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The effects of simulated stuttering and prolonged speech on the neural activation patterns of stuttering and nonstuttering adults

Luc F. De Nil [a,b,c,*], Deryk S. Beal [a,b,c], Sophie J. Lafaille [a,b], Robert M. Kroll [a,d], Adrian P. Crawley [b], Vincent L. Gracco [e,f]

[a] Department of Speech-Language Pathology, University of Toronto, 500 University Avenue, Room 160, Toronto, Ont., Canada M5G 1V7
[b] Toronto Western Research Institute, University Health Network, Toronto, Ont., Canada
[c] Hospital for Sick Children Research Institute, Toronto, Ont., Canada
[d] Speech Foundation of Ontario, Toronto, Ont., Canada
[e] School of Communication Sciences and Disorders, McGill University, Montreal, Que., Canada
[f] Haskins Laboratories, New Haven, CT, USA

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ABSTRACT

Functional magnetic resonance imaging was used to investigate the neural correlates of passive listening, habitual speech and two modified speech patterns (simulated stuttering and prolonged speech) in stuttering and nonstuttering adults. Within-group comparisons revealed increased right hemisphere biased activation of speech-related regions during the simulated stuttered and prolonged speech tasks, relative to the habitual speech task, in the stuttering group. No significant activation differences were observed within the nonstuttering participants during these speech conditions. Between-group comparisons revealed less left superior temporal gyrus activation in stutterers during habitual speech and increased right inferior frontal gyrus activation during simulated stuttering relative to nonstutterers. Stutterers were also found to have increased activation in the left middle and superior temporal gyri and right insula, primary motor cortex and supplementary motor cortex during the passive listening condition relative to nonstutterers. The results provide further evidence for the presence of functional deficiencies underlying auditory processing, motor planning and execution in people who stutter, with these differences being affected by speech manner.

1. Introduction

Recent brain imaging research has shown that as a group, persons who stutter demonstrate a distinctive pattern of functional neural activation during speech production relative to nonstuttering individuals. This distinctive pattern is evident even during perceptually fluent speech and is characterized by increased right hemisphere or bilateral activation of speech motor areas (Biermann-Ruben, Salmelin, & Schnitzler, 2005; Blomgren, Nagarajan, Lee, Li, & Alvord, 2003; De Nil, Kroll, Kapur, & Houle, 2000; Preibisch, Neumann et al., 2003), overactivation of sensorimotor areas and cerebellum (De Nil et al., 2000) and reduced activation in auditory areas (Braun et al., 1997; Fox et al., 1996; Ingham, Fox, Ingham, & Zamarripa, 2000).

The distinctive pattern of functional brain activation in adults who stutter is thought to reflect both genetic and early developmental influences as well as later acquired characteristics resulting from a lifetime of covert and overt coping behaviors. The extent to which these reactive behaviors influence the functional neural activation pattern is unknown but possibly significant given that changes to overt speech behavior may influence patterns of functional activation (Riecker, Kassubek, Gröschel, Grodd, & Ackermann, 2006; Schulz, Varga, Jeffires, Ludlow, & Braun, 2005). Elucidating the effects of specific speech modifications on brain function in adults who stutter and comparing these to the activation changes observed in nonstuttering individuals may provide further information on the locus and potential contribution of brain processes in stuttering which are more or less amenable to external influences. As such, the outcomes of the current study will allow for better informed interpretation of the results of previously published and future neuroimaging studies.

In a number of studies of stuttering speakers, speech tasks in which the participants used their habitual (natural or not modified) speaking style was compared to a speech style known to induce fluency. For instance, Fox et al. (1996, 2000) used positron emission tomography to examine stuttering participants' performance during unmodified reading aloud versus choral reading (i.e., reading a passage out loud together with a fluent reader), a task known to be fluency-enhancing. Their results revealed a pattern of activation associated with the

* Corresponding author. Address: Department of Speech-Language Pathology, University of Toronto, 500 University Avenue, Room 160, Toronto, Ont., Canada M5G 1V7.
E-mail address: luc.denil@utoronto.ca (Luc F. De Nil).

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habitual speech of stutterers that included bilateral motor system activation, overall overactivation in the motor system and reduced left lateralized auditory activation. The modified choral reading task resulted in an activation pattern associated with a reduction in the overactivation of the motor areas and a reversal of the auditory underactivation. Braun et al. (1997) and Stager, Jeffries, and Braun (2003) compared brain activations of both nonstuttering and stuttering individuals during habitual speech versus fluency-enhancing paced speech and singing. In each study, both nonstuttering and stuttering participants were found to have increased activation in the auditory association areas during paced speech and singing.

Other studies have examined brain activation differences before and after fluency shaping therapy for stuttering. Such treatment in adults essentially teaches a modified articulatory pattern that is more conducive to speech fluency. Interestingly, people who stutter demonstrated a similar pattern of overactivation in the motor system, bilateral activation in the motor system and reduced auditory activation prior to and immediately following treatment (De Nil, Kroll, Lafaille, & Houle, 2003; Neumann et al., 2003, 2005). De Nil et al. (2003) found that the overactivation observed in the motor cortex pre- and immediately post-treatment was reduced significantly after 1 year of maintenance treatment, and became more similar to activation patterns seen in nonstuttering individuals. Neumann et al. (2003), however, reported that 2 years after treatment, the overactivation in the right frontal and parietal, bilateral temporal, limbic regions and putamen, which was noted immediately post-therapy, could still be observed. Comparing these two studies by De Nil et al. (2003) and Neumann et al. (2003) it is not clear whether the overactivation which was observed 2 years post-treatment by Neumann et al., but which was not reported 1 year post-treatment by De Nil et al., indicates a persistence of overactivation or possibly a re-emergence of such overactivation in the second year post-treatment.

Changing the speech manner in stuttering individuals through treatment or fluency-enhancing conditions clearly results in significant changes in brain activation. Typically, these observed changes have been interpreted as resulting from increased speech fluency under such speaking conditions. However, the observed activation changes may also reflect the changed motor behavior, regardless of whether or not an increase in speech fluency accompanies this change. In the present study, we compared neural activation associated with passive listening to habitual overt production of auditorily presented words in stuttering and nonstuttering individuals as a replication of previous neuroimaging studies. In addition, we examined whether two modified speech tasks, namely simulated stuttering and prolonged speech, representing voluntary modified speech behaviors not unlike those used in a number of fluency interventions, would result in within- and between-group differences in neural activation. By asking both the stuttering and nonstuttering participants to produce speech in this way, we anticipated to be able to better untangle the activation effects that result from such modified observable behavior and that can be observed for both stuttering and nonstuttering participants, from those activation differences that are specific to the group of stuttering individuals. It was predicted that both voluntary stuttering and prolonged speech would result in significantly increased activation in the speakers and that this overactivation would be more pronounced and widespread in the stuttering group.

2. Methodology

2.1. Participants

Fifteen stuttering and 15 nonstuttering men recruited from the Toronto area participated in the current study. All participants were right handed as assessed by the Edinburgh Handedness Inventory (Oldfield, 1971), and all had a negative history of neurological deficits and hearing, speech or language difficulties (except for developmental stuttering for the stutterers). Each participant was screened by a speech-language pathologist for normal hearing. The two participant groups were similar in age ($t(28) = 0.497$, $p = .623$), with a mean age of 31.7 years for the stuttering participants ($SD = 7.5$; range 21–47 years), and 33.0 years ($SD = 7.2$; range: 24–48 years) for the nonstuttering speakers. The stuttering participants were all identified as having developmental stuttering by a qualified speech-language pathologist, and their Stuttering Severity Index (Riley, 1994) scores ranged from 8 to 49 with two participants classified as very mild, 1 as mild, 9 as moderate, 1 as severe and 2 as very severe.

2.2. Task design

The fMRI experiment consisted of four tasks counterbalanced across participants. Each task consisted of the random auditory presentation of 20 words and 20 silent stimuli, using the MRI-compatible Commander XG audio headphone system (Resonance Technology, Northridge, CA). Participants practiced all tasks prior to the scanning session and again prior to the presentation of each of the four individual tasks in the scanner. The second practice session was used to confirm the participants' compliance with the task instructions. The four experimental tasks consisted of one passive listening task and three overt speech repetition tasks. For each of the four tasks, all word stimuli were presented auditorily as described for the listen task. The four tasks were:

Listen to single words (Listen): Participants were presented with 20 single two-syllable words presented binaurally using MRI-compatible headphones. The stimuli were presented at a participant-defined comfortable loudness level.

Repeat single words using a habitual speech pattern (Repeat): Participants were instructed to repeat the words out loud using their habitual (natural) speech pattern.

Repeat single words using a simulated stuttered speech pattern (Simulate): Participants were instructed to repeat each word out loud while repeating the first sound or syllable multiple times (e.g., baseball—*/b-b-b-baisbal/*).

Repeat single words using a prolonged speech pattern (Prolong): Participants were instructed to repeat each word out loud while prolonging the sounds in each word (e.g., flower—*/f:l:o:w:er:/*).

2.3. Stimuli

Eighty two-syllable English nouns matched for number of phonemes, frequency, familiarity and concreteness were generated from the MRC Psycholinguistic Data Base Machine Usable Dictionary version 2.0 (http://www.psy.uwa.edu.au/MRCDataBase/uwa_mrc.htm). Examples of stimulus words are: *trolley, candle, blossom, woman, butcher, railroad, whiskey, bedroom, midnight*. Each word was digitally recorded in a soundproof booth as it was being read aloud by a male native speaker of standard Canadian English. These recordings were used as auditory stimuli during the MRI scan and presented aurally using Superlab 2.0.4 (Cedrus Inc.).

2.4. Imaging

A 1.5-T Echospeed MRI system (GE Medical Systems, Milwaukee, WI) and a standard quadrature head coil were used to obtain all images. For anatomical images, a *T*1-weighted 3D IR (inversion recovery)-prepared FSPGR sequence (flip angle = 20°, TE = 5.2 ms, TR = 12 ms, prep. time = 300 ms) was used to generate 124 1.5-mm-thick sagittal slices (256 × 256 matrix, 30 × 30 cm field of view). For functional imaging, 29 5-mm-thick (gap = 1mm) $T2^*$-

weighted sagittal slices were acquired with a gradient echo sequence using a single-shot spiral trajectory through *k*-space (Glover & Lee, 1995), flip angle = 85°,TE = 40 ms, TR = 10 s, 64 × 64 matrix, 24 × 24 cm field of view. Each single 2-s acquisition frame was preceded by an 8-s silent interval during which single word stimuli were presented, resulting in a total interstimulus interval of 10 s. This stimulus sequence was repeated 40 times, each sequence containing one of the randomly assigned word ($n = 20$) or silent ($n = 20$) audio stimuli. For the listen task, stimuli were presented 3 s into each sequence. For the overt tasks, the stimuli were presented 0.5 s into each stimulus sequence. The timing of the experiment was designed in such a way that the 2-s scan would occur approximately 5 s following the onset of either the auditory presentation or the overt production of the word (Fig. 1). Previous studies have shown that the peak of the BOLD response is expected to occur at approximately 5–6 s following single word stimuli (Friston, 1997; Hickok, Love, Swinney, Wong, & Buxton, 1997; Josephs, Turner, & Friston, 1997).

2.5. Analysis

All images were processed and analyzed using SPM2 (Welcome Department of Imaging Neuroscience). The images were realigned to the first image by rigid body transformation, and transformed by non-linear transformation to normal anatomical space (Friston et al., 1995) using the Montreal Neurological Institute template. The data were smoothed spatially with a Gaussian kernel of full width half maximum (FWHM) of 10 mm. The realignment parameters were applied as motion regressors for all experiments. All spatial coordinates are listed in MNI space.

The first level contrast images (word minus baseline) for each task were analyzed using a Finite Impulse Response (FIR) stick function (Manoach, Greve, Lindgren, & Dale, 2003). Each acquired frame was considered a single stick function by setting the SPM FIR window to 2 s and setting the SPM defaults time bin to 1. These first level contrast images were then entered into a second level random effects analysis. For the within- and between-group comparisons of the random effects analyses one group paired *t*-tests or two group independent *t*-tests were performed as appropriate. Activations were localized using the SPM Anatomy Toolbox (Eickhoff et al., 2005), identifying peak activations as well the spatial extent of the cluster. In any instances where the toolbox failed to identify specifically a particular cortical or subcortical area, the nearest brain region was listed in the tables (identified as **adjusted localization*). For presentation purposes only, fMRI data presented in the figures were overlaid on the canonical single subject *T*1 template provided with SPM2. All statistical analyses were done using a corrected family-wise error (FWE) of 0.05 unless otherwise indicated.

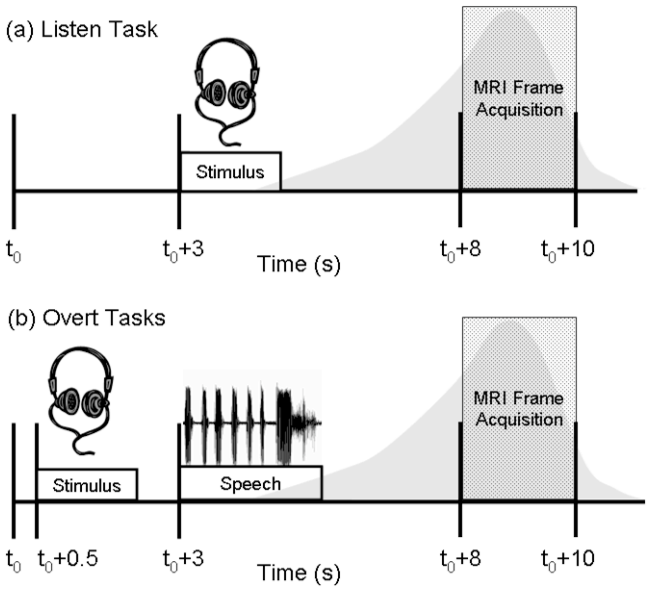

Fig. 1. Experimental design of listen (a) and overt (b) tasks.

In addition to the functional image analyses, a number of behavioral measures were obtained from the participants' audio recorded verbal responses. These measures included speech onset, word production duration, and number of word segment repetitions. Intra-rater reliability showed very high correlation between raters' measurements: onset time ICC = .996 ($p < .001$); word duration ICC = .989 ($p < .001$); and number of repetitions ICC = .915 ($p < .001$).

2.6. Listener perception study

A listener perception study was completed in order to investigate to what extent naïve listeners could perceptually differentiate between the utterances of stuttering and nonstuttering participants. A total of 180 utterances (approximately 20% of the total number of utterances of all participants) were randomly selected from the stuttering participant group for each of the three overt speech tasks (natural speech, simulated stuttered speech, prolonged speech; 60 from each task). These randomly selected words were paired with a randomly selected but identical word from the nonstuttering group for presentation. For half of the paired stimuli, a stuttering participant's production was presented first, followed by a production of the same word by a nonstuttering participant. For the other half of the stimuli, productions by nonstuttering participants were presented first. The word pairs were presented in a random order. Twenty naïve listeners, who were either qualified speech-language pathologists or graduate students who had completed advanced course work in speech fluency disorders, were asked to identify the stuttering participant for half of the word pairs and the nonstuttering participant for the other half of the word pairs.

3. Results

3.1. Behavioral measures

Each group of participants generated 300 overt single word productions (15 participants × 20 utterances) in each of the three speech conditions. To examine whether the speech tasks may have induced genuine involuntary stuttering, the second author and a research assistant independently listened to all utterances for the purpose of identifying genuine involuntary stuttering as characterized by blocks, arrhythmic and irregular speech sound repetitions and prolongations and struggle behavior. In the stuttering group 4 (1.3%) utterances in the habitual speech pattern condition were perceptually identified as stuttered, the same number of utterances (4 or 1.3%) in the simulated stuttering and two utterances (0.6%) in the prolonged speech condition were identified as evidencing real stuttering. None of the utterances by the nonstuttering participants were identified as stuttered. The speech onset times and overall word duration results and number of simulated repetitions for the stuttering and nonstuttering participants for each overt task are presented in Table 1. None of the between-group differences for any of the three behavioral measures were statistically significant. With regard to the perceptual listener study, the likelihood of correctly identifying a speaker as either a stuttering or a nonstuttering person for the habitual speech task

was 66.75 ($t = 9.68$, $p < .05$), for simulated stuttering 61.36 ($t = 6.82$, $p < .05$), and for prolonged speech 60.35 ($t = 6.43$, $p < .05$).

3.2. Functional neural activation

3.2.1. Passive listening

When instructed to listen to single words without any overt response, both the nonstuttering and the stuttering participants showed left lateralized activation in the temporal gyrus (Fig. 2a and b and Table 2). Statistically corrected significant peak activations for the nonstuttering participants were observed in the left superior temporal gyrus (BA 22) extending into the primary auditory cortex (BA 41–42) and the parietal operculum. Similar to the nonstuttering speakers, significant activation in the stuttering group also was localized in the temporal cortex. In contrast to the nonstuttering speakers, however, the peak activation in the temporal cortex for the stuttering speakers was observed in the left middle temporal gyrus, with this cluster of activation extending into the primary auditory cortex and the parietal operculum, similar to what was observed in the nonstuttering participants.

Significant between-group differences ($p \leqslant .001$ uncorrected) for the listen task were also found (Table 4). Compared to the stuttering participants, the nonstuttering speakers showed increased activation in the thalamus, bilaterally in the medial aspect of the superior frontal gyrus, right cerebellum, and right insula. Relative to the nonstutterers, the stutterers showed two large clusters of significantly increased activation. One cluster was left lateralized and peaked in the middle temporal gyrus, extending into the superior temporal gyrus including the primary auditory cortex. The second cluster was right lateralized and included the right insula and primary motor cortex extending into the supplementary motor area. Two additional smaller areas of significant activation were found in the right superior temporal gyrus, at the level of anterior and posterior BA 22.

3.2.2. Overt speaking using a habitual speech pattern

When asked to repeat heard single words using their habitual speech, both nonstuttering and stuttering participants showed significantly increased cortical activation relative to the baseline task (Fig. 2c and d and Table 2). Activation for the nonstuttering participants was primarily lateralized with several peak activations in the left superior temporal gyrus. Although peak activations were localized in the left superior temporal gyrus, the clusters extended anteriorly into the postcentral gyrus, primary motor and premotor cortex, and Broca's area (BA 44), consistent with the motor planning and execution involved in this task. Additional activation was observed medially in the anterior portion of the cingulate cortex, in the right parahippocampal gyrus and the region of the midbrain.

The significant activation in the stuttering participants during the overt habitual speak task, while also left lateralized, was less extensive than that observed in the nonstuttering participants. Activation was limited to the motor and premotor cortex, including the precentral gyrus, supplementary motor area and medially in the cingulate gyrus. In contrast to the activation patterns seen in the nonstuttering speakers, no significant activation was observed in auditory cortex in either hemisphere.

Significant between-group differences ($p \leqslant .001$ uncorrected) were found with the nonstuttering participants showing greater activation at the level of the left superior temporal gyrus and the midbrain (Table 4). No significant greater activation was observed in the stuttering group.

3.2.3. Overt speaking using a simulated stuttered speech pattern

Instructing the nonstuttering participants to speak using simulated stuttered speech compared to their habitual speaking pattern did not result in any differences in activation that survived the statistical correction threshold. In contrast, the stuttering speakers showed significantly increased activation bilaterally (Table 3). A large significant activation cluster was right lateralized with a peak in the superior temporal gyrus (Fig. 3a) and included the primary auditory cortex, the parietal operculum and extended anteriorly to BA 44 (homologues of Broca's area). Further increased right hemisphere activation was observed in the rolandic operculum and the supramarginal gyrus. Left lateralized increased activation in the stuttering participants involved the superior temporal gyrus, including the primary auditory cortex and parietal operculum, as well as more frontal motor regions located in the rolandic operculum and insula.

Not surprisingly given the lack of within-group differences for the nonstuttering speakers, between-group analysis of the data did not yield any significantly increased activation in the nonstuttering group compared to the stuttering speakers ($p \leqslant .001$ uncorrected). However, stuttering speakers showed significantly increased activation in the right inferior frontal gyrus (BA 44) compared to their fluent controls (Table 4).

3.2.4. Overt speaking using a prolonged speech pattern

When instructed to speak in a prolonged speech pattern, again the nonstuttering speakers showed no increased activation compared to the habitual speak task. The stuttering speakers, in contrast, showed increased activation in the right superior temporal

Table 1
Group means and standard deviations of speech onset time, word duration and number of repetitions for nonstuttering ($n = 13$) and stuttering ($n = 14$) speakers

Measure	Task	Group	Mean	Standard deviation
Onset (s)	Repeat	Controls	2.010	0.221
		Stutterers	2.161	0.421
	Simulate	Controls	2.065	0.253
		Stutterers	2.186	0.318
	Prolong	Controls	2.229	0.268
		Stutterers	2.321	0.397
Duration (s)	Repeat	Controls	0.698	0.071
		Stutterers	0.845	0.140
	Simulate	Controls	2.578	0.696
		Stutterers	2.851	0.684
	Prolong	Controls	3.596	0.997
		Stutterers	3.765	0.690
Repetition (#)	Simulate	Controls	7.19	2.53
		Stutterers	6.86	3.35

Note. Speech onset was significantly slower in the prolonged speech than in typical speech ($t(26) = 3.77$, $p = .001$) or simulated stuttering ($t(26) = 4.10$, $p < .001$), (paired samples t-tests). Word duration differed significantly between all overt tasks ($F(2, 50) = 173.01$, $p < .001$). Data is missing from two nonstuttering speakers and one stuttering speaker due to technical difficulties.

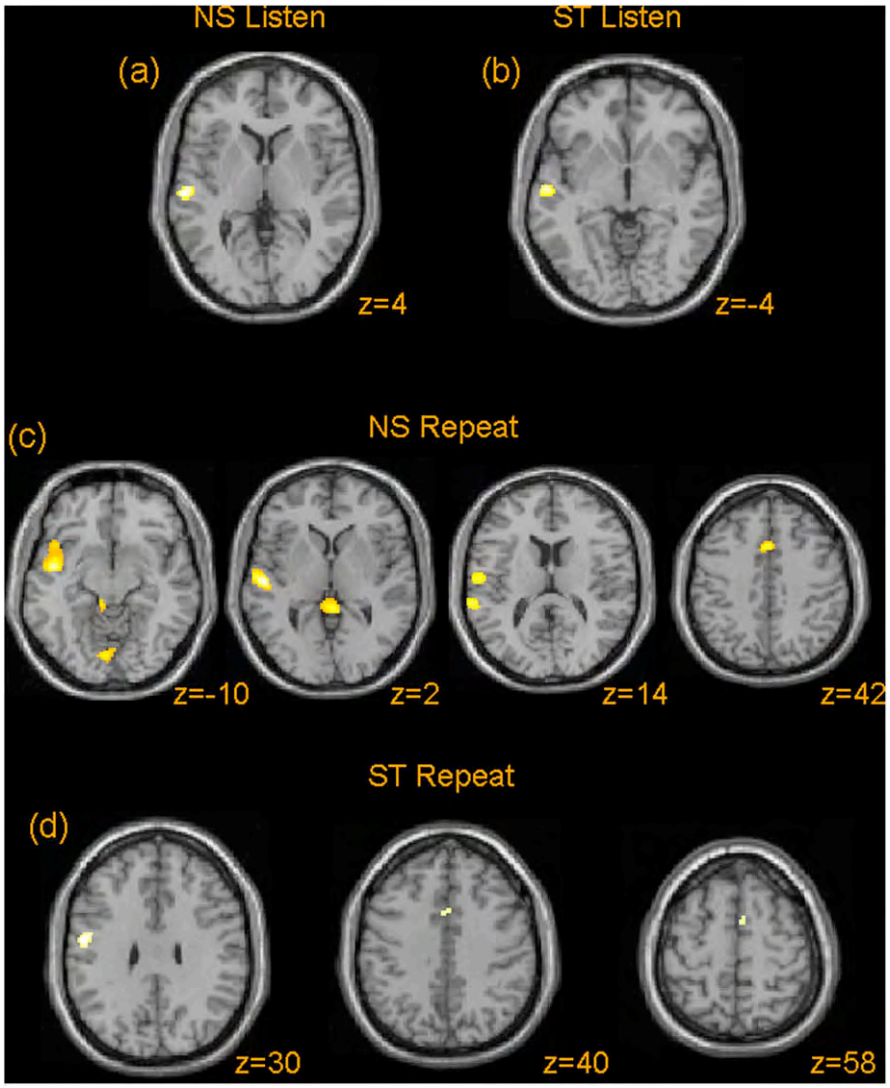

Fig. 2. Average activation ($n = 15$) during passive listening (a and b) and repeat (habitual) speech (c and d) for nonstuttering (NS) and stuttering (ST) adults. Full activation details can be found in Table 2.

gyrus including the primary auditory cortex (Table 3 and Fig. 3b). No significant between-group differences were found ($p \leqslant .001$ uncorrected).

4. Discussion

Results reported in previous functional imaging studies of persons who stutter have shown increased right and/or bilateral cortical activation of sensory and motor cortical areas involved in the planning and execution of speech movements (Biermann-Ruben et al., 2005; Blomgren et al., 2003; De Nil et al., 2000; Preibisch, Neumann et al., 2003). Several studies have also demonstrated decreased activation in primary auditory cortex (Braun et al., 1997; Fox et al., 1996; Ingham et al., 2000). In the current study, functional brain activation during a variety of speech tasks was evaluated to identify differences between stuttering and nonstuttering speakers, and to determine to what extent these differences were affected by changes in the manner of speech production.

4.1. Behavioral measures

No between-group differences in speech initiation were observed between the stuttering and nonstuttering speakers in any of the three overt speech tasks. Compared to habitual speech, participants in both groups showed a trend for slower speech onset times during simulated stuttering and significantly slower onset times during prolongation. The increased initiation times in these modified speech tasks suggest that execution was more deliberate and less automatic compared to habitual speech. Similarly, the absence of word duration differences between the two groups suggests that the task instructions resulted in similar modified speech behavior. This is further confirmed by the observation that no differences were observed between the two groups in number of word segments repeated during the simulated stuttering task. Essentially, the behavioral data suggest that the overt speech tasks resulted in speech productions that were similar for both groups. Nevertheless sophisticated but naïve listeners were still able to identify word productions as being produced by either a stuttering or nonstuttering speaker at a level that was somewhat better than chance. Apparently at least some of the utterances were produced in a qualitatively different manner by some of the stuttering speakers compared to their nonstuttering controls. These differences did not manifest themselves as overt stuttering given the very low percentage of perceptual stuttering across all recorded utterances. Because of these perceptual differences, it cannot be excluded that differences in functional activation that we observed between

Table 2
Peak activations for nonstuttering and stuttering participants at $p \leqslant .05$ corrected FWE for both the listen minus baseline and the repeat minus baseline contrast

Peak activation location	Laterality	MNI *x*	MNI *y*	MNI *z*	*Z* score	Cluster size
Listen—baseline						
Control subjects						
Superior temporal gyrus	L	−58	−20	4	5.47	156
Stuttering subjects						
Middle temporal gyrus	L	−58	−14	−4	5.59	164
Repeat—baseline						
Control subjects						
Superior temporal gyrus	L	−54	−16	2	5.88	807
Superior temporal gyrus	L	−46	−2	−10	5.66	504
Midbrain	L and R	−6	−34	−8	5.52	336
Cingulate gyrus	L	0	16	42	5.35	121
Superior temporal gyrus	L	−62	−36	14	5.35	144
Midbrain	L	−10	−22	−18	5.32	23
Lingual gyrus	R	−4	−80	−12	5.23	182
Parahippocampal gyrus	R	24	−18	−18	5.12	16
Stuttering subjects						
Precentral gyrus	L	−52	−8	30	5.13	98
Cingulate gyrus	R	2	12	40	4.86	45
Supplementary motor area	R	6	6	58	4.82	11

Note. Second level random effects analyses were performed using a within-group *t*-test.

Table 3
Peak activations for stuttering participants at $p \leqslant .05$ corrected FWE for the simulated stuttering minus repeat and the prolonged minus repeat contrast

Peak activation location	Laterality	MNI *x*	MNI *y*	MNI *z*	*Z* score	Cluster size
Stutter—repeat						
Superior temporal gyrus	L	−46	−30	18	5.87	126
Superior temporal gyrus	R	62	−18	0	5.70	1042
Cingulate gyrus*	L	−14	0	34	5.54	46
Rolandic operculum	R	38	−24	22	5.25	40
Insula	L	−32	4	12	5.14	22
Rolandic operculum	L	−52	−4	6	5.12	46
Subcortical	R	30	−4	20	5.07	22
Supramarginal gyrus	R	58	−30	32	5.05	30
Prolong—repeat						
Superior temporal gyrus	R	62	−6	−4	5.00	12

Note. Second level random effects analyses were performed using a paired (between tasks) *t*-test.
* Adjusted localization.

Table 4
Peak activations for subtractions between nonstuttering and stuttering participants at $p \leqslant .001$ uncorrected value

Peak activation location	Laterality	MNI *x*	MNI *y*	MNI *z*	Z score	Cluster size
NS > ST listen						
Thalamus	L	−12	−14	16	4.18	925
Superior frontal gyrus	L and R	0	52	38	3.57	84
Cerebellum	R	6	−40	−10	3.50	31
Insula*	R	28	−34	18	3.50	69
ST > NS listen						
Middle temporal gyrus	L	−64	−22	0	3.83	130
Rolandic operculum	R	42	2	14	3.68	143
Insula	R	32	22	−2	3.35	26
Superior temporal gyrus	R	48	−36	20	3.29	12
Superior temporal gyrus	R	54	−2	−14	3.23	15
NS > ST speak						
Midbrain*	R	10	−12	−16	3.63	18
Superior temporal gyrus*	L	−34	2	−18	3.61	27
Brainstem	L and R	0	−20	−22	3.23	12
ST > NS stutter						
Inferior frontal gyrus	R	54	6	24	3.35	16

Note. Second level random effects analyses were performed using a between-group *t*-test.
* Adjusted localization.

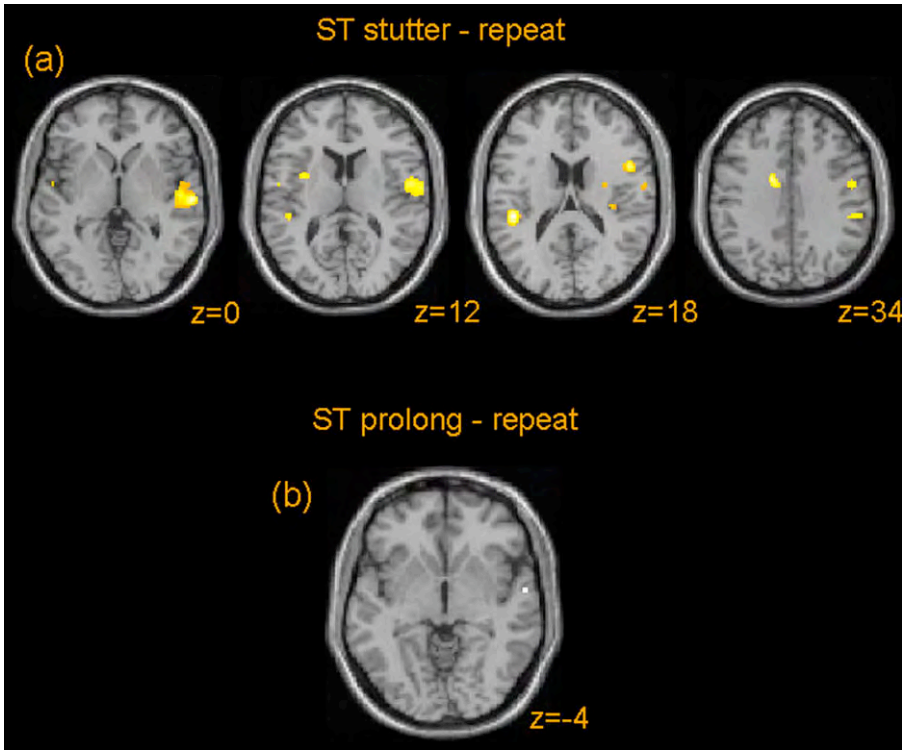

Fig. 3. Activation during simulated stutter minus repeat (a) and prolong minus repeat speech (b) for stuttering (ST) adults. No significant activations were observed for the nonstuttering participants. Full activation details can be found in Table 3.

the two groups during the simulated stuttering task were due in part to these subtle qualitative differences in speech production (Riecker et al., 2006; Schulz et al., 2005). The possibility of such qualitative differences in speech production will need to be considered in other studies in which fluent or even modified speech of stuttering and nonstuttering speakers is compared.

4.2. Passive listening

Passive listening to words resulted in left lateralized activation in the temporal cortex for both groups. For the nonstuttering participants, this activation was primarily focused in Brodmann areas 22 and 41/42 of the superior temporal gyrus. These areas are strongly interconnected and have an important speaker- and language-independent role during auditory processing of speech stimuli (Demonet, Thierry, & Cardebat, 2005; Patel, Bowman, & Rilling, 2006). These same areas were also found to be significantly activated in the stuttering speakers, but peak activation was localized in the middle temporal gyrus, which is primarily associated with higher level cognitive processing of auditory stimuli (Liebenthal, Binder, Spitzer, Possing, & Medler, 2005; Noppeney, Josephs, Kiebel, Friston, & Price, 2005). While this difference needs to be interpreted with caution given the smoothing applied to our data, it may point to differential cognitive processes in stuttering and nonstuttering speakers when presented with word stimuli. It has been argued that stuttering speakers may use a more sequential-analytical approach when asked to read words (De Nil et al., 2000) and the present findings suggest that this can be extended to listening to words. This is further supported by the between-group observation of relatively stronger right lateralized activation in insula and right precentral cortical areas in the stuttering speakers during the passive listening task suggesting more articulatory oriented strategies among stutterers (De Nil, 2004).

The lack of right temporal cortex activation in both groups was somewhat surprising but may reflect the fact that our linguistic stimuli were phonologically and phonetically complex two-syllable words, putting a higher demand on linguistic neural processing. Such processing has been shown to be primarily left lateralized in most speakers (Meyer, Zysset, von Cramon, & Alter, 2005; Scott & Johnsrude, 2003).

4.3. Overt speech

Overt repetition of auditorily presented words using a habitual speech pattern resulted in left hemisphere biased activation for both nonstuttering and stuttering participants. As expected, strong auditory cortex peak activation was observed in the nonstuttering speakers, (Kemeny et al., 2006; Shuster & Lemieux, 2005). This peak activation was located in a cluster that extended into primary and premotor (SMA) areas, known to be important for speech production (Demonet et al., 2005; Kemeny et al., 2006; Riecker, Wildgruber, Dogil, Grodd, & Ackermann, 2002; Riecker et al., 2005) and BA 44 in Broca's area, which has been shown to be involved in phonological decision processes (Heim et al., 2005). Similarly, the observed activation in the anterior cingulate is consistent with other studies which have shown this medial region to be involved in the production of overt (Abrahams et al., 2003; Jurgens, 2002) and covert speech (Shergill, Tracy, Seal, Rubia, & McGuire, 2006), and listening to one's own voice (Allen et al., 2005).

Our overt speech data did not demonstrate overall increased activation of sensorimotor cortex, nor increased bilateral activation, in the stuttering speakers. While surprising in light of previously reported findings, it is possible that the use of single words may have resulted in less extensive activation compared to longer utterances (Preibisch, Raab et al., 2003), although bilateral activation has been reported even when using single word utterances (De Nil et al., 2000). It could be argued that the results might have been influenced by the fluency-enhancing effects of rhythmic or paced speech as reported by Stager et al. (2003). While certainly deserving further investigation, this interpretation does not seem

highly plausible as rhythmic fluency-enhancing effects are typically seen at higher speech rates (e.g., 92 beats per minute in the Stager et al. study compared to the six words per minute used in the current study). Nevertheless, the three cortical areas that were found to be more highly activated in our stuttering subjects (precentral gyrus, cingulate gyrus, and SMA) also were among a number of cortical regions observed to be higher in activation for the stuttering subjects in the Stager et al. study during fluency-evoking conditions. However, this broad overlap needs to be interpreted with some caution as the coordinates of the activation peaks were different in the two studies. In our study, the peak activation in the precentral cortical region was more lateralized by 20 mm compared to that observed in the other study. Similarly, the SMA activation in our subjects was found to be more dorsal. Alternatively, the use of stringent multiple comparison corrections may have removed weaker activations which would be preserved when no correction for multiple comparisons is used as was the case in some other studies (e.g., Neumann et al., 2003).

Of particular interest was the observation that nonstuttering participants showed peak activation in the left superior temporal gyrus during the overt speech task but no such activation was present in the stuttering participants. Activation in the superior temporal gyri during overt speech has been interpreted as reflecting self-generated feedback and the transformation of auditory signals into motor speech gestures (Hickok, Buchsbaum, Humphries, & Muftuler, 2003; Hickok et al., 2000; Wise et al., 2001). The absence of significant auditory cortex activation during habitual speech in stuttering speakers has been reported before (Brown, Ingham, Ingham, Laird, & Fox, 2005; De Nil et al., 2000, 2003; Fox et al., 1996), and appears to be independent of the type of speech task used. The reason behind this reduced activation in stuttering speakers is not well understood but is believed to reflect a deficiency in auditory processing in stuttering individuals that may be related to the presence of structural as well as physiological differences in auditory cortex (Beal, Cheyne, De Nil, 2007; Beal, Gracco, Lafaille, & De Nil, 2007; Foundas, Leonard, & Hanna-Pladdy, 2002).

4.4. Simulated stuttering

Simulated stuttering resulted in no significantly increased activation for the nonstuttering speakers. In contrast, significant increased activation was observed bilaterally for the stuttering group, although it was biased towards the right hemisphere. Peak increases were observed bilaterally in the superior temporal gyrus, including the primary auditory cortex. Previous studies have reported an increase in activation of the superior temporal gyrus when adults who stutter were instructed to speak under fluency-enhancing conditions, such as choral speech, which was interpreted as being directly or indirectly related to increased fluency in these speakers (Fox et al., 1996; Ingham, Ingham, Finn, & Fox, 2003). The current findings may suggest an alternative interpretation by showing that increased auditory cortex activation is not necessarily associated with a decrease in speech dysfluency. Rather, it may reflect the heightened reliance on auditory feedback, or increased auditory stimulation, when speaking in a non-habitual manner. In contrast, in nonstuttering speakers, who do show significant activation of auditory cortex during habitual speech, such increases may be masked or remain subthreshold as a result of the subtraction used in the comparison.

Stronger right hemisphere biased activation also was observed in motor cortex associated with the planning and execution of speech movements, including the primary motor, premotor and inferior lateral frontal cortex, as well as the insula. It is interesting that such increased motor activation during simulated stuttering was evident in the stuttering but not the nonstuttering group. One possible interpretation is that voluntary simulated stuttering may have triggered involuntary real stuttering dysfluencies in stuttering participants resulting in the observed activation. While the perceptual identification of stuttering participants may seem to support this interpretation, it is important to note that listeners also were able to differentiate between the two groups in the habitual speak condition, in which no overactivation of motor cortex was observed. Alternatively, the increased activation during the simulated stuttering task may reflect increased task complexity and associated effort in producing such speech for the stuttering participants. Following a meta-analysis of a number of brain imaging studies, Brown et al. (2005) reported that adults who stutter had increased activation in most cortical and subcortical areas involved in vocal control and speech, and that the strongest increase was evident in the right primary motor cortex. Most studies included in Brown's meta-analysis used more complex and longer speech utterances than the current study. The present data may suggest that the increased attention and effort involved in producing simulated stuttering for the stuttering speakers triggered overactivation similar to that observed in more complex linguistic tasks. This interpretation is supported by recent observations that prolonged muscle activity, which results in increased effort, resulted in increased brain activation, especially in the supplementary and frontal motor areas (van Duinen, Renken, Maurits, & Zijdewind, 2007), while well practiced tasks resulted in less widespread activation of neural networks involved in motor execution (Milton, Solodkin, Hlustík, & Small, 2007). It has been shown that when stuttering speakers are consciously monitoring their speech, significantly greater bilateral overactivation can be observed in sensorimotor cortex (De Nil et al., 2003; Neumann et al., 2003, 2005), and that choral speech, previously shown to result in less overactivation in stutterers, is associated with a subjectively experienced reduction in effort (Ingham, Warner, Byrd, & Cotton, 2006).

Increased activation also was observed in the left insula and bilateral rolandic operculum. Lesions in the operculum have been reported to result in articulatory coordination difficulties (Tonkonogy & Goodglass, 1981). Similarly, the insula is strongly activated in stuttering speakers, even during silent speech (De Nil et al., 2000, 2003). Peak activation in the stuttering speakers was observed in the anterior portion of the insula, which has been speculated to play an important role in speech programing and lesions in this area often result in disruption of smooth articulatory coordination of speech movements (Dronkers, 1996). The observation of increased insular activation in our participants lend further support to the hypothesis that for stuttering speakers speech production is a more effortful and less automatic task (De Nil, 1999; Smits-Bandstra, De Nil, & Saint-Cyr, 2006), possibly leading to qualitative differences in overt speech which in turn may partially explain our perceptual judgment findings.

4.5. Prolonged speech

When asked to speak words in a prolonged manner, stuttering but not the nonstuttering speakers again showed increased cortical activation compared to the habitual speech condition, but less pronounced than in the simulated stuttering condition. This increased activation was exclusively right lateralized in the stuttering participants, and was limited to auditory cortex in the superior temporal gyrus. It was somewhat surprising that the prolonged speech condition resulted in less activation increase compared to the simulated stuttering task. The fact that most of our stuttering participants had gone through fluency shaping treatment prior to this experiment, and that the use of prolonged speech, but typically not voluntary stuttering, is highly practiced during such treatment, may offer a potential explanation for this difference between these two modified speech tasks, even if the prolongation task in our study resulted in speech that was very distinct of the very short

and subtle prolongations used by some stuttering speakers post-treatment and thus should not be considered highly automated.

5. Conclusion

In conclusion, the present findings show that voluntary modified speech, as predicted, for the stuttering speakers resulted in increased and differential activation of cortical regions bilaterally and/or right hemisphere lateralized. The increased reliance on the inferior frontal gyrus in the right hemisphere for the stuttering participants may reflect a reorganization of a deficit in the speech motor network in and around the left BA 44, as suggested by reports of disordered temporal activation of left hemisphere speech motor areas in stutterers when reading single words aloud (Preibisch, Neumann et al., 2003; Salmelin, Schnitzler, Schmitz, & Freund, 2000) and of white matter disconnectivity in and around BA 44 in the left hemisphere in stutterers compared to nonstutterers (Sommer, Koch, Paulus, Weiller, & Buchel, 2002; Watkins, Smith, Davis, & Howell, 2008).

An important observation was that the overactivation observed in the stuttering participants during the simulated stuttering task involved many of the same areas in which neural overactivation has been reported previously during predominantly fluent habitual speech, especially when such speech involves more complex and longer utterances. Additionally, increased auditory activation, previously reported to be associated with increased speech fluency, was evident in our data when stuttering participants were asked to increase dysfluency voluntarily. Overall, the present results suggest that at least some of the functional overactivations reported previously between stuttering and nonstuttering adults may reflect between-group differences in the level of automaticity, effort and attention present during speech production. If true, this would mean that the critical factor in understanding differences in neural activation between stuttering and nonstuttering speakers is not necessarily the level of overt speech fluency but the level of effort and automaticity during speech production. Similarly, the increase in auditory activation, previously reported for fluent speech (Fox et al., 1996; Ingham et al., 2000), apparently can also be observed during perceptually less fluent speech and, thus, may reflect that speech is produced in a non-habitual manner rather than that it is perceptually more fluent. Although the observation of increased auditory activation even during imagined fluent speech (Ingham et al., 2000) may seem to challenge this interpretation, there is ample evidence that even imagined motor behavior will activate the sensorimotor and related systems (Guillot et al., 2007; Lacourse, Turner, Randolph-Orr, Schandler, & Cohen, 2004; Mulder, 2007). It is these neural processes, rather than the peripheral movements themselves that are hypothesized to affect the level of brain activation.

A critical issue, of course is to what extent our simulated stuttering condition can be compared to true stuttering. This issue cannot be addressed satisfactorily in the present study as no 'true stuttering' condition was included for comparison. While such a comparison would be difficult to obtain given the highly intermittent nature of stuttering, especially during short utterances produced during fMRI scanning, it nevertheless would provide a crucial test for the present study and therefore is worth pursuing. The need for further study is highlighted by the differences between this study and the PET data reported by De Nil et al. (2000) in which higher levels of auditory activation was reported during single word production. While the differences between these two studies may reflect differences in scanning methods (PET versus fMRI) or temporal averaging (60 s in the PET study versus 10 s TR in the present study), there was also an obvious difference in level of stuttering between the two studies. However, even in the De Nil et al. (2000) paper, most stuttering individuals demonstrated no or very low levels of dysfluency during the task. This highlights the need for further study of individual or subgroup differences in brain activation for persons who stutter, especially under more natural speech conditions using complex connected speech.

Our data also raised a number of important questions. While our behavioral measures failed to reveal any acoustic differences between the speech of the two groups of participants, our perceptual data did show that some qualitative differences were present at least in the speech of some of the participants. The nature of these qualitative differences and their potential impact on functional imaging data needs to be investigated further. An additional issue is related to the potential long-term effects of intensive fluency treatment on the speech execution processes for fluent speech. Since none of the nonstuttering speakers had, obviously, undergone such treatment, one cannot assume that observed differences in neural activation during perceptually fluent speech, or even during experimentally induced modified speech such as used in the current study, are unaffected by speech production strategies acquired during previous treatments which are unique to the participants who stutter. Studies of children, who are less likely to have undergone such intensive treatment could shed further light on this important issue.

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