Neurolinguistic impairments in stroke-induced and progressive aphasia: Implications for treatment

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Talk Outline

• Agrammatic language patterns
  o Stroke-induced aphasia
  o Primary progressive aphasia (PPA)

• Recovery of sentence deficits in stroke-aphasia

• Neurobiology of recovered sentence processing

• Treatment of PPA
Author's personal copy
produced: M = 42%, SD = 15%). Participants presented with mild-to-moderate aphasia (WAB-AQ: M = 76.1, Range: 56.4–93), with relatively preserved verb (M = 98%, SD = 6%) and sentence comprehension (M = 72%, SD = 15%, see Table 1). All aphasic participants presented with left hemisphere lesions due to a cerebral vascular accident in the vicinity of the left middle cerebral or anterior temporal artery. Anatomical scans were performed for 12 of the 15 participants, showing variation in the location of the lesion and its extent across participants. Four of the patients presented with large lesions involving frontal, parietal and temporal regions, and one presented with additional subcortical involvement. Selected slices from these patients T1 MRI images are presented in Fig. 1, and a brief description of their lesions is provided in Table 2.

2.2. Materials

Thirty-five transitive and 35 intransitive verbs were selected to form sentence stimuli. The transitive verbs were obligatory two-argument verbs that take either animate or inanimate objects (e.g., pull). The intransitive verbs all were obligatory one-argument verbs with no possible direct or indirect object arguments (e.g., sneeze).

Despite appearances, linguistic evidence reveals that in both cases, the post-verbal NP is not a direct object of the verb, but rather an adjunct (see e.g. Carrier & Randall, 1992, 1993; Jones, 1988; Mittwoch, 1988; Zubizarreta, 1987). For example, unlike true objects of transitive verbs, these NPs cannot be passivized (2), pronominalized (3) or questioned (4). There is thus a clear distinction in the argument structure information associated with the two verb types.

(2) (a) A baby carriage was pulled.
(b) *A cute baby sneeze was sneezed.
(3) (a) John pulled a baby carriage and then his brother pulled it.
(b) *John sneezed a cute baby sneeze and then his brother sneezed it.
(4) (a) What did John pull?
(b) *What did John sneeze?

Both transitive and intransitive verbs required a human agent in subject position (i.e., unaccusative verbs, psych verbs, etc. were excluded). The complete list of the verbs used in the experiment is provided in the Appendix.

The verbs were embedded in sentences to comprise the experimental stimuli. All sentences were active constructions that included a human/animate subject and an object, which was realized as a coordinated NP (the N and the N). Correct sentences (e.g. Anne visited the doctor and the nurse) contained a transitive verb and a semantically congruent object. Sentences with argument structure

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Core Features of Agrammatism Stroke-Induced

- Nonfluent (Broca’s) aphasia
- Impaired comprehension (and production) of complex sentences (Caplan & Hildebrandt, 1998; Caramazza & Zurif, 1976; Grodzinsky 2000; Saffran et al., 1980; Thompson et al., 1995 and others)
- Impaired production of verbs (compared to nouns) (Berndt et al., 1997; Kim & Thompson, 2000, 2004; Miceli et al., 1984; 1988; Zingeser & Berndt, 1990)
- Impaired production of grammatical morphology (Arabatzi & Edwards, 2000, 2002; Bastiannse 1995; Bastiannse & Thompson, 2002; Friedman & Grodzinsky, 1997; Miceli & Caramazza, 1988; Thompson et al., 2002)
**Core Features of Agrammatism**

**Agrammatic Variant of PPA**

- **Impaired comprehension (and production) of complex syntax** (Gorno-Tempini et al., 2011; Thompson et al., 2012; Wilson et al., 2012)
- **Verb production deficits (compared to nouns)** (Gorno-Tempini et al., 2011; Hillis et al., 2004; Thompson et al., 2012)
- **Impaired production of grammatical morphology** (Thompson & Meltzer-Aascher, 2012)


*Archives of Neurology*
Frontotemporal Dementias

Primary Symptoms

Personality Behavioral Changes

Behavioral variant (bvFTD)

Language Changes

Primary Progressive Aphasia (PPA)
Progressive Aphasia

- Reported in 19th century
  - Pick (1892), Pick (1904), Franceschi (1908), Rosenfeld (1909), Mangazzini (1914)
- Gained attention in late 20th century
  - Mesulam (1982): 6 cases of “Slowly Progressive Aphasia”
- **Primary Progressive Aphasia (PPA)** (Mesulam, 1987)
  - Prominent language deficit *(primary)*
  - Caused by a neurodegenerative disease *(progressive)*
    - No evidence of stroke, tumor, hypothyroidism, psychiatric or other disorder
    - Cognitive impairments other than language not impaired *(at least initially)* *(aphasia)*
- Hundreds of cases now reported in literature
Percent Change in Test Scores Over 2 Years

Language and Related Tests

- Auditory Comprehension
- Repetition-Words
- Repetition-Sentences
- Oral Reading- Words
- Oral Reading-Sentences
- Confrontation Naming
- Word Fluency
- Reading Comprehension
- Praxis-Buccofacial
- Praxis Limb
- Calculation

Non Language Tests

- Memory-Orientation
- Memory 3W3S
- Line Orientation
- Facial Recognition
- Hooper VOT
- Reasoning-Raven’s Matrices
- Reasoning- Shipley
- Reasoning-Visual-Verbal

Case 3, Weintraub et al, 1990
Neuroimaging Findings

**Magnetic Resonance (MR) Imaging**
- No evidence of stroke, tumor, or other source of language deficit
- Left-lateralized atrophy in some patients

**Positron Emission Topography (PET)**
- Decreased blood flow in left hemisphere
- Shows up when MRI is within normal limits

Neuropathology on Autopsy

Frontotemporal lobar degeneration (FTLD) and Alzheimer’s disease (AD) are two major causes of neurodegenerative diseases. The tissue diagnosis shows that FTLD occurs in 70% of cases, while AD occurs in 30% of cases. The presence of plaques and tangles is a hallmark of Alzheimer’s disease. Normal brain tissue and tau inclusions in Pick’s disease are also shown for comparison.

Courtesy of Eileen Bigio, MD; CNADC
PPA subtypes

Primary Progressive Aphasia

Agrammatic PPA (PPA-G)

Semantic PPA (PPA-S)

Logopenic PPA (PPA-L)

(From: Gorno-Tempini et al., 2011)
Three PPA Subtypes; Language Deficits

<table>
<thead>
<tr>
<th>Agrammatic (PPA-G) (Progressive Nonfluent Aphasia) (PNFA)</th>
<th>Logopenic (PPA-L)</th>
<th>Semantic (PPA-S) (Semantic Dementia (SD))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sentence production: Impaired; Syntactic errors</td>
<td>Sentence production: Impaired; Grammatically correct but simple</td>
<td>Sentence production: Unimpaired; Grammatically correct</td>
</tr>
<tr>
<td>Sentence comprehension: Impaired for complex syntax</td>
<td>Sentence comprehension: Impaired for complex syntax</td>
<td>Sentence comprehension: Unimpaired</td>
</tr>
<tr>
<td>Naming: Impaired; verbs more impaired than nouns</td>
<td>Naming: Impaired; nouns more impaired than verbs</td>
<td>Naming: Severely impaired</td>
</tr>
<tr>
<td>Word comprehension: Unimpaired</td>
<td>Word comprehension: Unimpaired</td>
<td>Object knowledge: Impaired</td>
</tr>
<tr>
<td>Repetition: Impaired</td>
<td></td>
<td>Word comprehension: Impaired</td>
</tr>
</tbody>
</table>

Gorno-Tempini et al., 2004; Hillis et al., 2004; Hodges & Patterson, 1996; Mesulam et al., 2009; Thompson et al., 1997, 2012; Weintraub et al., 2008; Wilson et al., 2010
## Stroke Aphasia vs. Primary Progressive Aphasia (PPA)

<table>
<thead>
<tr>
<th>Stroke Aphasia</th>
<th>Primary Progressive Aphasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Language Deficit</td>
<td>Primary language Deficit</td>
</tr>
<tr>
<td>Vascular pathology</td>
<td>Neurodegenerative</td>
</tr>
<tr>
<td>Pathology follows organization of the vascular system</td>
<td>Pathology does not follow organization of the vascular system</td>
</tr>
<tr>
<td>Destroys all neural tissue nourished by affected artery</td>
<td>Spared tissue within regions of atrophy; may or may not be functional</td>
</tr>
<tr>
<td>Symptoms acute</td>
<td>Symptoms progressive</td>
</tr>
<tr>
<td>Potential for improvement with treatment</td>
<td>Potential for improvement with treatment questionable</td>
</tr>
</tbody>
</table>
## Narrative Language Production Patterns

<table>
<thead>
<tr>
<th>Participants</th>
<th>Years Post-onset (M)</th>
<th>Age (M)</th>
<th>Education (yrs) (M)</th>
<th>WAB AQ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPA-G</td>
<td>17</td>
<td>3.66</td>
<td>63.27</td>
<td>16.82</td>
</tr>
<tr>
<td>PPA-L</td>
<td>20</td>
<td>3.78</td>
<td>65.90</td>
<td>15.85</td>
</tr>
<tr>
<td>PPA-S</td>
<td>6</td>
<td>2.67</td>
<td>56.3</td>
<td>16.0</td>
</tr>
<tr>
<td>StrAg</td>
<td>20</td>
<td>4.53</td>
<td>52.8</td>
<td>16.3</td>
</tr>
<tr>
<td>Age-Matched Controls</td>
<td>13</td>
<td>63.23</td>
<td>16.31</td>
<td>99.82</td>
</tr>
</tbody>
</table>
Narrative Speech: Stroke-Induced Agrammatic Aphasia

“(Okay so) there’s the girl whose are (and) there’s nother two girls and her nother (uh) husband. And there and there his on (the) the girl. Not (the) the two girls the one her girl and she’s uh lossing they (no she’s in) she’s washing something”.

• Mean words-per-minute (WPM) ~ 50-60
  • (Control M: 130-150)
• Frequent grammatical errors (~50% grammatical sentences)
• Frequent pauses
“She made a (pumpkinpen pumpkined) pumpkin (in a to a inste uh ins) 0:03 into (a) a stage coach.
(And uh) and she maked four mices into (uh) horses.”

- Mean words-per-minute (WPM) ~ 50-60
- (Control M: 130-150)
- Frequent grammatical errors (~50% grammatical sentences)
- Frequent pauses
Narrative Language Production Patterns

Fluency Measures

• WPM
• MLU

Grammatical measures

• Proportion of grammatical sentences
• Noun to verb ratio
• Proportion of correctly inflected verbs

Thompson, Cho, Hsu, Wieneke, Rademaker, Witner, Mesulam & Weintraub (2012)
Fluency Measures: WPM and MLU-W across Participant Groups

**WPM**
- **PP-G:** Mean ~ 50 - 60
- **PPA-L:** Mean ~ 80 - 100
- **PPA-S:** Mean ~ 115 - 135

*(controls M: 130-150)*
Fluency by PPA Subtype

Fluency based on WPM. Nonfluent = at or below 113.4 WPM cut-off (control mean minus 1 SD)
Grammatical Measures

**Proportion of Grammatical Sentences**

**N:V Ratio**

**Proportion of Correctly Inflected Verbs**

* $p < .05$; ** $p < .01$; *** $p < .001$; * $p < .05$ (Mann-Whitney)
Comprehension and production of simple and complex sentences

Syntactic and morphosyntactic processing in stroke-induced and primary progressive aphasia

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Abstract. The paper reports findings derived from three experiments examining syntactic and morphosyntactic processing in individuals with agrammatic and logopenic variants of primary progressive aphasia (PPA-G and PPA-L, respectively) and stroke-induced agrammatic and anomic aphasia (StrAg and StrAn, respectively). We examined comprehension and production of canonical and noncanonical sentence structures and production of tensed and nontensed verb forms using constrained tasks in experiments 1 and 2, using the Northwestern Assessment of Verbs and Sentences (NAVS [57]) and the Northwestern Assessment of Verb Inflation (NAVI, Thompson and Lee, experimental version) test batteries, respectively. Experiment 3 examined free narrative samples, focusing on syntactic and morphosyntactic measures, i.e. production of grammatical sentences, noun to verb ratio, open-class to closed-class word production ratio, and the production of correctly inflected verbs. Results indicate that the two agrammatic groups (i.e., PPA-G and StrAg) pattern alike on syntactic and morphosyntactic measures, showing more impaired noncanonical compared to canonical sentence comprehension and production and greater difficulties producing tensed compared to nontensed verb forms. Their spontaneous speech also contained significantly fewer grammatical sentences and correctly inflected verbs, and they produced a greater proportion of nouns compared to verbs, than healthy speakers. In contrast, PPA-L and StrAn individuals did not display these deficits, and performed significantly better than the agrammatic groups on these measures. The findings suggest that agrammatism, whether induced by degenerative disease or stroke, is associated with characteristic deficits in syntactic and morphosyntactic processing. We therefore recommend that linguistically sophisticated tests and narrative analysis procedures be used to systematically evaluate the linguistic ability of individuals with PPA, contributing to our understanding of the language impairments of different PPA variants.

Keywords: Aphasia, primary progressive aphasia, agrammatism, syntactic processing, narrative speech

1. Introduction

Although there exists a large body of literature that describes the linguistic deficits associated with different types of aphasia caused by stroke (StrAph). Many individuals with stroke-induced agrammatic aphasia (StrAg) of Broca's type present a characteristic pattern of nonfluent speech, as well as grammatical, or (morpho)syntactic, deficits. The latter are exhibited by impaired comprehension and production of sentences with complex syntactic structures, in particular semantically reversible noncanonical sentences involving syntactic movement (e.g. [9,11,31,62]), impaired production of grammatical morphemes, in particular tense inflection, etc.
Sentence Comprehension and Production

Northwestern Assessment of Verbs and Sentences (NAVS; Thompson 2011)

What is NAVS?

The Northwestern Assessment of Verbs and Sentences (NAVS) was designed to examine comprehension and production of action verbs, production of verb argument structure in sentence contexts, and comprehension and production of canonical and non-canonical sentences in individuals with language disorders resulting from neurological disease. Results of testing provide a comprehensive profile of these abilities.

The NAVS consists of five subsets: the Verb Naming Test (VNT), the Verb Comprehension Test (VCT), the Argument Structure Production Test (ASPT), the Sentence Production Priming Test (SPPT), and the Sentence Comprehension Test (SCT). The VNT and VCT examine production and comprehension of isolated verbs that differ with respect to their argument properties. The ASPT evaluates production of these verbs together with their arguments in a sentence production task. Verb argument structure and optionality effects are examined based on verb types (i.e., one-, two-, and three-argument verbs) as singletons (i.e., in the VNT and VCT) and in a sentence context (i.e., in the ASPT). Production and comprehension of sentences by canonicity and sentence type are examined in the SPPT and the SCT, using six sentence types (i.e., three canonical forms: active, subject extracted wh-question (SWQ), and subject relative clause (SR); three non-canonical forms: passive, object extracted wh-question (OWQ), and object relative clause (OR)).

If you want to order the test or need more information, please visit www.northwestern.flintbox.com/public/project/9299/
Point to: The groom was carried by the bride.
The bride was carried by the groom.
Who is the man saving?  ???
<table>
<thead>
<tr>
<th>Aphasia Type</th>
<th>Number</th>
<th>Years Post-Onset (M)</th>
<th>Age (M)</th>
<th>Education (yrs) (M)</th>
<th>WAB AQ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Fluent</td>
<td>59 (15 m)</td>
<td>3.84</td>
<td>62</td>
<td>17</td>
<td>77.74</td>
</tr>
<tr>
<td>Fluent</td>
<td>57 (18 m)</td>
<td>3.72</td>
<td>64</td>
<td>16</td>
<td>69.8</td>
</tr>
</tbody>
</table>

(Caplan & Hildebrandt, 1998; Caramazza & Zurif, 1976; Grodzinsky 2000; Saffran et al., 1980; Thompson et al., 1995; and others)
## NAVS Results: PPA-G vs. PPA-L

<table>
<thead>
<tr>
<th>Aphasia Type</th>
<th>Number</th>
<th>Years Post-Onset (M)</th>
<th>Age (M)</th>
<th>Education (yrs) (M)</th>
<th>WAB AQ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPA-G</td>
<td>11</td>
<td>3.84</td>
<td>63.8</td>
<td>17</td>
<td>82.95</td>
</tr>
<tr>
<td></td>
<td>6 males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPA-L</td>
<td>22</td>
<td>3.72</td>
<td>62.9</td>
<td>16</td>
<td>88.50</td>
</tr>
<tr>
<td></td>
<td>9 males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke-Agrammatic</td>
<td>22</td>
<td>5.38</td>
<td>53.6</td>
<td>16</td>
<td>77.13</td>
</tr>
<tr>
<td></td>
<td>16 males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thompson et al. (2012). *Behavioral Neurology*
NAVSO Results: PPA-G vs. Stroke Agrammatism

Thompson et al. (2012). Behavioral Neurology
Northwestern Anagram Test

Grammatical processing deficits in PPA signal FTLD-T pathology (Mesulam et al, 2008)

Measures of grammatical processing need to adapt to input and output limitations of individual patients and track changes as disease progresses

NAT provides clinical options for measuring syntactic processing
Northwestern Anagram Test (NAT)

What is the NAT?

The Northwestern Anagram Test (NAT) was developed to examine non-verbal production of canonical and noncanonical sentences, using a set of word cards and action pictures. It is particularly useful for testing individuals with motor speech, cognitive (e.g., attention, memory), or other impairments that preclude ability to perform spoken sentence production tasks, such as those included on the Northwestern Assessment of Verbs and Sentences (NAVS).

The NAT consists of two versions: a Long and Short Version. The Long Version examines production of the same sentence types examined with the NAVS, including active sentences, passive sentences, subject extracted wh-questions, object extracted wh-questions, subject relatives, and object relatives. The Short Version examines production of subject and object extracted wh-questions only. Scores derived from the two versions are highly correlated with one another. In addition, scores on the NAT correlate highly with those derived from the Sentence Production Priming Test (SPPT) on the NAVS.

If you want to order the test or need more information, please visit www.northwestern.flintbox.com/public/project/19927

Thompson, Weintraub, & Mesualm, 2009
https://flintbox.com/public/project/19927
Sample Test Item

girl

boy

tickle

the

tickling

boy

girl

the

is
NAT Performance Patterns

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>YPO (M)</th>
<th>Age (M)</th>
<th>WAB AQ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPA-G</td>
<td>6</td>
<td>3.9 (0.6)</td>
<td>64.9 (3.0)</td>
<td>80.1 (1.4)</td>
</tr>
<tr>
<td>Stroke-Agr</td>
<td>11</td>
<td>6.8 (1.6)</td>
<td>57.7 (3.0)</td>
<td>66.0 (5.2)</td>
</tr>
<tr>
<td>t-Test</td>
<td></td>
<td>P=.11</td>
<td>P=.12</td>
<td>P=.02</td>
</tr>
</tbody>
</table>
Correlations
NAT and NAVS SPPT

- Total NAT and SPPT score
  Spearman R = .91, p < .001
- Canonical structures
  Spearman R = .68, p = .015
- Noncanonical structures
  Spearman R = .95, p < .001

The Northwestern Anagram Test: Measuring Sentence Production in Primary Progressive Aphasia

Sandra Weintraub, PhD, M.-Marsel Mesulam, MD, Christina Wieneke, BA, Alfred Rademaker, PhD, Emily J. Rogalski, PhD, and Cynthia K. Thompson, PhD

American Journal of Alzheimer’s Disease & Other Dementias (2009)
Classification of PPA by Subtype

Quantitative Template for Subtyping Primary Progressive Aphasia

Marsel Mesulam, MD; Christina Wieneke, BA; Emily Rogalski, PhD; Derin Cobia, PhD; Cynthia Thompson, PhD; Sandra Weintraub, PhD

Archives of Neurology (2009)
Primary Language Measures

- **Western Aphasia Battery** (WAB; Kertesz, 2006)
- **Boston Naming Test** (BNT; Kaplan et al., 1983)
- **Northwestern Naming Battery** (Thompson & Weintraub, 2014)
- **Peabody Picture Vocabulary Test**, items 157-192 (PPVT; Dunn & Dunn, 2006)
- **Northwestern Assessment of Verbs and Sentences** (Thompson, 2011)
- **Northwestern Anagram Test** (NAT; Thompson, Weintraub, & Mesulam, 2012)

Mesulam, Wieneke, Rogalski, Cobia, Thompson & Weintraub (2009). Archives of Neurology
Deficit/Atrophy Patterns in Mild PPA

Quantitative classification of primary progressive aphasia at early and mild impairment stages

M.-Marsel Mesulam,\(^1\) Christina Wieneke,\(^1\) Cynthia Thompson,\(^1,\,2\) Emily Rogalski\(^1\) and Sandra Weintraub\(^1\)

Figure 1. Quantitative template. Filled circles indicate impaired performance (<90% accuracy) in repetition tasks. Open circles indicate preserved repetition. The interval between 80% and 90% accuracy represents a grey zone where boundaries between subtypes are blurred. Numbers correspond to subject numbers in Tables 3 and 4. nc = non-canonical sentences.
On-Line Sentence Processing Patterns
Automatic processing of wh- and NP-movement in agrammatic aphasia: Evidence from eyetracking

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\textsuperscript{d}Department of Communication Sciences and Disorders, Northwestern University, Evanston, IL, USA
\textsuperscript{e}Department of Neurology, Northwestern University, Evanston, IL, USA

Dickey, Choy, & Thompson (2007); Dickey & Thompson (2009); Meyers, Mack, & Thompson (2012); Mack, Ji, & Thompson, 20012; Thompson & Choy (2009)

Tracking passive sentence comprehension in agrammatic aphasia

Aaron M. Meyer\textsuperscript{a}, Jennifer E. Mack\textsuperscript{a}, Cynthia K. Thompson\textsuperscript{a,b,c,*}
Locating Participant’s Eye

Center of pupil

Corneal Reflection
"One day, a bride and a groom were walking in the mall. The bride was feeling playful, so the bride tickled the groom. A clerk was amused."

Probe Question
"Point to the one that the bride was tickling ___ in the mall".

Dickey & Thompson (2009). Journal of Neurolinguistics
Aphasic vs Controls

Aphasic Correct vs Incorrect

Eye fixations to “groom” across regions

Dickey & Thompson (2009). *Journal of Neurolinguistics*
Gap-Filling in PPA

• Is online formation of syntactic dependencies impaired or intact in PPA-G? In other PPA subtypes?

“One day, a bride and groom were in a mall. The bride was feeling playful, so the bride tickled the groom. A clerk was amused.

Point to the one that the bride was tickling ___ in the mall.”
Participants
- 10 older adult controls
- 8 PPA-G
- 5 PPA-L (2)/PPA-S (3)

Results: PPA-G show
- Gap-filling (rise in target fixations during the verb + GAP region)
- Significantly slower rise in target fixations compared to controls
- Marginally slower as compared to PPA-L/PPA-S, who don’t differ from controls
Summary Sentence Deficits Patterns in Agrammatism

Both Stroke and Progressive Aphasia

• Off-Line Results
  o Syntactically complex sentences more difficult than simple sentences to comprehend and produce

• On-Line Results (eye-tracking)
  o ‘Normal’ syntactic computation of complex sentences (e.g., normal “gap-filling” for wh-movement structures)
  o Impaired integration of lexical items (content words) into the syntax
    • Thematic role assignment
Training Complex Sentences

Wh-movement
☞ Object relatives
☞ Object clefts
☞ Object extracted wh-questions

NP-movement
☞ Subject raising
☞ Passives

Treatment of Underlying Forms (TUF)
Object Relative Training

Target Sentence

Pete saw the cat who the dog watched.
Object Relative Training

Step 1: Thematic Role Identification

[Pete] saw [the cat] [the dog] watched [the cat]
Step 2: Object Relative Sentence Building
Clinician manipulates cards to combine clauses

[who]

[Pete] [saw] [the cat]  [the dog] [watched] [the cat]
Step 3: Participant Builds Sentence
Participant manipulates cards to combine clauses
Thematic role identification in re-built sentence

[Pete] [saw] [the cat]  [the dog] [watched] [the cat]
“Point to ‘It’s the cat who the dog is watching’”
Production Probe
Clinician model sentence structure, participant produces similar sentence

“For this picture you could say: ‘It’s the cat who the dog is watching’.”
Training Complex to Simple: Generalization across Structures

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Northwestern University
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Lewis P. Shapiro
San Diego State University and University of California, San Diego

Swathi Kiran
Northwestern University
Evanston, IL

The Role of Syntactic Complexity in Treatment of Sentence Deficits in Agrammatic Aphasia: The Complexity Account of Treatment Efficacy (CATE)

This experiment examined the hypothesis that training production of syntactically complex sentences results in generalization to less complex sentences that have processes in common with treated structures. Using a single subject experimental design, 4 individuals with agrammatic aphasia were trained to comprehend and produce filler-gap sentences with wh-movement, including, from least to most complex, object-extracted who-questions, object clefts, and sentences with object-relative clausal embedding. Two participants received treatment first on the least complex structure (who-questions), and 2 received treatment first on the most complex form (object-relative constructions), while untrained sentences and narrative language samples were tested for generalization. When generalization did not occur across structures, each was successively entered into treatment. Results showed no generalization across sentence types when who-questions were trained; however, as predicted, object-relative training resulted in robust generalization to both object clefts and who-questions. These findings support those derived from previous work, indicating not only that generalization occurs across structures that are linguistically related, but also that generalization is enhanced when the direction of treatment is from more complex to less complex constructions. This latter finding supports the authors’ newly coined “complexity account of treatment efficacy” (CATE).

COMPLEX

Pete saw the groom who(m) the bride carried _GAP_.

SIMPLE

It was the groom who(m) the bride carried _GAP_.

Who did the bride carry_GAP_?
Training Simple to Complex: No Generalization

The Role of Syntactic Complexity in Treatment of Sentence Deficits in Agrammatic Aphasia: The Complexity Account of Treatment Efficacy (CATE)

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Who did the bride carry _GAP_?

It was the groom who(m) the bride carried _GAP_.

Pete saw the groom who(m) the bride carried _GAP_.

SIMPLE

\[ \text{ Who did the bride carry } \_\text{GAP}\_? \]

COMPLEX

\[ \text{ It was the groom who(m) the bride carried } \_\text{GAP}\_. \]

\[ \text{ Pete saw the groom who(m) the bride carried } \_\text{GAP}\_. \]
who(i)(j) chased the man saw the artist (j) the thief
Complexity Account of Treatment Efficacy (CATE)

- Top-down training
- Training complex linguistic structures results in generalization to less complex structures
  - Linguistically related

- Computer simulations (Plaut, 1996)
- English as Second Language (Eckman, 1988)
- Phonological development (Gierut, 1998, 1999, 2007)
- Lexical semantic (naming) deficits (Kiran & Thompson, 2003; Kiran et al., 2008)
- Phonological dyslexia (Riley & Thompson, 2015)
fMRI Task
Sentence-Verification

Complex: Object Clefts
“It was the groom who the bride carried”

Simple: Subject Clefts
“It was the bride who carried the groom”
Neural Mechanisms of wh-Movement Structures

Inferior/Middle frontal, Precentral, Superior/Middle temporal gyri

Figure 3.
The winning model #12, with driving input on the trilFG node and modulation of the connection between trilFG and pSTS by object-clerk processing. Mean parameter estimates are given alongside the connections and the modulation. Those that exceed the statistical threshold ($p < 0.05$) are listed in bold print.

Neural plasticity and treatment-induced recovery of sentence processing in agrammatism

Cynthia K. Thompson a, b, *, Dirk-Bart den Ouden a, Borna Bonakdarpour a, Kyla Garibaldi a, Todd B. Parrish c

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b Department of Neurology, Northwestern University, USA
c Department of Radiology, Northwestern University, USA

Aphasic Participants showed treatment-induced recruitment of neural tissue

Left middle temporal gyrus (BA21)

Bilateral inferior and superior parietal (BA7, 39, 40)
$12M grant to Northwestern to aid research on aphasia

Brain disorder causes inability to understand or express words

BY NANCY A. SIMON
Special to the Tribune

More Americans suffer from aphasia — a brain disorder in which a person loses the ability to understand or express words — than Parkinson’s disease or muscular dystrophy. But few in the public have heard of the disease.

Thanks to a major federal grant, however, the study and treatment of aphasia, which can be triggered by stroke, gunshot or other brain trauma, is undergoing a major expansion.

The National Institutes of Health awarded Northwestern University a $12 million grant to establish the Center for the Neurobiology of Language Recovery, which Caplan will lead. It is part of a national network of brain centers.

Cynthia Thompson, professor of communication sciences at Northwestern, will lead the new center. “We know the network is there to help people regain language skills at higher levels when someone’s life is disrupted,” said Cynthia Thompson, professor of communication sciences at Northwestern who will lead the new center. “We know that network is there to help people regain language skills at higher levels when someone’s life is disrupted.”

David Caplan (MGH)
Swathi Kiran (BU)
Brenda Rapp (JHU)
Cynthia Thompson (NU)
Todd Parrish (NU)

But the brain is capable of relearning language skills, she said. Thompson said she has discovered that patients regain learning skills at higher levels when

Northwestern

Professor Cynthia Thompson is looking for answers to aphasia, a devastating disorder that essentially robs the brain of language.
Sentactics

Computer Automated Complex Sentence Treatment
Sentence Production

Object Relatives

Object Clefts

Object Wh-Questions

Sentence Comprehension

Object Relatives

Object Clefts

Object Wh-Questions

Thompson, Holland, Choy, & Cole (2010).

Aphasiology
Treatment of PPA

- Few published studies of treatment for PPA
- Pharmacological interventions (Johnson et al., 2010; Kertesz et al., 2008; Reed et al., 2004)
  - Null effects
- Language treatments (Beeson et al., 2011; Henry et al., 2008; Murray, 1998; Newhart et al., 2009)
  - Primarily case studies with one or two patients
  - PPA type not always specified or controlled
  - Naming treatment; no sentence treatment studies
    - Mixed findings
  - Non-invasive Brain Stimulation (NBS)
    - One study of sentence treatment
Language Treatment

- Beeson et al. (2011)
  - 1 PPA-L participant
  - 2 weeks intensive naming treatment
  - Improved lexical retrieval for trained and untrained items, maintained for 6 months
  - fMRI results showed increased activation in left and right hemispheres
Noninvasive Brain Stimulation (NBS)

tDCS: Transcranial Direct Current Stimulation

- Low current electrical stimulation
  - Anodal (V+) increases excitability
  - Cathodal (V-) decreases excitability

TMS: Transcranial Magnetic Stimulation

- Frequency controlled electric current
  - Low (<5Hz) disrupts function
  - High (>10Hz) enhances function
# Strengths, Weakness by NBS Method

<table>
<thead>
<tr>
<th>tDCS</th>
<th>TMS</th>
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<tbody>
<tr>
<td>• Safe</td>
<td>• Safe -- when used properly</td>
</tr>
<tr>
<td>• Can be used with behavioral treatment</td>
<td>• Focal sites may be stimulated</td>
</tr>
<tr>
<td>• Can be used clinically</td>
<td>• Measureable effects without behavioral treatment</td>
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<tr>
<td>• Can be used at home</td>
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<tr>
<td>• Inexpensive</td>
<td></td>
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<tr>
<td>+</td>
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<tr>
<td>• Non-focal stimulation</td>
<td>• Difficult to do with behavioral treatment</td>
</tr>
<tr>
<td>• Small effects without behavioral treatment</td>
<td>• Difficult to use clinically</td>
</tr>
<tr>
<td></td>
<td>• Requires training to administer</td>
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<tr>
<td></td>
<td>• Can be uncomfortable or painful</td>
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<td>• Equipment is expensive</td>
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Therapeutic applications

Depression
PTSD
Schizophrenia
Alzheimer’s disease
Motor impairment
Cerebellar deficits
Aphasia
rTMS and Alzheimer’s Disease (AD)

Object vs. Action Naming

rTMS: high frequency left and right DLPC

Mild AD

Severe AD
Anodal tDCS for treatment of PPA: Improved Language Abilities

• Cotelli et al.
  o One PPA-G participant
  o 20 sessions over 10 days; LH Broca’s area in AM, Wernicke’s in PM
  o Behavioral treatment: Auditory word-picture identification, picture naming, oral word reading, word repetition

• Tsapkini et al.
  o One PPA-G participant
  o 10 sessions: L dlPFC
  o Behavioral treatment: Picture naming and other treatment for anomia

• Wang et al.
  o One PPA patient (subtype unspecified)
  o 10 sessions: LH IFG, SMG
  o Behavioral treatment: Spelling
High Frequency rTMS for PPA: Improved Language Ability

- Finocchiaro, et al. (2006)
  - Case study of 60 yo man with PPA
  - High frequency rTMS (20 Hz) applied at 90% MT for 2 seconds
  - 10 times/day, 5 consecutive days
  - Stimulation target: LH medial IFG
  - Sentence production
    - Sentence completion task
    - Fill in missing noun or verb
  - Improved verb production in sentences

Also see Cotelli et al., Wang et al., and others
Summary and Unresolved Questions about Treatment for PPA

• Treatment improves language abilities in some patients with PPA
• Does treatment change the trajectory of language decline?
• Should treatment be compensatory only?
  o Verbal compensatory strategies (e.g., naming strategies)
  o Non-verbal compensatory strategies
    • gesture, drawing, communication notebook
    • electronic devices (banking client verbalization for future use)
• Should treatment exploit principles of neurolinguistics?
• Should treatment take advantage of principles of neuroplasticity?
• Research needed
Life Participant Approach to Aphasia

World Health Organization (WHO) framework

Focus:
The consequences of aphasia
Re-engagement in life
Enhancing life participation and quality of life
Northwestern University Aphasia Center
Promoting Communication and Community for People with Aphasia

TV & Film.

Journal Club.

Community Connection.

Cyber Hour.

Newsroom.

Book Club.

Conversation Group.

Games Club.

Toastmasters.

Exercise Club.

Music Club.
What have we learned?

- Agrammatic aphasic individuals (both stroke and progressive) show difficulty processing complex sentences in off-line and on-line tasks
  - Evidence of gap filling/sentence resolution in the vicinity of the verb
  - Patterns do not lend support to representational accounts of sentence deficits in aphasia
- Difficulty integrating lexical information into higher order representations

Lexical (Thematic) Integration Deficit
What have we learned?

- Treatment improves sentence comprehension and production
- Linguistically related structures recover together
- Generalization: complex $\rightarrow$ simple structures
  - The Complexity Account of Treatment Efficacy (CATE) (Thompson et al., 2003)
  - Counter to conventional treatment for language impairments, which train simple structures first

Train Complex Forms First

Not tested in PPA or with NBS in either stroke and PPA
What have we learned?

- Neuroimaging (fMRI) data show brain activation changes associated with recovery of language
  - Both stroke and PPA

Brain change possible long after stroke

Patients with PPA recruit spared neural tissue to support language
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