarily benefit patients with Broca's aphasia, it may also prove to be beneficial for patients with other types of aphasia.

The effect of SE on increased speech output can be very striking in some aphasic patients. It is important to emphasize that action observation and modeling is not a new concept in rehabilitation. For example, Ertelt et al. (2007) demonstrated that a four-week rehabilitation program that emphasized action observation yielded positive improvements in motor function among chronic stroke patients. A recent review by Small, Buccino, and Solodkin (2013) further explains how rehabilitation that utilizes modeling and action observation may modulate residual brain networks and, thereby, aid in stroke recovery. Positive effects of modeling motor actions have also been demonstrated in aphasia rehabilitation. A previous study by our group (Fridriksson, Baker, et al., 2009; Fridriksson, Moser, et al., 2009) revealed greater improvement in naming following a rehabilitation regiment where non-fluent aphasic patients paired pictures with audio-visual stimuli (showing the mouth of the speaker producing a word) compared to when pictures were paired with auditory only stimuli. Similar effects have been reported by Lee, Fowler, Rodney, Cherney, and Small (2010) and Sarasso et al. (2014). As far as we can tell, Rosenbek, Lemme, Ahern, Harris, and Wertz (1973) were among the first to explicitly utilize speech mimicking as a part of a published approach to treat adult neurogenic speech problems (their approach focused specifically on apraxia of speech). Melodic Intonation Therapy (MIT) also includes an aspect of real-time speech mimicking (Helm-Estabrooks, Nicholas, & Morgan, 1989). Although MIT and the treatment hierarchy outlined by Rosenbek and colleagues include steps that require the patient to speak in unison with the clinician, each of these approaches relies on multiple other steps that are thought to be more crucial for treatment success.

4.3. *Theoretical implications*

It is pertinent to ask why some patterns of cortical damage predict SE's benefits to speech fluency, while others do not demonstrate similar gains. Furthermore, how can theories of speech production inform future study of SE to further its utility as a therapy for impaired speech fluency? A brief discussion of current speech models is warranted before explaining SE's proposed mechanism of action relative to internal monitoring for speech production. The interaction between feedback and feedforward mechanisms for the purpose of speech production has been outlined in the recently developed Hierarchical State Feedback Control model (HSFC; Hickok, 2014), which builds on previous models (Houde & Nagarajan, 2011). According to the HSFC model, word (lemma) selection activates two levels of processing: 1). A higher-level cortical auditory-motor circuit that contains motor syllable programs in Brodmann's area (BA) 44, auditory syllable targets in the superior temporal sulcus and superior temporal gyrus, and an area the lies at the notch of the left Sylvian fissure at the temporal and parietal junction (area Spt; Hickok, Houde, & Rong, 2011) that accomplishes auditory-to-articulation transformations; and 2), a lower-level somatosensory motor circuit that is comprised of somato-phoneme

targets in the anterior supramarginal gyrus and S1 as well as motor phoneme programs in the ventral BA 6 and M1.

Based on the observation that non-fluent patients can produce fluent speech with the aid of SE, it appears that lower level speech motor commands at the level of BA 6 and M1 are relatively intact in these individuals, but that non-fluent speech occurs because of an impairment at the level of motor syllable programs in BA 44. This results in inability to access lower level motor commands and/or successfully utilize feedforward error correction mechanisms. We propose that there are two possible mechanisms by which SE may aid speech production in non-fluent aphasia. The first account posits that SE works at the lower-level of processing by providing non-fluent patients surrogate, multisensory targets to guide speech production. Based on data showing the influence of visual and heard speech on speech production (Fridriksson, Baker, et al., 2009; Fridriksson, Moser, et al., 2009, Fridriksson et al., 2012; Reisberg, McLean, & Goldfield, 1987), we hypothesize that the multisensory input provided by SE's AV model improves speech fluency by providing sensory targets at the level of proprioception (somato-phoneme targets), which subsequently interacts with the motor phoneme programs (vBA 6 and M1) to tune internal monitoring (Hickok, 2012) and guide speech production (Houde & Nagarajan, 2011). Although this account is plausible, we suggest it is not probable as enhanced activation at the level of the somatosensory motor circuit does not necessarily compensate for damage in BA 44, which is not included as part of this circuit.

An alternative account that is perhaps more plausible suggests that SE works at the higher-level cortical auditory-motor circuit of processing. This explanation proposes that SE activates auditory–visual syllable targets, perhaps rooted in the posterior middle temporal gyrus (Venezia et al., under review). Much like is the case for auditory syllable targets that are mapped onto articulation via the area Spt, the same processing route could be assumed for AV syllable targets. However, the fact that patients do not benefit from auditory only SE suggests that AV SE may assume an alternative route and bypass motor syllable programs in BA 44. Although we favor an explanation that suggests SE facilitates speech via activation of the auditory-motor circuit, our current data cannot definitively adjudicate between these two possible accounts. Nevertheless, it is possible that future studies might, for example, rely on structural connectivity analyses to determine if damage to white matter pathways that subserve either the higher-level cortical auditory-motor circuit or the lower-level somatosensory-motor circuit predicts SE success.

It is pertinent to point out that our theoretical explanations do not account for the specific role of mimicry in SE. Mimicking others probably plays an important role in speech development (Abravanel & DeYong, 1991; Abravanel & Sigafoos, 1984) and adult humans adapt their speech behaviors to others in their environment, including speech rate and utterance length (Cappella & Planalp, 1981; Matarazzo, Wiens, Matarazzo, & Saslow, 1968; Webb, 1972). Given that SE elicits fluent speech production in some aphasic patients whereas the same effect is not seen in actual speech repetition, it is clear that the real-time synchrony between the speech model and the entrained speaker is crucial. Accordingly, it could be the case that SE takes advantage of a mechanism that is not at all speech specific but may instead be crucial for social cohesion and cooperation (for discussion see Gueguen, Jacob, & Martin, 2009). However, far more research is needed to verify such accounts.

5. Conclusions

In this study, we show that SE improves fluency in individuals with non-fluent (Broca's) aphasia, likely accounting for impaired processing in Broca's area, specifically the IFGpo. Not only did we identify patterns of damage that support improved fluency in SE, we suggest two preliminary theoretical accounts for why SE may improve speech production in aphasic patients. Importantly, the IFGpo appears to be a crucial area for the formation of speech syllable programs, which guide internal monitoring prior to the programming of these movements in primary and supplementary motor areas. SE facilitates speech by either providing the speaker with somato-phoneme targets that facilitate fluent speech production via a lower-level somatosensory motor circuit or by activating auditory–visual syllable targets in a higher-level cortical auditory-motor circuit. Ultimately, localizing areas that mediate a response to treatment may add additional information to the precise localization of damage that underlies non-fluent speech.

Potential conflicts of interest

The authors have no other disclosures, financial or otherwise, to declare.

J.F. conceived the study; J.F., L.B., A.B., and C.R. compiled and analyzed the data; J.F., A.B. and G.H. interpreted the data; J.F. and A.B. wrote the article with contributions from all authors.

Acknowledgment

The research reported here was supported by a grant from the National Institutes on Deafness and other Communication Disorders (DC009571).

REFERENCES

Abravanel, E., & DeYong, N. G. (1991). Does object modeling elicit imitative-like gestures from young infants? *Journal of Experimental Child Psychology*, 52(1), 22–40.

Abravanel, E., & Sigafoos, A. D. (1984). Exploring the presence of imitation during early infancy. *Child Development*, 381–392.

Ashburner, J., & Friston, K. J. (2005). Unified segmentation. *NeuroImage*, 26(3), 839–851.

Brett, M., Leff, A. P., Rorden, C., & Ashburner, J. (2001). Spatial normalization of brain images with focal lesions using cost function masking. *NeuroImage*, 14(2), 486–500.

Buchsbaum, B. R., Baldo, J., Okada, K., Berman, K. F., Dronkers, N., D'Esposito, M., et al. (2011). Conduction aphasia, sensory-motor integration, and phonological short-term memory–an

aggregate analysis of lesion and fMRI data. *Brain and Language, 119*(3), 119–128.
Cappella, J. N., & Planalp, S. (1981). Talk and silence sequences in informal conversations III: interspeaker influence. *Human Communication Research, 7*(2), 117–132.
Caramazza, A. (1984). The logic of neuropsychological research and the problem of patient classification in aphasia. *Brain and Language, 21*(1), 9–20.
Dabul, B. L. (2000). *Apraxia battery for adults* (2nd ed.). Austin, TX: Pro-ed.
Damasio, H., & Damasio, A. R. (1980). The anatomical basis of conduction aphasia. *Brain, 103*(2), 337–350.
Darley, F. L. (1982). *Aphasia*. Philadelphia: WB Saunders Company.
Ertelt, D., Small, S., Solodkin, A., Dettmers, C., McNamara, A., Binkofski, F., et al. (2007). Action observation has a positive impact on rehabilitation of motor deficits after stroke. *NeuroImage, 36*, T164–T173.
Fridriksson, J., Baker, J., Whiteside, J., Eoute, D., Moser, D., Vasselinov, R., et al. (2009). Treating visual speech perception to improve speech production in non-fluent aphasia. *Stroke, 40*, 853–858.
Fridriksson, J., Fillmore, P., Guo, D., & Rorden, C. (2014). Chronic Broca's aphasia is caused by damage to Broca's and Wernicke's areas. *Cerebral Cortex*. http://dx.doi.org/10.1093/cercor/bhu152.
Fridriksson, J., Hubbard, H. I., Hudspeth, S. G., Holland, A. L., Bonilha, L., Fromm, D., et al. (2012). Speech entrainment enables patients with Broca's aphasia to produce fluent speech. *Brain, 135*(12), 3815–3829.
Fridriksson, J., Moser, D., Ryalls, J., & Bonilha, L. (2009). Modulation of frontal lobe speech areas associated with the production and perception of speech movements. *Journal of Speech, Language, and Hearing Research, 52*(3), 812–819.
Geschwind, N. (1965). Disconnection syndromes in animals and man. *Brain, 88*, 237–294.
Goodglass, H., & Kaplan, E. (1972). *The assessment of aphasia and related disorders* (pp. 1–80). Philadelphia: Lea & Febiger.
Goodglass, H., Kaplan, E., & Barresi, B. (2001). *Boston diagnostic aphasia examination* (3rd ed.). Philadelphia: Lippincott Williams & Wilkins.
Gueguen, N., Jacob, C., & Martin, A. (2009). Mimicry in social interaction: its effect on human judgment and behavior. *European Journal of Social Sciences, 8*(2), 253–259.
Helm-Estabrooks, N., Nicholas, M., & Morgan, A. (1989). *MIT, melodic intonation therapy manual*. San Antonio: Special Press.
Hickok, G. (2012). Computational neuroanatomy of speech production. *Nature Reviews Neuroscience, 13*(2), 135–145.
Hickok, G. (2014). Towards an integrated psycholinguistic, neurolinguistic, sensorimotor framework for speech production. *Language, Cognition and Neuroscience, 29*(1), 52–59.
Hickok, G., Houde, J., & Rong, F. (2011). Sensorimotor integration in speech processing: computational basis and neural organization. *Neuron, 69*(3), 407–422.
Hickok, G., & Poeppel, D. (2000). Towards a functional neuroanatomy of speech perception. *Trends in Cognitive Sciences, 4*(4), 131–138.
Hickok, G., & Poeppel, D. (2004). Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. *Cognition, 92*(1), 67–99.
Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nature Reviews Neuroscience, 8*(5), 393–402.
Houde, J. F., & Nagarajan, S. S. (2011). Speech production as state feedback control. *Frontiers in Human Neuroscience, 5*.
Kertesz, A. (2007). *The western aphasia battery-revised*. New York: Grune & Stratton.
Kreisler, A., Godefroy, O., Delmaire, C., Debachy, B., Leclercq, M., Pruvo, J. P., et al. (2000). The anatomy of aphasia revisited. *Neurology, 54*(5), 1117–1123.
Lee, J., Fowler, R., Rodney, D., Cherney, L., & Small, S. L. (2010). IMITATE: an intensive computer-based treatment for aphasia based on action observation and imitation. *Aphasiology, 24*(4), 449–465.
Matarazzo, J. D., Wiens, A. N., Matarazzo, R. G., & Saslow, G. (1968). Speech and silence behavior in clinical psychotherapy and its laboratory correlates. In J. Schlier, H. Hunt, J. D. Matarazzo, & C. Savage (Eds.), *Research in psychotherapy* (pp. 347–394). Washington, DC: American Psychological Association.
McNeil, M. R., & Kimelman, M. D. (2001). Darley and the nature of aphasia: the defining and classifying controversies. *Aphasiology, 15*(3), 221–229.
Reisberg, D., McLean, J., & Goldfield, A. (1987). "Easy to hear but hard to understand" a lip-reading advantage with intact auditory stimuli. In B. Dodd, & R. Campbell (Eds.), *Hearing by eye: The psychology of reading* (pp. 97–113). London: Lawrence Erlbaum.
Rorden, C., Bonilha, L., Fridriksson, J., Bender, B., & Karnath, H. O. (2012). Age-specific CT and MRI templates for spatial normalization. *NeuroImage, 61*(4), 957–965.
Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesions. *Behavioural Neurology, 12*(4), 191–200.
Rorden, C., & Karnath, H.-O. (2004). Using human brain lesions to infer function: a relic from a past era in the fMRI age? *Nature Reviews Neuroscience, 5*, 812–818.
Rosenbek, J. C., Lemme, M. L., Ahern, M. B., Harris, E. H., & Wertz, R. T. (1973). A treatment for apraxia of speech in adults. *Journal of Speech and Hearing Disorders, 38*(4), 462–472.
Sarasso, S., Määttä, S., Ferrarelli, F., Poryazova, R., Tononi, G., & Small, S. L. (2014). Plastic changes following imitation-based speech and language therapy for aphasia a high-density sleep EEG study. *Neurorehabilitation and Neural Repair, 28*(2), 129–138.
Schwartz, M. F. (1984). What the classical aphasia categories can't do for us, and why. *Brain and Language, 21*(1), 3–8.
Small, S. L., Buccino, G., & Solodkin, A. (2013). Brain repair after stroke—a novel neurological model. *Nature Reviews Neurology, 9*(12), 698–707.
Venezia, J., Fillmore, P., Hickok, G., & Fridriksson, J. (2015). *Perception drives production across sensory modalities: A cortical network for sensorimotor integration of visual speech* (Under review).
Webb, J. T. (1972). Interview synchrony: an investigation of two speech rate measures in an automated standardized interview. In B. Pope, & A. W. Siegman (Eds.), *Studies in dyadic communication* (pp. 115–133). New York: Pergamon.