Research with Transcranial Magnetic Stimulation to Improve Naming in Nonfluent Aphasia

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Four Topics for this Presentation

1. Review current <u>TMS treatment protocol</u> with Nonfluent aphasia patients to improve naming

3. <u>Overt Naming fMRI</u> studies, Pre- and Post- a series of TMS treatments

5. TMS plus Speech Therapy studies

7. <u>DTI studies of two parts of Broca's area</u>: Pars Triangularis (PTr) vs. Pars Opercularis (POp) connections to Arcuate Fasciculus and posterior language zones. Since 1996, functional imaging studies with *nonfluent* aphasia patients, have observed *unusually high activation* in *R perisylvian* language homologues

during

various language tasks.

Rosen et al., 2000



Belin et al., 1996 Perani et al., 2003 Naeser et al., 2004 Rosen et al., (2000) concluded that "...the anomalous R frontal response after L frontal damage may reflectthe loss of active inhibition or competitive interaction from the homologous L frontal area, oran inefficient 'dead-end' strategy."

Belin et al. (1996) have suggested that increased, abnormal activation patterns may not necessarily be related to recovery rather, *increased abnormal activation* may be *...a marker of maladaptive plasticity*.

Rationale for rTMS to Improve Naming in Nonfluent Aphasia:

Since 1 Hz rTMS can be used to suppress a cortical ROI (approximately 1 cc in size), we apply slow, 1 Hz rTMS to specific RH ROIs where *high activation on fMRI* in nonfluent aphasia was observed.

Hypothesis: That 1 Hz rTMS will decrease this "over-activation" and promote inhibition in R hemisphere ROIs and promote better overall modulation, in the bilateral neural network for naming. Topic 1. Current <u>TMS treatment</u> protocol with Nonfluent aphasia patients to improve naming

Inclusion Criteria

 Phase 1: Locate "Best Response" RH cortical ROI to suppress with 1 Hz rTMS

 Phase 2: Suppress the "Best Response" RH ROI for a longer period of time, and during ten sessions.

Inclusion Criteria, Nonfluent Aphasia Patients:

Single, unilateral, L hemisphere stroke At least 6 months poststroke onset R-handed; Native speaker of English Ages 41-80 Yr.; No seizure within 1 Yr. Nonfluent Speech - Elicited, Propositional Speech 1-4 Word, Longest Phrase



Boston Diagnostic

Cookie Theft Picture Description

Minimum Criterion for Entry: Must be able to name at least 3 Pictures of first 20 Pictures Boston Martin, Nicholas et al., 2005 Brain Lang

rTMS Protocol with Nonfluent Aphasia

Two phases of rTMS for each nonfluent patient Real rTMS protocol described here, Sham rTMS protocol, identical

Phase 1

- Locate the Best Response RH, cortical region of interest (ROI) to suppress with rTMS
- Examine at least 4 separate RH cortical ROIs, in separate rTMS sessions
- Each ROI suppressed with slow, 1 Hz rTMS, 90% motor threshold (L FDI), 10 min.
- <u>Best Response ROI</u> is determined by Snodgrass & Vanderwart picture naming (and Response Time)

immediately post- rTMS to suppress an ROI. 20 pictures on a S&V

List.

Baseline was established earlier, across 5 S&V Lists for Picture Naming. Best Response ROI, Picture Naming (20-item S&V List) = +2 SD above Baseline (Effect is temporary)

Phase 2

- Suppress <u>Best Response RH, ROI</u>
- Longer Treatment (20 Minutes)
- More Days (10 Days)
- To examine whether naming can be improveded in the improveded of the second s

Vertical Ascending Sulcus often considered to separate Pars Triangularis (BA 45), Pars Opercularis (BA 44)



Frey, Campbell, Pike, Petrides, 2008

Sample Phase 1 rTMS Session, Suppression of a R Hemisphere ROI

Pre- rTMS Baseline Naming: Five, 20-item Snodgrass & Vanderwart Picture Lists

Immediate Post- rTMS Naming: One List of 20 Pictures, Snodgrass & Vanderwart

Naeser, Martin, Fregni, Theoret, Kobayashi, Nicholas, Baker, Maria-Tormos, Steven, Pascual-Leone. Suppression of **Right Anterior Broca's** Area Improves Naming in Chronic Nonfluent Aphasia. Presented at The 8th Internat. Conference on Functional Mapping of the Human Brain, June 2-6, 2002; Sendai, Japan. NeuroImage 2002 Abstract #133. Submitted





Phase 1 Results: Significant effect of site-specific rTMS suppression on both: number of pictures named correctly (F= 14.63; df 3,15; p=0.0001) and RT for word production (F= 5.62; df 3,15;

p=0.009).

Patients named significantly more items after 1 Hz rTMS to suppress R PTr than to R POp (Fisher's PLSD post-hoc p<0.001)

R M1 (p<0.01)

R STG (p<0.005).

Naeser et al., 2002; Submitted

Phase 2 rTMS

- Suppress Best Response RH Cortical ROI, as located from Phase 1, for each Nonfluent patient
- Longer Treatment Time (20 Minutes)
- More Days (10 Days) 5 Days / Week for 2 Weeks

To examine whether naming can be improved for 2 mo. or longer, post- rTMS treatment.

Patients are asked not to receive any individualized speech therapy during the study.

Naeser, Martin, Nicholas et al., 2005 Brain Lang

Language Outcome Measures (Pre- and Post- Phase 2 rTMS)

First 20 items Boston Naming Test (BNT)

(Pre-TMS, minimum criterion for Entry: 3 pictures named on BNT.)

Boston Diagnostic Aphasia Exam

- Phrase Length, Cookie Theft Picture Description
- Naming subtests

Naeser, Martin, Nicholas et al., 2005 Brain Lang

Structural MRI scans for 4 chronic aphasia patients, Phase 2 rTMS Study



Primary Language Outcome Measures: Naming scores for each chronic aphasia patient, pre-rTMS, and at 2 weeks, 2 Mo. and 8 Mo. post- Phase 2 rTMS treatments



Phase 2 Results (n=4) Naming Tests, Post- rTMS

		Pre- rTMS	2Wk Post- rTMS	2Mo Post- rTMS	8Mo Post - rTMS	
BNT						
First 20 Items	Mean	8	8.5	10.5	12.5	
	S.D.	4.69	4.66	4.66	6.14	
			t=1.732	t=8.66	t=2.635	
			p=.18	p=.003	p=.08	
BDAE						
Animals	Mean	3.75	5	5	7.5	
	S.D.	3.86	3.92	4.32	4.44	
			t=5.00	t=5.00	t=2.611	
			p=.02	p=.02	p=.08	
BDAE						
Tools/Implements	Mean	3.25	3.5	6	5.75	
	S.D.	1.89	2.38	2.94	1.71	Naeser.
			t=.397	t=3.67	t=8.66	Nichola
			p=.72	p=.04	p=.003	2005 B

Naeser, Martin, Nicholas et al., 2005 *Brain Lang*

Results, post- Phase 2 rTMS Propositional Speech Improvement also observed in number of words per longest phrase length in elicited, propositional speech **BDAE (Cookie Theft Picture)** for two nonfluent patients at 2 Mo. post-rTMS: **One patient (mild-mod. nonfluent)** *increased* from a 3-word longest phrase, to a 5-word longest phrase.

Another patient (moderate nonfluent) *increased* from a *1-word longest phrase*, to a *3-word longest phrase*. Naeser, Martin, Nicholas et al., 2005 Brain Lang

Possible mechanism for rTMS effect:

Paradoxical Functional Facilitation

While it may seem paradoxical to suggest that promoting inhibition in R Pars Triangularis, would promote improved naming or improved speech, there are animal studies, and human case reports, which suggest that *direct or indirect neural "damage"* to specific areas in the central nervous system may result in *facilitation of behavioral functions* (Kapur, 1996, review).

Kapur has labeled this phenomenon "*paradoxical functional facilitation (PFF)*."

PFF is known as the "Sprague effect" in animal studies. For example, new collicular lesions may bring about an improvement in visual functioning following an initial occipital lesion.

In humans, there are case studies whereby ambidextrous adults who had stuttered since childhood, no longer stuttered, following unilateral brain damage in adulthood (e.g., stroke or head injury), even as soon as 10 days postonset (Helm-Estabrooks et al., 1986).

Vuilleumier et al., (1996) reported the disappearance of left-sided unilateral neglect, brought on by a right parietal infarct, after the occurrence of a new lesion in the area of the left frontal eye field in the previously undamaged left hemisphere. Topic 2: Overt Naming fMRI Studies Pre- and Post- rTMS Series P1, Nonfluent Aphasia Patient Good Responder, rTMS Treatment

- R-handed engineer
- LMCA stroke with moderate R hemiparesis
- Age 48, onset

At 9 yr. poststroke, enrolled in rTMS Treatment protocol

At Entry:

- Boston Naming Test: 11 pictures named.
- Cookie Theft Picture Description: 3 word phrase length

P1, Nonfluent Aphasia, Good Responder Results, post- Phase 2 rTMS Treatments



At 2 mo. and 8 mo. post- Phase 2 TMS

- Improved Boston Naming Test scores
 - Improved phrase length (Cookie Theft Picture, BDAE)
 - From 3-word, to 5-word longest phrase length

Overt Naming fMRI Studies, Pre- Post- TMS Series P1, Nonfluent Aphasia, Good Responder



Structural T1-weighted MRI, 3D SPGR scan Lesion present in cortex and subjacent white matter (WM):

Lesion in Broca's area

Pars triangularis (PTr) and pars opercularis (POp)

Some sparing of Medial Subcallosal Fasciculus (MScF), WM deep to Broca's area (red arrows)

Lesion in Middle 1/3 periventricular white matter (M 1/3 PVWM) (white arrow)

- Lesion in lowest premotor and sensorimotor cortex and subjacent WM Sparing mid-to-upper sensorimotor region (mouth)
- Lesion in most of Wernicke's area and
- Portion of supramarginal gyrus area

Overt Naming fMRI Method: Block Design



- Minimizes motion artifact
 - Barch et al., 1999
 - Eden et al., 1999
 - Birn et al., 2004
- Takes advantage of <u>hemodynamic response delay</u>
 - Increased bloodflow remains approx. 4 8 s after task
- Task related information obtained after task

Martin, Naeser, Doron et al., 2005 *NeuroImage* Martin, Naeser, Ho et al., 2009 *Brain Lang, in press*

Snodgrass & Vanderwart, black and white pictures

P1, Nonfluent Aphasia, Good Responder Overt Naming fMRIs Pre- and Post-TMS Series



P1, Nonfluent Patient, Good Responder

Conclusions: Overt Naming fMRIs Pre- and Post- Series of rTMS Treatments

Suppression of Right Pars Triangularis with rTMS:

- Promoted significant <u>increase in L Supplementary</u> <u>Motor Area (L SMA) post- rTMS</u>, over time.
- Gradual shift to <u>more LH activation</u> in remaining L perisylvian language areas
- Improved naming and propositional speech

Many functional neuroimaging studies with a variety of aphasia patients have stressed that activation in LH perilesional and remaining LH language areas is important for better

recovery.

Heiss, Kessler, Thiel, Ghaemi, Karbe, 1999 Warburton, Price, Swinburn, 1999 Perani, Cappa, Tettamanti, Rose, Scifo, Miozzo, Basso, Fazio, 2003 Connor, Blasi, Young, Tucker, Snyder, Kwentus, et al., 2004

Studies also report that after speech therapy, new L hemisphere activation is associated with improvement.

Small, Flores, Noll, 1998 Leger, Demonet, Ruff, 2002 Cornelissen, Laine, Tarkiainen, Jarvensivu, Marin, Salmelin, 2003

P2, Poor Responder, rTMS Series Overt Naming fMRIs, Pre- and Post- rTMS

- Left Hemisphere stroke
- Received tPA (Clot formation from Patent Foramen Ovale)
- No R hemiparesis
- Age 56, M
- R-handed
- Master's Degree, High school teacher

At 2 yr. poststroke, enrolled in rTMS protocol

At Entry:

- Cookie Theft Picture Description: Severe nonfluent speech, 1 - word phrase length, and <u>Stereotypies</u>
- Boston Naming Test: Mean of 1.6 pictures, across 3 test times.

Patient did not meet minimum criterion of 3 pictures named on Boston Naming Test.

P2, Poor Responder Results, Post- Phase 2 rTMS



At 2 mo. and 6 mo. post- Phase 2 rTMS

- No change in BNT scores
- No change in phrase length (Cookie Theft Picture, BDAE)

Note:

At 4 mo. post- rTMS patient was given a handheld augmentative speech device

Efforts at verbalization reduced (personal observation)

Overt Naming fMRI Studies, Pre- Post- rTMS Series P2, Severe Nonfluent Patient <u>with Stereotypies</u> Poor Responder, 1.5 Yr. Poststroke



Structural T1-weighted MRI, 3D SPGR LH lesion extends to high supraventricular slices, <u>almost to brain vertex</u> (white arrows).

Lesion Broca's area

Pars triangularis (PTr) and pars opercularis (POp)

Medial Subcallosal Fasciculus (MScF), white matter (WM) deep to Broca's area (red arrows)Lesion in about half of middle 1/3 periventricular white matter

- Lesion in most of premotor and motor cortex
 - Lesion in white matter deep to L
 supplementary motor area (SMA) (white arrows)

Likely undercutting of fibers from SMA which pass through the MScF to anterior cingulate (BA 24) and head of caudate deep to Broca's area.

- Lesion in most of Wernicke's area and
- Portion of posterior middle temporal gyrus

Structural MRIs, P1 (Good Responder) and P2 (Poor Responder) Duffau et al., (2003) describe the posterior portion of the middle frontal gyrus (at *junction of superior frontal sulcus with the precentral sulcus*), as an <u>'epicenter' for naming</u>, observed during intraoperative stimulation. P1, no lesion present in this area; P2, lesion present here (vertical arrow).





P2, Poor Responder Conclusions: Overt Naming fMRIs Pre- and Post- Series of rTMS Treatments Suppression of Right Par Triangularis with rTMS: • Little change in activation on overt naming fMRI

• *Little change in naming or propositional speech* post- rTMS

 <u>Unusual lesion site pattern</u>, with high, superior frontal lobe lesion extension. P2 had received tPA.

> The patients who receive tPA may have unusual lesion site patterns.

P2, Poor Responder

- Patient <u>did not meet minimum criterion at Entry</u>: Mean of 3 pictures named on Boston Naming Test, across 3 test sessions.
 - His Mean score for BNT was only 1.6 pictures named, across 3 test sessions.
 - Patient produced <u>stereotypies</u>, as part of severe nonfluent speech
- Patient had been given a hand-held augmentative speech device starting at 4 mo. post- rTMS. The effect on naming, from use of this device is unknown.

Topic 3: Studies with TMS followed by Speech/Language Therapy

- Post-Phase 2, Begin Speech Therapy months later.
 OR
- New Pilot Study: Begin Speech Therapy <u>immediately</u> after, each 20 minute- rTMS treatment:
 - 10 rTMS treatments, each followed by 3 hours of Constraint-Induced Language Therapy (CILT)
- <u>Rationale</u>: rTMS may modulate bi-lateral neural networks for language, so that patients can attain a better outcome from Speech Therapy.

P3, Severe Nonfluent, Global Aphasia, Good Responder Started Speech Therapy 8 Months Post- Phase 2 rTMS

Severe nonfluent (1-word Phrase Length, but *did <u>not produce stereotypies</u>*), global aphasia

6.5 Yr. Poststroke, Age 58 Yr., F (college-educated)

At Entry: 1- word Phrase Length Named 4 pictures on the Boston Naming Test



Naeser, Martin, Nicholas, Baker et al. 2005, Neurocase

P3, Severe nonfluent (1-word Phrase Length), global aphasia 6.5 Yr. Poststroke, Age 58 Yr., F, Subcortical Lesion only, that included lesion in two white matter areas near ventricle:



1) MScF, Medial Subcallosal Fasciculus. Stratum Subcallosum St Sbc (red arrow).

Yakovlev & Locke, 1961





2) Middle 1/3 periventricular white matter (PVWM)



Naeser, Palumbo, Helm-Estabrooks et al., Brain, 1989; Duffau et al., 2002

Phase 1 rTMS: Location of four RH ROIs each suppressed with 1 Hz rTMS for 10 minutes during separate rTMS sessions, to locate the "Best Response" RH ROI to suppress in order to immediately improve picture naming. P3, severe global aphasia patient, Good Responder



P3, Phase 1 rTMS Results for each of four RH ROIs, each suppressed for 10 minutes

Picture Naming results immediately post-rTMS to each ROI



P3, Post- Phase 2 rTMS Results after suppression of R PTr Good Responder (6.5 Yr. Poststroke)



<u>At 8 Months post- Phase 2 rTMS</u>, P3, a severe nonfluent patient was referred for Speech Therapy, the first time since her stroke (7.5 Yr. Poststroke).

Prior to this, her speech was too severe for a Verbal treatment program; she had used a nonverbal, computer-assisted program (C-ViC).

She was enrolled in the program, Voluntary Control of Involuntary Utterances (VCIU) and after 5 sessions, she could *name 28/40 pictured items without prompting.*

VCIU Program in *Manual of Aphasia Therapy* 2004, Helm-Estabrooks, Albert

P1, Nonfluent Aphasia Patient, Good Responder Started Intensive <u>Verb Production</u> Therapy at 24 Months post- Phase 2 TMS

Pre-TMS 17/60 28% Pictures Named 9 Yr. Poststroke 3 Mo. Post-TMS 25/60 42% Pictures Named 10;4 Yr. Poststroke

16 Mo. Post-TMS 35/60 58% Pictures Named 11;5 Yr. Poststroke



24 Mo. Post-Phase 2 TMS 12 Yr. Poststroke

P1 entered a Constraint-Induced Aphasia Treatment Program (CIAT) to emphasize <u>Verb Production</u> within Informative exchanges -Family, Vacation, Work.

> Emerson College Boston, MA Speech Pathology Program, 2005

Intensive Treatment 75-minutes, 4x / Wk. 20 Hrs. 4 weeks A B A B design Goral & Kempler 2008, Aphasiology 46 Mo. Post-TMS 25/60 42% Pictures Named 13;11 Yr. Poststroke



P1, significant increase in number of Verbs produced during Narrative Generation (Family, Vacation, Work) post-treatment period 2, of CIAT for Verb Production.

10 GORAL AND KEMPLER



At 24 Mo. Post-rTMS (12 Yr. Poststroke) P1 entered a modified Constraint-Induced Aphasia Treatment (CIAT), with single-subject, to emphasize verb production within informative exchanges. Goral & Kempler 2008, Aphasiology

Figure 1. Mean percent verbs and nouns produced (bars) and the ratio of verbs to number of verbs and nouns multiplied by 100 (line) for three narratives pre- and post-treatment.

New Pilot Study: Start Speech Therapy <u>immediately</u> after a 20-min. rTMS Treatment

 Start <u>immediately</u>, post- each 20 minute- rTMS Treatment:

10 rTMS treatments, each followed by 3 hours of Constraint-Induced Language Therapy (CILT)

5 Days per week, for 2 weeks.

Constraint-Induced Language Therapy (CILT)

A therapy program observed to improve object and action naming, where patients may <u>only</u> respond with <u>verbal</u> <u>output</u> (no gestures, writing, sound effects).

Pulverrmuller et al., 2001; Meinzer et al., 2005; Maher et al., 2006



Opaque screen is placed between therapist and patient, to discourage use of gesture or writing.

New Pilot Study: TMS plus Constraint-Induced Language Therapy (CILT)

Inclusion Criteria:

1. Patient has completed all follow-up Language Testing, post- Phase 2 rTMS, with significant improvement Boston Naming Test and/or Naming Subtests on BDAE, Good Responder.

2. Remaining inclusion criteria are the same as for the regular rTMS study: Ages 41-80; no seizures within 1 year; R-handed; single LMCA stroke; Native speaker of English

rTMS Method:

Suppress <u>same</u> Best Response RH ROI as previous series. 10 rTMS Treatments, 1 Hz, 90% MT, 5 Days / Wk., 2 Wks.

TMS plus Constraint-Induced Language Therapy (CILT) Pre- and Post- Language Testing:

Pre-testing: Parts of BDAE, and BNT (x3) (Baseline)

Post- testing: at 1 and 6 Mo. post-intervention: Same tests

Language Outcome Measures:

Significant improvement defined, >2 SD above Baseline on BDAE, BNT.

To examine for possible changes that might occur during intervention, <u>Naming Probe Testing</u> was administered using BDAE naming subtests (Actions, Animals, Tools/Implements), and BNT:

- Pre-TMS 10-12x, 4-5 week period
- Daily, immediately post- each CILT session
- Post-TMS 10-12x, 4-5 week period

These time-series data were analyzed using Double Bootstrap method. http://www.stat.wmich.edu/slab/Software/Timeseries.html (McKnight, McKean, Huitema, 2000)

P3, Severe nonfluent (1-word Phrase Length), global aphasia Now 12 Yr. Poststroke, Age 58 Yr., F, Subcortical Lesion only (Previous rTMS Treatment Series, 6.5 Yr. Poststroke)



1) MScF, Medial Subcallosal Fasciculus. Stratum Subcallosum St Sbc (red arrow).

Yakovlev & Locke, 1961





2) Middle 1/3 periventricular white matter (PVWM)



Naeser, Palumbo, Helm-Estabrooks et al. 1989 Brain; Duffau et al., 2002



Constraint-Induced Language Therapy (CILT)

Therapy Materials, Pictures to be Named

Prior to Intervention (rTMS plus CILT): Baseline, picture naming ability was tested 3x on 250 color pictures

During CILT Treatment Sessions: 33% of color pictures presented, were <u>always</u> named on Baseline testing (3/3).

> 33% of color pictures presented, were <u>sometimes</u> named on Baseline testing (1 or 2/3)

33% of color pictures presented for naming, were <u>never</u> named on Baseline testing (0/3)

Pictures to be named were presented in groups of 6 pictures at a time, 2 of each level of difficulty, unique to that patient. 18 Pictures / day









Average = 4.6

Average = 6.0

Average = 6.5

Double Bootstrap Method for Autoregression for Interrupted Time Series McKnight, McKean, Huitema, 2000



Average = 1.9

Average = 3.0

Average = 4.0

Double Bootstrap Method for Autoregression for Interrupted Time Series McKnight, McKean, Huitema, 2000



Double Bootstrap Method for Autoregression for Interrupted Time Series McKnight, McKean, Huitema, 2000

P3, Severe Nonfluent, Global Aphasia Patient, BDAE Action Naming Pre- and Post- Intervention (TMS plus CILT). Previous Scores are also reported, when Intervention was TMS alone.





P3, Severe Nonfluent, Global Aphasia Patient, BDAE Tools/Implements Naming Pre- and Post- Intervention (TMS plus CILT). Previous Scores are also reported, when Intervention was TMS alone.





P3, Severe Nonfluent, Global Aphasia Patient, BDAE Single Word Repetition Pre- and Post- Intervention (TMS plus CILT). Previous Scores are also reported, when Intervention was TMS alone.





P3, Severe Nonfluent Global Aphasia Now 12 Yr. Poststroke (Previous rTMS Treatment Series, 6.5 Yr. Poststroke)

Results, <u>Outcome Measures</u>: at 1 and 6 Months post- <u>TMS plus CILT</u>:

Significant improvement (>2 SD above Baseline):

BDAE Action Naming

Tools/Implements

Single Word Repetition

Conclusions, TMS plus CILT Case Study:

 Improvement in <u>Action Naming</u> was observed only following her second TMS series, with CILT

Improvement may have been associated with better modulation of R POp, an area with <u>mirror neurons</u>.

(Rizzolatti & Craighero 2004; Wilson et al. 2004; Iacoboni 2008)

 Suppression of R PTr may have promoted less inhibition of R POp from R PTr, via U-fibers.

Topic 4: DTI studies of parts of Broca's area

Connections for two parts of Broca's area, with posterior language zones follow <u>different</u> white matter pathways, in the left hemisphere.
Posterior Broca's area (likely Pars Opercularis) connects with anterior supramarginal gyrus via arcuate fasciculus.
Anterior Broca's area (likely Pars Triangularis) connects with temporal lobe, via the extreme capsule.



We have undertaken a DTI study that examined these pathways in the Right Hemisphere, as well as in Left. Kaplan, Naeser et al. *Submitted*





Frey, Campbell, Pike, Petrides, 2008

DTI Study of Arcuate Fasciculus Projections to parts of Broca's Area



Left Hemisphere 3 Subregions of Broca's Area



Anterior Pars Triangularis
 Posterior Pars Triangularis
 Pars Opercularis

Normal Control, 55 Yr,. M

* In this DTI study, the Ascending Vertical Ramus was used to separate Pars Opercularis from Pars Triangularis

Labeled Right Hemisphere Lateral View



Right Hemisphere 3 Subregions of Broca's Area



Normal Control, 68 Yr,. M

Kaplan, Naeser, Martin, Ho et al. Submitted

Connections to Arcuate Fasciculus from "Broca's Area" are primarily from Pars Opercularis, not from Pars Triangularis, in the Right Hemisphere, and in the Left.

Connections to POp from Arcuate Fasciculus in **Left Hemisphere**, Normal Control, 55 Yr., M



Connections to POp from Arcuate Fasciculus in **Right Hemisphere**, Normal Control, 68 Yr., M



Note, posterior connections from arcuate fasciculus are to supramarginal gyrus, not temporal lobe; higher slice, necessary to view. Anterior Pars Triangularis
Posterior Pars Triangularis
Pars Opercularis

Kaplan, Naeser, Martin, Ho et al. *Submitted*

DTI Study: U-Fibers in RH between posterior PTr, and POp

Normal Control, 69 Yr., F



Right Anterior Pars Triangularis
 Right Posterior Pars Triangularis
 Right Pars Opercularis

Kaplan, Naeser, Martin, Ho et al. *Submitted* Normal Control, 62 Yr., M



Differential Effects of Suppression of Right Pars Triangularis vs. Pars Opercularis

We hypothesize that the integrity of mirror neurons (R POp, BA 44) in humans is critical not only to language acquisition but also to possibly foster *recovery from nonfluent aphasia*.

Neurons in PTr (BA 45) might serve to modulate activity of mirror neurons in BA 44 through inhibitory interaction.

If so, in nonfluent aphasia, *hyperactivity of neurons in R BA 45*, would excessively suppress *R BA 44* and possibly *hinder recovery from aphasia*.

Naeser et al. 2002; Naeser et al. 2005 Brain Lang; Martin, Naeser, Ho et al. 2009 Brain Lang, in press; Kaplan et al. submitted

Differential Effects of Suppression of PTr vs. POp cont'd. Suppression of hyperactivity in R BA 45 might permit better modulation of R BA 44 (and other L and R temporo-parietal regions of the temporo-parietal-premotor network important for object naming and verb production). Price, Warburton, Moore, Frackowiak, Friston, 2001 Damasio, Tranel, Grabowski, Adolphs, Damasio, 2004

Gold & Buckner, 2002

Better modulation, in turn, can lead to improved object naming and verb production in chronic, nonfluent aphasia.

Naeser et al. 2002; Naeser et al. 2005 Brain Lang; Martin, Naeser, Ho et al. 2009 Brain Lang, in press; Kaplan et al. Submitted



A Diagonal Sulcus is present in the Inferior Frontal Gyrus in 50% of hemispheres. Within "Broca's Area," the Diagonal Sulcus is not reliable to separate Pars Triangularis from Pars Opercularis (Amunts, et al. 2004)

Cytoarchitectonic Studies of Broca's area, BA 45 (PTr), and BA 44 (POp): Two cases showing one R hemisphere; one L hemisphere, where Diagonal Sulcus was present. In the R hemisphere case, the *Diagonal Sulcus separated BA 45 from BA 44*.

In the L hemisphere case, the *Diagonal Sulcus was within BA 44*.

Thus, the Diagonal Sulcus is not reliable on surface anatomy alone, to separate BA 45, from BA 44.

= BA 44, POp



FIGURE 1. Size and location of Brodmann's areas 44 and 45

Right Broca's Area: Diagonal Sulcus (ds) separates BA 44, POp (Red) from BA 45, PTr (Yellow)

Nishitani, Schurmann, Amunts, Hari, 2005



= BA 45, PTr

fs arl brff

Right Broca's Area: Diagonal Sulcus (ds) separates BA 44, POp (Red) from BA 45, PTr (Yellow) ^{Brain 3}

Amunts et al., 2004

Left Broca's Area: Diagonal Sulcus (ds) is within BA 44, POp (Red). Brain 8

Amunts et al., 2004