Purpose: Reorganization of language networks in aphasia takes advantage of the facts that (a) the brain is an organ of plasticity, with neuronal changes occurring throughout the life span, including following brain damage; (b) plasticity is highly experience dependent; and (c) as with any learning system, language reorganization involves a synergistic interplay between organism-intrinsic (i.e., cognitive and brain) and organism-extrinsic (i.e., environmental) variables. A major goal for clinical treatment of aphasia is to be able to prescribe treatment and predict its outcome based on the neurocognitive deficit profiles of individual patients. This review article summarizes the results of research examining the neurocognitive effects of psycholinguistically based treatment (i.e., Treatment of Underlying Forms; Thompson & Shapiro, 2005) for sentence processing impairments in individuals with chronic agrammatic aphasia resulting from stroke and primary progressive aphasia and addresses both behavioral and brain variables related to successful treatment outcomes. The influences of lesion volume and location, perfusion (blood flow), and resting-state neural activity on language recovery are also discussed as related to recovery of agrammatism and other language impairments. Based on these and other data, principles for promoting neuroplasticity of language networks are presented.

Conclusions: Sentence processing treatment results in improved comprehension and production of complex syntactic structures in chronic agrammatism and generalization to less complex, linguistically related structures in chronic agrammatism. Patients also show treatment-induced shifts toward normal-like online sentence processing routines (based on eye movement data) and changes in neural recruitment patterns (based on functional neuroimaging), with posttreatment activation of regions overlapping with those within sentence processing and dorsal attention networks engaged by neurotypical adults performing the same task. These findings provide compelling evidence that treatment focused on principles of neuroplasticity promotes neurocognitive recovery in chronic agrammatic aphasia.

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Recovery of language following brain damage takes advantage of two now well-known facts. First, the brain is an organ of plasticity, with neuronal changes occurring throughout the life span, including following brain damage. Attesting to this, many stroke survivors with aphasia show improved language abilities and associated rewiring of the language network even several years poststroke (Allen, Mehta, McClure, & Teasell, 2012; Crosson et al., 2019; Hartwigsen & Saur, 2019; Kiran & Thompson, 2019). Second, plasticity is highly experience dependent. That is, the malleability of the neural networks for language is influenced by language experience: People with aphasia who receive language treatment show improved language ability, whereas those who receive no treatment often do not. Another well-known observation is that not all people with aphasia show the same degree of recovery. This is likely because of the many factors that influence it: both organism-intrinsic (i.e., lesion characteristics, patterns of impaired language) and organism-extrinsic (i.e., environmental) variables, and as with any learning system, recovery from aphasia involves a synergistic interplay between the two (see Kiran & Thompson, 2019, for a review). Understanding how these variables affect the recovery of language is important not only for the sake of knowledge about brain damage and recovery of function but also, and critically, clinically. A major goal in clinical practice is to be able to provide optimal treatment and predict treatment outcome for people with aphasia based on the behavioral (and neural) patterns patients present. Although the field has not yet reached this goal, this review article discusses a body of...
relevant work, completed in my lab over the past three decades, that addresses it in the domain of sentence processing. The results of studies examining the neurocognitive effects of Treatment of Underlying Forms (TUF; Thompson & Shapiro, 2005), a metalinguistic intervention approach, on sentence processing in individuals with agrammatic aphasia are presented, followed by a summary of recent studies focused on neural variables that potentially influence treatment-induced improvements in aphasia across language domains. The most recent findings reported here were derived from a multisite, 5-year, National Institutes of Health–funded project, which examined the neurocognitive effects of treatments for anoma (Boston University and Massachusetts General Hospital), dysgraphia (Johns Hopkins University), and aggrammatism (Northwestern University). Based on our collective findings, and those of others, principles for promoting neuroplasticity as related to recovery of sentence processing are discussed in the final section of this review article. Before turning to these discussions, I first briefly address the neurocognitive mechanisms of sentence processing in neurotypical adults, which provide a basis for interpretation of the patient data, and discuss critical psycholinguistic concepts upon which TUF is based.

**Sentence Processing in Healthy People**

A large literature focused on sentence processing in neurotypical adults indicates that both understanding and producing sentences involve rapid analysis and integration of structural and conceptual information. Sentences that follow the canonical word order of a particular language (e.g., Agent–Verb–Theme in English; as in Sentence 1 in Box 1) are preferred over sentences in which the linear order of sentence constituents violates this pattern (i.e., noncanonical structures in Sentences 2 and 3 in Box 1; F. Ferreira, 2003; Hanne, Burchert, De Bleser, & Vabissh, 2015; Kamide, Scheepers, & Altman, 2003; Knoerlle, Crocker, Scheepers, & Pickering, 2005; Meyer, Mack, & Thompson, 2012; Townsend & Bever, 2001). Rather than the Agent argument (i.e., the doer of the action) coming before the Verb and the Theme argument (i.e., the recipient of the action) following the verb, as in canonical active sentences, in noncanonical sentences, the Theme is encountered before the Agent (i.e., the boy [Theme] precedes the woman [Agent] in 2 and 3). According to linguistic theory, noncanonical sentences involve movement of the Theme from its original (underlying) position after the verb, leaving a Copy or Trace (t) in its place, to a landing site at an earlier position in the sentence (e.g., Chomsky, 1986; Marantz, 1995), creating a dependency between the two positions, marked by (\(i\)). This means that solving “who did what to whom” requires (or depends on) consideration of both verb arguments and other materials in the sentence. Object-cleft structures (2) involve wh-movement, formed by displacement of the Theme argument to a clause-initial nonargument position (i.e., the position typically occupied by wh-question words, as in “Who did John kiss?”).

The technical term for this position is the **Specifier position of the Complementizer Phrase**. In contrast, passive sentences (3) involve supplanting of the Theme to an earlier argument position (i.e., the position typically occupied by the subject of the sentence, technically referred to as the **Specifier position of the Inflection Phrase**).

**Box 1. Sample canonical and noncanonical sentences.**

1. The woman \(_{AGENT}\) weighed the boy \(_{THEME}\). (canonical: active; no movement)
2. It was the boy \(_{THEME}\) who \(_{i}\) the woman \(_{AGENT}\) weighed \([t]\). (noncanonical: object cleft; wh-movement)
3. The boy \(_{THEME}\) was weighed \([t]\) by the woman \(_{AGENT}\). (noncanonical: passive; NP-movement)

In sentence comprehension, noncanonicity violates healthy listeners’ preference that (or prediction that) the first noun phrase (NP) encountered is the Agent of the action, in anticipation of a canonical structure. When it is discovered downstream that the first NP is not the Agent, thematic role reassignment and syntactic reanalysis are required in order to accurately integrate thematic information into the syntactic structure. Psycholinguistic studies using cross-modal priming, eyetracking, and other real-time experimental paradigms have shown that noncanonical compared to canonical sentences are harder to process for healthy listeners (del Río, López-Higes, & Martín-Aragoneses, 2012; Mack & Thompson, 2017; Swinney & Zurif, 1995; Tanenhaus, Carlson, & Trueswell, 1989; Zurif, Swinney, Prather, Wingfield, & Brownell, 1995; and many others). Production of noncanonical sentences also is more computationally costly than producing canonical ones—again because the order of constituent production differs from the basic order of the language. Therefore, preplanning production of a noncanonical sentence is more difficult than preplanning a canonical sentence, although healthy speakers are able to use an incremental (word-by-word) production strategy for both complex and simple sentences. However, healthy speakers may also use structural planning in production of complex sentences, which requires planning up to the verb (Konopka, 2012; Lee, Yoshida, & Thompson, 2015; Wagner, Jescheniak, & Schriefers, 2010).

Studies examining the neural mechanisms of sentence processing also find that the networks for noncanonical and canonical sentence processing differ. In a recent functional magnetic resonance imaging (fMRI) study with 21 healthy participants, we found overlapping cortical activation for the two sentence types, with engagement of additional regions for noncanonical compared to canonical structures (Europa, Gitelman, Kiran, & Thompson, 2019). Participants listened to canonical active and subject cleft structures, as well as noncanonical passive and object cleft structures; viewed pictures depicting reversible transitive actions; and indicated by button press whether the sentences matched the scenes. They also performed a control task with reversed speech and scrambled pictures (of target sentences and scenes). As shown in Figure 1, results indicated greater activation for noncanonical compared to

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1. NIDCDP50DC012283 (PI: C. K. Thompson).
canonical sentences in the left inferior frontal gyrus (IFG; pars opercularis), middle frontal gyrus (MFG), paracingulate gyrus, posterior middle temporal gyrus (pMTG), superior left occipital cortex, and fusiform gyrus (FG).

A recent meta-analysis of the results of neuroimaging studies in healthy participants, using activation likelihood estimation (Turkeltaub, Eden, Jones, & Zeffiro, 2002), largely confirmed these findings (Walenski, Europa, Caplan, & Thompson, 2019). Based on the results of 37 studies contrasting noncanonical and canonical sentence comprehension, greater activation for noncanonical sentences was found, with clusters of significant activation for the contrast noncanonical > canonical structures in the left IFG, MFG, and superior frontal gyrus (SFG) as well as the left pMTG and angular gyrus (AG) and the paracingulate gyrus, bilaterally (see Figure 2).

**Sentence Processing in Agrammatic Aphasia**

The computational details involved in processing sentences are particularly relevant for understanding and treating patients with agrammatic aphasia. Agrammatic aphasia, referred to as agrammatism, was introduced in 1877 by Adolf Kussmaul (1822–1902) and has been recognized since then as a general speech production pattern associated with Broca’s aphasia, characterized by production of grammatically impoverished sentences due to a lack of verbs (compared to nouns) and word order errors (particularly in semantically reversible sentences, in which both participants in a sentence can plausibly serve as either the Agent or Theme, e.g., *The dog chased the cat. cf. The dog chased the bone.*).

Figure 1. Regions of significant activation derived from 23 neurotypical adults while performing a sentence verification task for noncanonical > canonical sentences. Reprinted from Europa et al. (2019) under the Creative Commons Attribution License (CC BY). Copyright © 2019 Europa, Gitelman, Kiran, and Thompson.

Figure 2. Significant clusters for noncanonical versus canonical sentence comprehension derived from a meta-analysis of neuroimaging studies of sentence processing. Numbers 1–7 correspond with clusters of significant activation. Reprinted from Walenski et al. (2019). Copyright © 2019 Wiley Periodicals, Inc. Cluster 1 = left frontal pole; Cluster 2 = left inferior frontal gyrus pars opercularis, pars orbitalis, and middle frontal gyrus; Cluster 3 = left middle frontal gyrus; Cluster 4 = left superior frontal gyrus, medial superior frontal gyrus, and bilateral paracingulate gyri; Cluster 5 = right insula; Cluster 6 = left posterior middle temporal gyrus; and Cluster 7 = left angular gyrus. The scale bar reflects the activation likelihood estimation values.
grammatical morphemes. These differentiable patterns have been noted in studies published since then (Miceli, Mazzucchi, Menn, & Goodglass, 1983; Saffran, Berndt, & Schwartz, 1989; and others). Miceli et al. (1983), for example, described two Italian-speaking agrammatic patients: The utterances of one patient were largely composed of disjoint sequences of phrases, with the omission of main verbs, whereas the other patient rarely omitted verbs but had two to three times more omissions of articles and prepositions than the first one. These patterns suggest that the underlying neurocognitive mechanisms associated with the two forms of agrammatism likely differ. Dickey and Thompson (2007) reported compelling evidence supporting this idea in an experimental treatment study. A patient (M. D.) with aphasia and sentence production difficulty associated with impaired word order and grammatical morphology was provided with TUF focused on training wh-movement structures, which resulted in improved production of trained sentences and generalization to untrained structures with wh-movement. However, treatment had no effect on production of grammatical morphemes (e.g., verb tense/agreement and complementizers) or sentences with NP-movement.

The work discussed in this review article explicitly focuses on breakdown and recovery of the former deficit pattern—aktaphasie—although, often, the patients we study show impairments of both types. In our work, we use the general term, agrammatism, to describe our study participants.

Agrammatism also extends to impairments in syntactic comprehension (termed asyntactic comprehension; Grodzinsky, 1990). First noted by Salomon (1914), research has shown that comprehension of syntactically complex sentences with noncanonical word order is impaired. Semantically reversible canonical sentences are also often impaired because real-world knowledge cannot be used to determine the thematic roles of participants within the sentences (Caplan & Futter, 1986; Cho-Reyes & Thompson, 2012; Parisi & Pizzamiglio, 1970; Schwartz, Saffran, & Marin, 1980; Zurif & Caramazza, 1976; Zurif, Caramazza, & Myerson, 1972). Thompson and colleagues tested both comprehension and production of canonical (i.e., active sentences such as “The dog chased the cat.”) and subject cleft sentences such as “It was the dog that chased the cat.”) and noncanonical (i.e., passive and object cleft structures such as “The cat was chased by the dog.” and “It was the cat that chased the dog.”, respectively) sentences, with results showing that patients with agrammatic aphasia performed significantly more poorly than those with anomic aphasia on noncanonical compared to canonical forms in both domains (Cho-Reyes & Thompson, 2012; Thompson, Meltzer-Asscher, et al., 2013; see Figure 3).

Theories addressing the source of sentence production impairments have suggested that economy of effort underlies agrammatic speech (Goodglass, 1997): Patients produce primarily content words with reduced syntactic scaffolding, permitting communication of information using a minimum number of words. Similarly, adaptation theory (Kolk & Heeschen, 1992) suggests that agrammatic speakers adapt to their impairment by producing fewer words and reducing syntactic information, hence decreasing processing cost and memory demands. On the comprehension side, noncanonical sentences in agrammatic aphasia have been explained by several theories, including that traces are deleted from the syntactic representation (Grodzinsky, 1986; Zurif, Swinney, Prather, Solomon, & Bushell, 1993), that slowed processing precludes successful comprehension (Ferrill, Love, Walenski, & Shapiro, 2012; Love, Swinney,
Walenski, & Zurif, 2008; Swinney & Zurif, 1995; also see Burkhardt, Avrutin, Piñango, & Ruigendijk, 2008; Burkhardt, Piñango, & Wong, 2003), or that domain-general systems, which subserve sentence parsing and comprehension (e.g., working memory), are impaired (Caplan, Michaud, & Hufford, 2013; Caplan & Waters, 2013; Ullman, 2004). Alternatively, our eyetracking research using visual world paradigms suggests that both sentence production and comprehension fail due to abnormal thematic processes. For production, use of abnormal sentence planning strategies, that is, underuse of incremental processing and overuse of structural planning, leads to faulty grammatical encoding and thematic integration (Cho & Thompson, 2010; Lee & Thompson, 2011; Lee et al., 2015). Agrammatic patients, for example, use verb phrase planning, rather than a word-by-word strategy to produce sentences, and because verb production is impaired, the sentences they produce often are ungrammatical. Such impairments, therefore, may underlie Kolk and Heeschen’s (1992) adaptation theory. However, thematic processes are also impaired for comprehension: Agrammatic patients show impaired thematic prediction, failing to use an Agent-first strategy as do healthy listeners (Mack, Ji, & Thompson, 2013; Meyer et al., 2012). Furthermore, they do not show the ability to reassign thematic roles, resulting in faulty thematic integration and failed comprehension of noncanonical sentence structures (Dickey, Choy, & Thompson, 2007; Dickey & Thompson, 2009; Mack et al., 2013; Meyer et al., 2012; Thompson & Choy, 2009; Yee, Blumstein, & Sedivy, 2008; also see Blumstein et al., 1998).

**Treatment of Sentence Deficits in Aphasia: Neurocognitive Recovery Patterns**

I now turn to discussion of TUF (Thompson & Shapiro, 2005), which was explicitly developed for treatment of the aforementioned sentence deficits seen in agrammatic aphasia. First, the treatment itself is summarized; this is followed by a summary of studies examining the behavioral and neurocognitive effects of treatment. Notably, the participants who entered into our studies met strict inclusionary criteria (i.e., see Box 2).

**TUF**

TUF is based on both linguistic and processing accounts of verbs and sentences. From a linguistic perspective, words are stored in the lexicon together with word class information (e.g., noun [n], verb [v]) and information about the syntactic environment in which they occur. For example, verbs specify the participant [thematic] roles such as Agent, Theme (see Figure 4A), as well as subcategorization frames, which specify the syntactic form of the arguments (e.g., whether a theme argument is expressed as an NP [e.g., The boy chased the girl] or a prepositional phrase [e.g., The boy waited for the girl] and the position in the sentence they will occupy [e.g., subject or object position]). Once selected from the lexicon, syntactic operations serve to amalgamate these elements to build the syntactic structure of the sentence (e.g., S [sentence] = NP + verb phrase [VP]; Chomsky, 1995, 1998; Marantz, 1995; see also Adger, 2003; see Figure 4B). Simply put, a lexical item (e.g., V) is selected from the lexicon and merges with an NP (i.e., the object of the verb), which is assigned the thematic role of Theme, forming a higher order category (i.e., a VP). The VP then merges with the subject NP, assigned the role of Agent, to

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**Box 2. Inclusionary criteria for participants entered into studies examining the effects of TUF.**

**LANGUAGE**

- Language profile consistent with Broca’s aphasia, based on performance on the Western Aphasia Battery—Revised (Kertesz, 2007).
- Relatively spared single word comprehension (both objects and actions), based on performance on the Northwestern Naming Battery (NNB; Thompson & Weintraub, 2014), Auditory Comprehension subtest.
- Greater difficulty naming actions compared to objects, based on performance on the NNB (Thompson & Weintraub, 2014), Confrontation Naming subtest. Note: The Boston Naming Test (Kaplan, Goodglass, & Weintraub, 1983) and Northwestern Assessment of Verbs and Sentences (NAVS; Thompson, 2011) Verb Production Test or an Object and Action Naming Test (Druks & Masterson, 2000) may also be used to test this.
- Deficits in production of verb argument structure, with poorer production of Theme arguments compared to Agents, based on performance on the NAVS (Thompson, 2011), Argument Structure Production Test.
- Greater difficulty comprehending and producing non-canonical compared to canonical sentences, based on performance on the NAVS (Thompson, 2011), Sentence Comprehension Test and Sentence Production Priming Test, respectively.
- Narrative production: (a) reduced mean length of utterance (normal mean = 132.2), (b) reduced words per minute (normal mean = 11.11 to 12.15), (c) reduced proportion of syntactically correct sentences (normal mean = 93.0–97.2; normal means from Hsu & Thompson, 2018, and Thompson et al., 2012).
- No evidence of semantic impairments, based on performance on the Pyramids and Palm Trees Test (Howard & Patterson, 1992), Picture Version.

**COGNITIVE**

- Average or above performance on the following:
  - Wechsler Memory Scale—Revised, Fourth Edition: Spatial Attention, Symbol Span, Logical Memory (Parts 1 and 2), Designs (Parts 1 and 2), and Logical Memory Tests (Wechsler, 1997).
  - Target Cancellation Test (Mesulam, 1985).
  - Trail-Making Test (Parts A and B; Tombaugh, 2004).
  - Wisconsin Card Sorting Test (Grant & Berg, 1948).

**OTHER**

- Vision (may be corrected) within normal limits, based on performance on the Lea Symbols Vision test (Hyvärinen, Näsänen, & Laurinen, 1980)
- Pass audiometric screening at 500, 1000, and 2000 Hz at 40 dB in at least one ear.
- Edinburgh Handedness Inventory (study participants must be right-handed; Oldfield, 1971)
form an NP-V-NP (i.e., Agent–Verb–Theme) sentence (S; see Figure 4B). Based on models of sentence processing (e.g., Bock & Levelt, 1994; V. S. Ferreira, 2010; Levelt, 1999), sentence constituents are assigned thematic roles (e.g., Agent, Theme) and grammatical functions (e.g., subject, object) during grammatical encoding.

TUF follows this in a series of metalinguistic steps that first build a simple active sentence, emphasizing the lexical (thematic) properties of verbs and their subcategorization frame. Participants are trained to comprehend and produce transitive (i.e., two-argument) verbs such as chase and to select and map their arguments (i.e., Agent–Theme [doer/receiver]) to the subject and object positions, respectively, in canonical sentences. Next, steps for building complex, non-canonical sentences and thematic role reanalysis and integration are emphasized. For detailed training steps, see https://anr.northwestern.edu/clinical-and-research-tools/#TUF.

Research has shown that these components of treatment promote improved sentence processing in people with aphasia. Verb as core treatment, advanced by Loverso, Selinger, and Prescott (1979), and Verb Network Strengthening Treatment (Edmonds, Mammino, & Ojeda, 2014) train verb production and highlight the semantic selection restrictions of verbs (e.g., words that can be used as objects/subjects of the verb, i.e., what may be chased: Dogs chase cars, not houses; who may do the chasing: Dogs chase, but apples don’t; Jackendoff, 1990). Similarly, Verb Argument Structure Treatment (VAST; Thompson, Riley, den Ouden, Meltzer-Asscher, & Lukic, 2013) trains verb production and comprehension, with emphasis on verb argument structure in simple active sentences. These approaches have shown improved verb production (and comprehension) as well as improved simple sentence production. Mapping Therapy (Fink, 2001; Rochon, Laird, Bose, & Scofield, 2005; Schwartz, Saffran, Fink, Myers, & Martin, 1994) and TUF train patients to map meaning to the syntax (i.e., map thematic roles to sentence structure) and also result in improved sentence processing in both simple and complex sentences. The critical difference between these latter approaches is that the Mapping Therapy focuses on comprehension (i.e., Schwartz et al., 1994) or production (i.e., Rochon et al., 2005) and trains simple sentences, testing (or later training) complex structures, whereas TUF focuses on both comprehension and production and trains complex sentences, testing generalization to less complex sentences. Both the Mapping Therapy and TUF engender improved sentence production and/or comprehension; however, TUF results in greater generalization from trained to untrained forms (cf. Barbieri, Mack, Chiappetta, Europa, & Thompson, 2019; Schwartz et al., 1994).

**Behavioral Effects of the TUF: Off-Line Performance Patterns**

Findings from our studies testing the effects of TUF have shown acquisition (both production and comprehension) of target structures (with both wh-movement and NP-movement) across studies, which have included primarily patients with stroke-induced aphasia, but also patients with the agrammatic variant of primary progressive aphasia (PPA-G; see the Appendix). Across studies and participants, we discovered two novel recovery patterns: (a) Patients relearn trained forms and show generalization to untrained, linguistically related (but not linguistically unrelated) structures.
(Ballard & Thompson, 1999; Barbieri, Mack, et al., 2019; Jacobs & Thompson, 2000; Thompson et al., 1997; Thompson, Shapiro, & Roberts, 1993; Thompson, Shapiro, Tait, Jacobs, & Schneider, 1996), and (b) training complex structures results in generalization to untrained linguistically related structures of lesser complexity, but training simple sentences rarely affects complex ones (Thompson, Ballard, & Shapiro, 1998; Thompson, Choy, Holland, & Cole, 2010; Thompson, den Ouden, Bonakdarpour, Garibaldi, & Parrish, 2010; Thompson, Shapiro, Kiran, & Sobecks, 2003) in keeping with the Complexity Account of Treatment Efficacy (CATE; Thompson et al., 2003). Notably, the effects of complexity have been shown in several linguistic domains, including naming (Kiran & Thompson, 2003; Sandberg & Kiran, 2014; Sandberg, Sebastian, & Kiran, 2012) and phonological dyslexia (Riley & Thompson, 2014) in people with aphasia and in children with developmental phonological impairments (see Gierut, 2007, for a review).

Across studies focused on training sentences with wh-movement, results show that participants with agrammatism improve in their ability to comprehend and produce trained structures (e.g., object clefts such as “It was the woman who the man followed.”), with generalization to untrained structures of lesser syntactic complexity (i.e., object wh-questions such as “Who did the man follow?”), but not syntactically unrelated structures with NP-movement (i.e., passive structures such as “The woman was followed by the man.”). Conversely, training less complex wh-movement structures does not improve more complex wh-movement structures. Similarly, participants trained to comprehend and produce NP-movement structures (i.e., passive sentences) show acquisition of trained structures as well as generalization to syntactically less complex structures that also involve NP-movement (e.g., active sentences with unaccusative verbs, e.g., The man fell by the river; see Figure 5). Of a total of 48 participants who completed treatment, only six did not show these patterns. One, in Thompson et al. (1993), did not show generalization to linguistically related object wh-questions due to difficulty with wh-morpheme selection. Another participant, in Thompson, den Ouden, et al., (2010), showed quite high baseline performance on object wh-question structures, and therefore, generalization from object clefts to simpler structures could not be tested. Three patients, however, failed to show generalization to structures of lesser complexity. Notably, all evinced Western Aphasia Battery–Aphasia Quotients (AQs) below 60 (two from Ballard & Thompson, 1999, trained on complex wh-movement structures; one from Barbieri, Mack, et al., 2019, trained on complex NP-movement structures), although two participants in Barbieri, Mack, et al., (2019) also had low AQs, but nevertheless showed substantial acquisition and generalization effects. Finally, only one participant (from Thompson & Shapiro, 1994) showed generalization from simple wh-movement structures (i.e., object wh-questions) to complex structures (object clefts). This patient, however, had PPA, which may have influenced learning and generalization, although the patient with PPA-G from Thompson et al. (under review) showed generalization patterns for both wh- and NP-movement structures such as those seen in the majority of patients with stroke-induced agrammatic aphasia (see below for a summary of the results for this patient). Additional studies examining the CATE in patients with PPA are needed to completely understand generalization patterns in this patient group.

In a recent study by Barbieri, Mack, et al. (2019), 14 participants with agrammatic aphasia, resulting from stroke, received a 12-week course of treatment focused on long passive sentences with adjunct clauses (e.g., The woman was followed by the man in the park.), with age-, education-, language impairment–matched across participants (n = 5) comprising a control group that received no treatment. At baseline, posttreatment, and 3 months following, we examined comprehension and production of trained and untrained long passives, syntactically related short passives (i.e., truncated passives with and without adjunct clauses), active transitive sentences (e.g., The man followed the woman.), and actives with unaccusative verbs (e.g., The woman fell in the park.), as well as unrelated Wh-movement (i.e., object cleft) structures in both participant groups. Results showed acquisition of trained and syntactically related, untrained

**Figure 5.** Proportion of studies using the Treatment of Underlying Forms to improve wh- and noun phrase–movement structures showing generalization from complex to simple sentences, and vice versa.
structures across language domains. However, no change in unrelated structures (i.e., object clefts) was found (see Figure 6).

**Effect of Treatment on Online Sentence Processing**

Does treatment-induced improvement in off-line sentence comprehension and production result in more normal-like sentence processing strategies, or does off-line improvement reflect development of nonlinguistic heuristic strategies for understanding and/or producing sentences? This question has been of interest in our recent work, which we have addressed by charting participants’ eye movements as they produce or listen to sentences. Notably, across studies, we found that participants who respond successfully to treatment show an emergence of normal sentence processing strategies.

Because this work required the measurement of eye movements over time, we first examined test–retest reliability in young healthy control participants (n = 21) and adults with aphasia (n = 12; Mack, Wei, Gutierrez, & Thompson, 2016) using an auditory sentence–picture matching task (after Meyer et al., 2012). On two separate occasions, 1 week apart, participants listened to active and passive sentences and selected between two pictures depicting semantically reversible scenes (e.g., *a boy kissing a girl; a girl kissing a boy*) as their eye movements were monitored during prespecified sentence regions (NP1 *the woman*, Verb [V] kissing/kissed, NP2 *the man*, Sentence End [E]). Both groups showed little eye movement variability across test points, with intraclass correlations (see Shrout & Fleiss, 1979) for the aphasic group in the good (.59–.75) and excellent (> .75) ranges for active sentences in the NP2 region and for passive sentences in the sentence end region, respectively.

Next, we used two eyetracking tasks—to evaluate pre- to posttreatment changes in online production and comprehension of passive and active sentences. A syntactic priming task (after Cho & Thompson, 2010) was used to test production: Each trial required participants to read/repeat an active or passive sentence and 1,500 ms later to produce a sentence describing an action scene using a different verb (Mack, Nerantzini, & Thompson, 2017). For comprehension, the aforementioned auditory sentence–picture matching task was used (Mack & Thompson, 2017). Results of both studies showed posttreatment changes in eye movements. Following treatment, participants (n = 10) showed evidence of incremental processing during production of passive sentences, particularly in the region prior to

Figure 6. The proportion (Prop) of correct responses on production (top) and comprehension (bottom) probe tasks for the treatment and control groups. FP = full passive (trained and untrained items); UP = untrained passive; AUC = unaccusative; OC = object cleft; ns = not significant. Adapted with permission from Barbieri, Mack, et al., 2019. Copyright © 2019 Elsevier Ltd.

*p < .05, **p < .01, ***p < .001, −p < .1
The majority of studies examining the neural mechanisms recruited to support language recovery have focused on patients with naming deficits, evaluating the effects of naming treatment (e.g., Fridriksson, Morrow-Odom, Moser, Fridriksson, & Baylis, 2006; Fridriksson et al., 2007; Sandberg, Bohland, & Kiran, 2015; van Hees et al., 2014). Only a handful have investigated the neuroplastic effects of treatment for sentence processing deficits (e.g., Barbieri, Mack, et al., 2019; Cherney & Small, 2006; Mohr, Difrancesco, Harrington, Evans, & Pulvermüller, 2014; Thompson, den Ouden, et al., 2010; Wierenga et al., 2006). Using primarily blood-oxygen-level-dependent (BOLD) signal data derived from fMRI as the dependent measure, studies show that language treatment results in increased activation (upregulation) following language treatment in nonlesioned cortical tissue in the left hemisphere, in the contralesional right hemisphere, or in both. Downregulation of neural activity following treatment has also been noted in a few studies (e.g., Abel, Weiller, Huber, Willmes, & Specht, 2015). A review of the aphasia treatment literature between 1996 and 2016 (Thompson, 2017) identified a total of 41 studies, which included 628 aphasic participants across studies. Of those, 90 study participants showed upregulation of neural activation in the right hemisphere, 99 showed increased activity in the left hemisphere, and 439 showed bilateral recruitment of neural tissue associated with treatment-induced language improvement. These findings indicate that the best candidate brain areas for supporting language recovery in chronic aphasia remain an unresolved issue and likely relate to individual variability in the neural mechanisms impaired by stroke and concomitant variability in impaired language processing within and across language domains. The type of treatment provided also affects outcomes, likely due to differences in the linguistic processes exploited, which engage differential, albeit overlapping, neural networks (see Gainotti, 2015; Kiran & Thompson, 2019, for reviews).

Our studies testing the effects of TUF on neural processing have shown that people with agrammatic aphasia recruit available tissue within the normal sentence processing network in the left and/or right hemisphere to support recovery. In one study, we examined the effects of training wh-movement structures (object clefts) and found pre- to posttreatment upregulation in undamaged regions within

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**Neuroplastic Effects of Treatment**

The majority of studies examining the neural mechanisms recruited to support language recovery have focused on patients with naming deficits, evaluating the effects of naming treatment (e.g., Fridriksson, Morrow-Odom, Moser, Fridriksson, & Baylis, 2006; Fridriksson et al., 2007; Sandberg, Bohland, & Kiran, 2015; van Hees et al., 2014). Only a handful have investigated the neuroplastic effects of treatment for sentence processing deficits (e.g., Barbieri, Mack, et al., 2019; Cherney & Small, 2006; Mohr, Difrancesco, Harrington, Evans, & Pulvermüller, 2014; Thompson, den Ouden, et al., 2010; Wierenga et al., 2006). Using primarily blood-oxygen-level-dependent (BOLD) signal data derived from fMRI as the dependent measure, studies show that language treatment results in increased activation (upregulation) following language treatment in nonlesioned cortical tissue in the left hemisphere, in the contralesional right hemisphere, or in both. Downregulation of neural activity following treatment has also been noted in a few studies (e.g., Abel, Weiller, Huber, Willmes, & Specht, 2015). A review of the aphasia treatment literature between 1996 and 2016 (Thompson, 2017) identified a total of 41 studies, which included 628 aphasic participants across studies. Of those, 90 study participants showed upregulation of neural activation in the right hemisphere, 99 showed increased activity in the left hemisphere, and 439 showed bilateral recruitment of neural tissue associated with treatment-induced language improvement. These findings indicate that the best candidate brain areas for supporting language recovery in chronic aphasia remain an unresolved issue and likely relate to individual variability in the neural mechanisms impaired by stroke and concomitant variability in impaired language processing within and across language domains. The type of treatment provided also affects outcomes, likely due to differences in the linguistic processes exploited, which engage differential, albeit overlapping, neural networks (see Gainotti, 2015; Kiran & Thompson, 2019, for reviews).

Our studies testing the effects of TUF on neural processing have shown that people with agrammatic aphasia recruit available tissue within the normal sentence processing network in the left and/or right hemisphere to support recovery. In one study, we examined the effects of training wh-movement structures (object clefts) and found pre- to posttreatment upregulation in undamaged regions within

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**Figure 7.** Eye movements recorded during performance of a sentence production (syntactic priming) task for active (black) and passive (blue) sentences. (A) Age-matched controls, (B) agrammatic aphasic participants prior to treatment, and (C) agrammatic aphasic participants following treatment. N1 = first noun phrase; V = verb; N2 = second noun phrase; E = end of sentence. Adapted from Mack et al. (2017) under the Creative Commons Attribution License (CC BY). Copyright © 2017 Mack, Nerantzini, and Thompson.
the left frontotemporal network, including the MTG, the AG, and the superior parietal lobule (SPL), as well as right hemisphere homologs, specifically the supramarginal gyrus (SMG) and the SPL (Thompson, den Ouden, et al., 2010). Similar findings were derived from Barbieri, Mack, et al. (2019) for NP-movement structures (passive sentences). However, posttreatment > pretreatment activation maps indicated significant upregulation in only the right hemisphere in both posterior and anterior brain regions (see Figure 9). Whereas the untreated participant group showed no changes in activation from pre- to posttesting, regions of upregulation for the treated patients showed overlap with several regions recruited by the healthy participants for the same passive > control contrast. In anterior brain regions, the healthy participants showed left IFG, MFG, and precentral gyrus activation, and right SFG activation; the patients showed right MFG and precentral recruitment only. Posteriorly, bilateral activation in the SPL, lateral occipital cortex (LOC), and FG as well as recruitment of the left superior temporal gyrus (STG) and SMG, and of the right AG, was found for healthy participants; the patients showed right SMG, AG, SPL, and LOC upregulation.

Interestingly, we found similar treatment-induced shifts in activation in a recent treatment trial for a patient (D. K.) with the agrammatic subtype of PPA (Thompson, Barbieri, Mack, Wilkins, & Xie, under review). A longitudinal, single-subject, multiple-probe design was used to evaluate the effects of the TUF focused first on training NP-movement structures (i.e., passive sentences), followed by training of wh-movement structures (i.e., object clefts). Production and comprehension of both NP- and wh-movement structures were tested throughout the study: prior to and immediately following, 6 months, and 1 year following each treatment phase. In addition, structural and functional magnetic resonance scans were obtained prior to and following each treatment phase to evaluate changes in neuronal atrophy over time and neural activation associated with treatment, respectively.

The behavioral effects of treatment were identical to those seen in patients with stroke-induced agrammatic aphasia: D. K. acquired both structures when treatment was provided and showed generalization to untrained, linguistically related structures during both treatment phases. Prior to passive sentence treatment, structural neuroimaging revealed cortical atrophy (measured using nonparametric voxel-based morphometry) constrained to the left hemisphere in the hippocampus and the basal ganglia. Activation shifts, from pre to post passive treatment, were noted in both the left and right hemispheres, with large bilateral clusters of significant activation in the frontal region,
including the SFG, MFG, and IFG (pars opercularis is in the left; pars triangularis is in the right), precentral gyrus (left), and supplementary motor area (right). Posttreatment upregulation of neural activity was also found bilaterally in posterior brain regions, including the inferior parietal lobule (AG and posterior SMG), the right anterior SMG, and the FG (occipital regions), extending to the superior LOC in the left and to the lingual gyrus and cerebellum in the right. Notably, following passive sentence treatment, no regions of significant downregulation were found.

Prior to object cleft treatment, atrophy had increased in the left hippocampus and caudate nucleus and spread to the anterior parahippocampal gyrus and planum polare. In addition, significant atrophy was apparent in the right caudate nucleus and right putamen. In spite of this increased atrophy, following object cleft treatment, D. K. showed further shifts in activation, with upregulation in the left frontal pole and IFG (pars triangularis). Additional upregulation in the right hemisphere included tissue in the inferior parietal lobule, near the AG, and within the anterior SMG and posterior STG. Downregulation was also found bilaterally at posttreatment in the frontal pole.

Table 1 summarizes activation patterns found in our work focused on passive and object cleft sentence processing in healthy listeners as well as in patients with stroke-induced agrammatic aphasia and for D. K., following treatment. The patients showed activation overlapping with that found for healthy control participants in the left IFG, MFG, and precentral gyrus, and in the right SFG for one or both contrasts (i.e., passive > control; object cleft > subject cleft). The patients also showed right hemisphere activation in the IFG, MFG, and precentral gyrus that was not found in healthy participants. Posteriorly, activation for the aphasic participants overlapped with that seen in the healthy participants in the left MTG, SMG, AG, SPL, LOC, and FG as well as in the right AG, SPL LOC, and FG. Additionally, the patients showed upregulation following treatment in right hemisphere homologs of the STG, SMG, and insula. Collectively, these findings indicate that agrammatic aphasic participants recruit left and right hemisphere regions activated by healthy control participants as well as right hemisphere homologs of left-brain areas engaged by healthy listeners to support recovery of sentence processing.

### Variables Related to Neural Recruitment Patterns in Patients With Aphasia

Our neuroimaging results, and those of others, show some differences in neural recovery patterns across study participants, which may be attributed to several factors, including the source of brain damage. Differences between stroke and neurodegenerative disease, for example, likely influence patterns of neural reorganization. PPA typically and preferentially affects tissue within the left perisylvian language network, but notably, patterns of neural degeneration do not follow the cerebral vasculature as do lesions resulting from stroke (Mesulam et al., 2009). Furthermore, the slow destruction of tissue by neurodegenerative disease and the residual survival of neurons even in the most atrophied cortical regions leave tissue available for reorganization of synaptic circuitry in PPA (Sonty et al., 2003). Conversely, stroke results in cell death and necrosed regions of the brain that are completely unavailable to support recovery.

Other intrinsic brain variables with potential to influence the neural recruitment patterns associated with treatment of stroke-induced aphasia include lesion volume and location, cerebral perfusion, and resting-state neural activity. We have begun investigating their impact and briefly discuss our findings below.

**Lesion volume and location.** Some studies suggest that small left hemisphere lesions are associated with better recovery, whereas larger lesions predict poorer language recovery (Hope, Seghier, Leff, & Price, 2013; also see Plowman, Hentz, & Ellis, 2012, for a review). One explanation for this is that, assuming that recruitment of ipsilesional tissue promotes better recovery, smaller lesions leave greater tissue volume within the left hemisphere available for remapping of the language network, whereas large left hemisphere lesions limit left hemisphere tissue available for reorganization of function, and hence, right hemisphere recruitment is required. Supporting this in part, Skipper-Kallal, Lacey, Xing, and Turkeltaub (2017a) found that total lesion volume in the left hemisphere predicted right hemisphere activation for both overt naming and covert word retrieval. However, the relation between lesion volume and behavioral recovery is not straightforward. Our work in the domain of sentence processing has shown that participants with both large (Barbieri, Mack, et al., 2019) and smaller (Thompson, den Ouden, et al., 2010) left hemisphere lesions (see Figure 10) show quite similar patterns of impaired sentence processing and response to treatment (as discussed above). Patients with smaller left hemisphere lesions showed upregulation of neural activation in both the right and the left hemispheres, whereas those with larger lesions recruited only right hemisphere regions to support improvements in sentence processing.

Lesion location is likely equally, if not more, important than lesion volume for predicting language recovery. Hillis et al. found that damage to the left posterior STG and fibers within the superior longitudinal and arcuate fasciculi negatively influence the recovery of naming in both acute and chronic patients with aphasia, and these findings were independent of total lesion volume (Hillis et al., 2018). In line with this, Bonilha, Fridriksson, and colleagues found that sparing of tissue in left temporal parietal regions and within the basal ganglia is associated with improvements in naming (Bonilha, Gleichgerrcht, Nesland, Rorden, & Fridriksson, 2016; Fridriksson, Richardson, Fillmore, & Cai, 2012; also see Heiss, Thiel, Kessler, & Herholz, 2003; Naeser, Helm-Estabrooks, Haas, Auerbach, & Srivinasa, 1987; but see Skipper-Kallal, Lacey, Xing, & Turkeltaub, 2017b, who reported no relationships between naming skills and damage in any given left hemisphere region when lesion volume was controlled). The role of tissue within domain-general neural networks has also received recent attention. Two studies on naming treatment by Kiran and coworkers (Kiran, Meier,
Kapse, & Glynn, 2015; Sandberg et al., 2015) found bilateral posttreatment increases in connectivity between IFG and MFG, a region implicated in cognitive control (Fedorenko, Duncan, & Kanwisher, 2013), working memory (Curtis & D'Esposito, 2003), and attention (Corbetta, Patel, & Schulman, 2008). Following training of object cleft sentences, we also found increased activation in bilateral MFG, SPL, and intraparietal sulci, regions that are part of the dorsal attention network (DAN; Corbetta et al., 2008; Thompson, den Ouden, et al., 2010); bilateral upregulation of the SPL was also found following VAST (Thompson, Riley, et al., 2013). Similar increased activation in bilateral intraparietal sulci was found following treatment of phonological skills in a patient with agrammatic primary progressive aphasia (PPA) performing the same task (DeMarco, Wilson, Rising, Rapcsak, & Beeson, 2018). Treatment-induced recruitment of domain-general networks possibly reflects increased engagement of top-down attentional-executive mechanisms, such as self-monitoring and response inhibition (Geranmayeh, Brownsett, & Wise, 2014; Kurland, Baldwin, & Tauer, 2010). Barbieri, Mack, et al. (2019) explicitly tested the relation between treatment-induced improvement in passive

Table 1. Regions of significant activation for healthy controls for passive > control and object cleft > subject cleft contrasts and regions of posttreatment upregulation and downregulation of activation for stroke-agrammatic patients and a patient with agrammatic primary progressive aphasia (PPA) performing the same task.

| Brain region                      | Passive > control | Upregulation (posttreatment > pretreatment) | Object cleft > upregulation (posttreatment > pretreatment) |
|-----------------------------------|-------------------|---------------------------------------------|----------------------------------------------------------|
|                                   | Healthy           | Stroke-agrammatic | PPA (D. K.) | Healthy | Stroke-agrammatic | PPA (D. K.) |
|                                   | participants a    | participants b   |            |         | participants b   |            |
| Inferior frontal gyrus            | L                 | R               | L           | L       | L               | L           |
| Middle frontal gyrus              | L                 | R/R             | R/L/R       | L       | L               | L           |
| Superior frontal gyrus            | R                 | R               | L/R         | L       | L               | L           |
| Superior temporal gyrus_post      | L                 | R               | L           | L       | L               | L           |
| Middle temporal gyrus             | R                 | L               | R/L         | L       | L               | L           |
| Supramarginal gyrus               | L/R               | R               | L/R/L       | L       | L               | L/R         |
| Angular gyrus                     | R                 | R               | L/R         | L/L/R   | R               | L/R         |
| Superior parietal lobule          | L/R               | R               | L/R/L       | L       | L               | L/R         |
| Lateral occipital cortex          | L/R               | R               | L/R/L       | L       | L               | L/R         |
| Fusiform                          | L/R               |                 |             |         |                 |             |
| Insula                            | L/R               |                 |             |         |                 |             |

Downregulation (pretreatment > posttreatment)

| Brain region                      | Downregulation (pretreatment > posttreatment) |
|-----------------------------------|----------------------------------------------|
| Inferior frontal gyrus            | NA                                           |
| Middle frontal gyrus              | NA                                           |
| Prefrontal gyrifrontal pole       | NA                                           |
| Superior temporal gyrus           | NA                                           |
| Supramarginal gyrus               | NA                                           |
| Insula                            | NA                                           |

Note. L = left; R = right; NA = not applicable.

aFrom Barbieri, Mack, et al., 2019. bFrom Thompson, den Ouden, et al., 2010.

Figure 10. Lesion overlap map for treated participants in (a) Barbieri, Mack, et al. (2019) and (b) Thompson, den Ouden, et al. (2010). Lighter shades indicate areas with a higher proportion of participants displaying lesioned tissue.
sentence comprehension and production and two networks: the sentence processing network and the DAN. Results showed a positive relation between treatment gains, as measured by performance on off-line tasks, and upregulation of neural activation in regions within both networks. Notably, however, differential activation in the two networks was correlated with changes in online processing, as measured by eyetracking. As depicted in Figure 11, upregulation within the right hemisphere sentence processing network, but not the DAN, was significantly correlated with improved thematic prediction. Conversely, a significant relation was found between upregulation in the right dorsal attention, but not the sentence processing network, and thematic integration.

With regard to lesion volume and location, we found that participants with larger lesions within the left hemisphere sentence processing network showed greater upregulation of neural activity within right hemisphere homologs of the sentence processing network, indicating a positive relation between lesion volume and recovery (i.e., larger lesions were associated with greater treatment gains). Conversely, participants with smaller lesion volumes within the left DAN showed greater upregulation of activation within this network in the right hemisphere, indicating a negative relation between lesion volume and recovery (i.e., smaller lesions were associated with greater improvement). Although seemingly counterintuitive, these findings indicate that participants who showed upregulation of activation in both networks (and who most benefited from treatment) presented with large lesions within the left hemisphere sentence processing network, but relatively spared tissue within regions implicated in domain-general processes in the left hemisphere. These findings suggest a complex interaction between lesion location and recovery of language and point to a need for additional research addressing how lesions within both language and domain-general processing networks impact treatment outcomes.

Cerebral perfusion. Changes in cerebral perfusion (blood flow), resulting from stroke, which are common in acute stroke (Hillis et al., 2006; Reineck, Agarwal, & Hillis, 2005), persist into the chronic phase of recovery (Brumm et al., 2010; Richardson et al., 2011; Thompson, den Ouden, et al., 2010; Thompson, Walenski, et al., 2017). We used arterial spin labeling to evaluate perfusion in a group of patients with chronic stroke aphasia (n = 35) compared to that of healthy age-matched controls (n = 16; Thompson et al., 2017). Results showed decreased perfusion in perilesional tissue (supporting the results of a similar study by Richardson et al., 2011), with the greatest hypoperfusion in tissue closest to the lesion. We also found abnormally increased perfusion values within regions of the right hemisphere. The relation between abnormal perfusion and behavioral/neural recovery, however, is unclear. In one study, we found a negative correlation between regions of posttreatment upregulation of neural activation and perfusion.

Figure 11. Relation between increased (posttreatment > baseline) activation in the sentence processing (SPN) and dorsal attention (DAN) networks and changes in online thematic prediction (a, b) and online thematic integration (c, d). A significant relation between upregulation in the right SPN and a decrease in the proportion of fixations to the target (11a) reflects a shift toward use of an agent-first strategy during processing of passive sentences. 11d shows a significant relation between upregulation in the right DAN and an increase in target fixations from the verb region to the end of the sentence. Adapted from Barbieri, Mack, et al. (2019) under the Creative Commons Attribution License (CC BY). Copyright © 2019 Barbieri, Mack, Chiappetta, Europa, & Thompson.
(Thompson, den Ouden, et al., 2010). That is, regions within both the left and right hemispheres with low perfusion values showed lesser posttreatment activation as compared to regions with greater perfusion values. Fridriksson et al. (2006) found a similar pattern associated with treatment-induced recovery of naming. However, Thompson et al. (2017) found no relation between language performance and perfusion values across regions within the left or right hemisphere, including perilesional regions. We replicated this finding in our most recent study with 72 participants with aphasia (Walenski et al., in preparation). In addition, we examined changes in perfusion in treated (n = 46) and untreated (n = 16) participant groups at baseline and 3 months later. For both groups, there was no significant difference in perfusion over time in perilesional rings, 0–6, 6–12, and 12–18 mm away from the lesion, in either the left or the right hemisphere. Moreover, within the group of individuals who received treatment, there was no correlation between perfusion values over time (posttreatment > pretreatment perfusion) and response to treatment (posttreatment language score > pretreatment language score). These findings suggest that perfusion may not be the most important brain variable related to recovery of language and the neural networks that support it.

**Resting-state neural activation.** We have begun to examine the relation between resting-state functional MRI values and language recovery. In one study (Dickerson et al., 2019), using resting-state functional MRI and data derived from 68 aphasic patients, fractional amplitude of low-frequency fluctuations (fALFF) values (i.e., the proportion of the BOLD signal that falls within the low frequency range of 0.01–0.08 Hz; Zou et al., 2008) were calculated across voxels within functional language networks (i.e., in regions of interest within syntactic processing [n = 13], spelling [n = 13], and naming [n = 13] networks; Harvard/Oxford atlas; Desikan et al., 2006). These values were used to index resting-state activation with the severity of naming, based on performance on the NNB (Confrontation Naming subtest; Thompson & Weintraub, 2014); spelling, based on scores derived from the Psycholinguistic Assessment of Language Performance in Aphasia (Subtest 40; Kay, Lesser, & Coltheart, 1992); and sentence processing, based on scores derived from the NAVS (combined scores from the Sentence Comprehension Test and the Sentence Production Priming Test; Thompson, 2011). Results using linear modeling with fixed effects for average fALFF values for regions of interest within each network, months poststroke, and lesion volume showed that the left IFG (pars opercularis) and a cluster including the left MFG, precentral gyrus, and SFG predicted deficits in sentence processing; spelling scores were predicted by fALFF scores in the left SMG (posterior division); and fALFF values within the left AG and SMG (posterior divisions) and right IFG (pars opercularis) and MFG predicted naming ability. These findings suggest that fALFF values reflect language abilities—with lower values in critical brain regions associated with greater domain-specific language severity—indicating that the brain’s activity at rest reflects language impairment profiles.

In another study, we used fALFF values to predict treatment outcomes across the three language domains (Jorga et al., in preparation). For this analysis, the bold data from 70 of our patients were decomposed using group independent component analysis; fALFF values were calculated to determine participant-specific time series for each component, and using these fALFF imaging predictors, treatment effects were modeled with elastic net regression. Results of correlational analyses indicated a strong relationship between predicted outcomes and actual language change scores derived from treatment for agrammatism (r = .940) and dysgraphia (r = .925), but correlations for anomia were poorer (r = .40). However, using both fALFF values and pretreatment behavioral data as predictors, we found high prediction accuracy across all three language domains. This finding suggests that resting-state data alone, or combined with pretreatment language performance scores, may have prognostic value for patients with chronic aphasia.

**Promoting Treatment-Induced Neuroplasticity**

Klein and Jones (2008) summarized 10 principles shown to be important for promoting neuroplasticity based on animal and human studies of (primarily motor) recovery and suggested that they may also enhance plasticity and language reorganization in people with aphasia. Since then, research examining neural recovery in aphasia has shown that six of these principles (presented in Table 2) are relevant to language recovery (see Kiran & Thompson, 2019). Based on the results of our work in the domain of sentence processing, three of these (bolded in Table 2) are particularly relevant: Use, Improve, or Lose it (Principle 1); Specificity Rebuilds Targeted Networks (Principle 2); and Complexity Promotes Learning and Generalization (Principle 6).

Principles 1 and 2 suggest that treatment focused on processes known to be used by healthy people to compute language rebuilds relevant domain-specific neural networks. In the aphasia treatment literature, several treatments based on psycholinguistic and cognitive neuropsychological research and models of language have been developed, which aim to improve specific language processes (Kiran & Thompson, 2003; Schwartz et al., 1994; Thompson & Shapiro, 2005). In general, studies have shown positive treatment outcomes. Furthermore, several impairment-based approaches have shown neural changes associated with improved language processing (Kiran et al., 2015; Thompson, den Ouden, et al., 2010; Wierenga et al., 2006).

| **Table 2.** Principles for promoting neuroplasticity in aphasia (from Kiran & Thompson, 2019), with principles most relevant to sentence processing treatment in bold. |
|----|
| **1.** | Use, improve, or lose it |
| **2.** | Specificity rebuilds targeted networks |
| **3.** | Salience is essential |
| **4.** | Repetition and intensity strengthen neural pathways |
| **5.** | Promote generalization; avoid interference |
| **6.** | Complexity promotes learning and generalization |
As discussed above, TUF exploits both lexical and syntactic processes involved in sentences and, in turn, impacts the neural mechanisms associated with treating these components. Thompson, Riley, et al. (2013) found that treatment using the VAST, which reflects the first component of the TUF—mapping verb arguments onto the syntax in simple sentences—resulted in recruitment of neural tissue overlapping with that found for verb production in healthy speakers (den Ouden, Fix, Parrish, & Thompson, 2009). These regions included the left SFG and precentral gyrus as well as bilateral MTG and SPL, although the patients recruited additional regions: the right SFG and STG, the left SMG, and the AG, bilaterally. Notably, the SMG and AG have been shown to be engaged for verb comprehension in healthy individuals and in aphasic individuals, with spared tissue in these regions (Meltzer-Asscher, Schuchard, den Ouden, & Thompson, 2012; Thompson, Bonakdarpour, & Fix, 2010; Thompson et al., 2007). Additionally, as noted above, TUF has been shown to rebuild sentence processing networks in patients with agrammatic aphasia, resulting in recruitment of regions activated for processing of noncanonical sentences in healthy listeners. These findings indicate that treatment focused on promoting the use of normal processing strategies drives brain functions engaged in normal sentence production and comprehension, resulting in enhancement of that function. Further research is needed to identify the neurocognitive mechanisms associated with the components of TUF and whether different components recruit overlapping regions within the network. Research also is needed to further identify the differential effects of these and other approaches that exploit normal language processes.

Principle 1 also indicates that, when treatment does not exploit what is known about normal sentence processing, engagement of neural tissue within that network may be minimal. This is supported by our findings (i.e., Barbieri, Mack, et al., 2019) as discussed above, indicating that participants who received a 3-month course of TUF show pre- to posttreatment neural activation shifts in the sentence processing network. Conversely, control participants, matched for age, education, and other variables with the treated participants, showed no changes in neural upregulation during this time period. Furthermore, results of our large-scale collaborative study of the effects of treatment for patients with chronic anomia, dysgraphia, or agrammatism (n = 85; 61 treatment, 24 controls) showed that, whereas all treatment groups showed significant domain-specific behavioral improvements, as well as associated neural changes, only the agrammatic participants who received TUF showed shifts in activation from baseline and to posttesting using a story comprehension fMRI task (Barbieri, Higgins, et al., 2019). No changes in activation were found on this task in the anomic or dysgraphic participant groups, who received word-level treatment, or in the control participants. However, the agrammatic participants showed posttreatment upregulation that, when overlaid onto activation maps derived from a group of healthy individuals performing the same task, showed overlap in the right hemisphere sentence processing network: right hemisphere regions that were either active (i.e., pMTG, IFG) or homologs to active left hemisphere regions (i.e., SFG, precentral gyri) in healthy individuals (see Figure 12). These findings indicate that the language domain targeted affects re-organization of language networks. Sentence-level language, but not word-level language, intervention impacts brain mechanisms associated with sentence processing.

Principle 6 is derived from the construct of complexity that has emerged as a general principle for treating a range of language disorders in both children and adults (Gierut, 2001, 2007; Gray & Kiran, 2016; Keane & Kiran, 2015; Kiran, 2008; Riley & Thompson, 2014; Thompson & Shapiro, 2007). While challenging the long-standing clinical notion that treatment should begin with simple structures, CATE (Thompson et al., 2003) points to the facilitative effects of using more complex structures as a starting point for treatment. The most important implication of CATE is that generalization to untrained linguistically related, simpler structures results from this approach, whereas training simple structures does not improve complex ones. From a neuroplasticity perspective, these findings suggest that the neural mechanisms engaged for complex linguistic processes are also engaged for simpler ones, if/when the complex and simple materials are related. In the domain of sentence processing, complex sentences entail processes inherent in simpler, linguistically related sentences (e.g., thematic role assignment and syntactic mapping). Hence, strengthening the neural network for processing complex sentences unlocks networks required for processing simpler ones.

Discussion

This review article summarizes a body of work conducted in my research laboratory focused on understanding the neurocognitive processes engaged for normal sentence processing and, in turn, how these processes may be exploited to improve sentence processing in individuals with agrammatic aphasia. Results of this research show that treatment that considers what is known about the linguistic representation and processing of sentences in healthy people improves sentence processing in aphasic individuals with sentence deficits. Across studies examining the effects of TUF (Thompson & Shapiro, 2005), results show that this approach improves trained structures and results in generalization of production and comprehension of less complex, linguistically related sentences. These findings highlight the benefit of training complex structures, that is, the CATE (Thompson et al., 2003), which is supported by studies across language domains (e.g., naming, reading, and sentence processing; see Kiran, 2007; Thompson, 2007; Thompson & Shapiro, 2007). TUF also impacts online sentence processing routines, resulting in posttreatment use of normal-like strategies for both sentence comprehension and production, and recruits brain mechanisms that overlap with those engaged by healthy people for sentence processing. These findings support the fact that neuroplasticity is highly experience dependent and further validate principles.
for promoting neuroplasticity, that providing specific treatment designed to stimulate critical components of normal sentence processing fosters the engagement of neural mechanisms associated with those components. When treatment is withheld or when word-level rather than sentence-level treatment is provided, sentence processing networks are not affected.

Further research, of course, is needed to fully understand not only the brain mechanisms engaged for syntactic computation in healthy people but also how brain damage impacts these mechanisms in people with aphasia. Indeed, the community of researchers whose work focuses on understanding the neural basis of normal syntactic processing is small relative to that concerned with lexical/semantic and other aspects of language processing, and although several models of syntax and the brain have been proposed, existing models are incomplete and controversial. Similarly, the aphasia literature is dominated by studies of lexical/semantic impairments, the treatment for them, and, although still in its infancy, the underlying neural mechanisms impaired by and recruited to support recovery of naming. In contrast, studies of syntactic processing in aphasia are comparatively few, and only a handful have addressed the neuroplasticity of sentence processing networks. The dearth of studies examining treatment for sentence-level impairments in aphasia is puzzling. Normally, people use sentences when communicating with one another. Of course, single words may be sufficient for communication in some contexts; nevertheless, treatment that attempts to boost sentence processing may enhance general language recovery. Future research needs to examine this postulate in controlled studies that test the relative benefits of sentence- and word-level treatments. Studies testing the relative effects of different approaches to sentence-level treatment are also needed, as is systematic research evaluating the individual and collective contribution of the components of sentence-level treatment.

A note about social validity: What are the functional effects of treatment focused on sentence-level and/or word-level impairments? What are the clinical implications of the results of controlled aphasia treatment studies? These important issues have not been fully addressed in studies examining the effects of any impairment-based treatments for aphasia. However, our findings that generalized comprehension and production of untrained sentences in off-line tasks occur with sentence-level treatment, online sentence comprehension and production improve, and changes in neural activation following treatment show up in a naturalistic story comprehension task suggest that the effects of treatment extend beyond training. Furthermore, some of our studies of TUF have found posttreatment improvements in the structure and content of narrative language production, including increases in the proportion of verbs produced with correct arguments (Thompson et al., 1997) and increases in correct information units (Ballard & Thompson, 1999; Jacobs, 2001). These findings support the use of TUF in clinical practice for people with agrammatic aphasia. Nevertheless, the functional outcomes of aphasia treatment are largely unknown. Future research needs to include additional functional outcome measures to better understand the impact of sentence-level and word-level treatment on functional communication. It may be that the addition of functional components to impairment-based treatment, for example, using principles of Promoting Aphasic Communication Effectiveness (Davis, 1980; Davis & Wilcox, 1981, 1985), may be needed to boost the use of trained forms (words and/or sentences) for communication in real-life contexts. N. Martin, Thompson, and Worrall (2007) discuss this issue at length in their book focused on aphasia rehabilitation and conclude that both impairment-based and consequence-based treatments, or treatments that combine both approaches, are necessary to achieve optimal recovery and use of language to communicate in naturalistic settings (also see Galletta & Barrett, 2014).

This review article also highlights the observation that, although a high percentage of our participants, carefully selected for verb and sentence impairments, have shown the aforementioned recovery patterns in response to the TUF, some have not, including those with AQs lower than 60. In general, patients with mild to moderately severe agrammatism show better response to treatment than those with more severe agrammatism (Ballard &}
Thompson, 1999; Barbieri, Mack, et al., 2019), in keeping with notions about general patterns of recovery in aphasia (Lazar et al., 2010; Pedersen, Vinter, & Olsen, 2004). This indicates that TUF may not be the best approach for treatment of participants with more severely impaired sentence processing impairments. Instead, it is recommended that treatment focused on verbs and verb argument structure in active sentence contexts (i.e., the first steps of the TUF) precede training of complex sentences for these patients. Furthermore, it is unclear whether participants who do not meet our strict inclusionary criteria would benefit from the TUF. Future research investigating the effects of TUF in more heterogeneous groups of participants with aphasia is needed to identify patient variables associated with responsiveness to treatment. Treatment outcome inconsistencies may result, to some extent, from differences in demographic variables, including age and sex. In the aphasia recovery literature, studies show better outcomes in younger (vs. older) people with aphasia and in females (vs. males; e.g., Laska, Hellblom, Murray, Kahan, & Von Arbin, 2001; McGlone, 1977; Pedersen et al., 2004). The age of stroke lesions is another factor that relates to recovery: Newer strokes (in the acute phase of recovery) show greater changes in language than older strokes (in the chronic phase of recovery; e.g., Bakheit, Shaw, Carrington, & Griffiths, 2007; Demeurisse et al., 1980; see Kiran & Thompson, 2019, for a review). These variables have not been explicitly studied with regard to recovery from agrammatism.

Lesion-related variables must also be considered when examining recovery from aphasia and the neuroplasticity of language networks. While some studies have shown better outcomes in patients with smaller (vs. larger) lesions (Maas et al., 2012), others have found no differences based on lesion size (Ansaldo, Arguin, & Lecours, 2002; Heiss & Thiel, 2006; Hillis, 2007; Mattioli et al., 2014). The studies discussed in this review article suggest that lesion volume alone does not predict recovery of sentence processing. Patients with large left hemisphere lesions show behavioral recovery patterns almost identical to those with smaller lesions. Rather, our data (and those of others) suggest that lesion location within the left hemisphere may be a better predictor of language recovery. Lesions that include tissue within both language and domain-general networks may turn out to impede recovery. Recent research has also shown that better language outcomes are predicted by the extent to which white matter tracts, such as the uncinate and the superior/inferior longitudinal fasciculi in the left hemisphere (Hope et al., 2013) or the long segment of the arcuate fasciculus in the right hemisphere, are compromised by stroke (Forkel et al., 2014). Further research addressing this issue in patients with impairments across language domains is needed to fully understand the impact of, and interplay between, lesion volume and location within both cortical tissue and white matter tracts on language recovery and neural plasticity.

We have only begun to evaluate the impact of brain variables such as perfusion (blood flow) and resting-state neural activation on neural plasticity and associated improvements in language. The extant data, including those from our lab and those derived from other research laboratories, suggest that stroke-induced abnormalities in perfusion are not directly associated with language performance, nor are they predictive of treatment outcome. Our preliminary work on resting-state neural activity, however, holds promise for predicting responsiveness to treatment. Future research addressing the impact of these (and other) neural variables as well as their potential interaction with language/cognitive impairment patterns and treatment variables is needed to develop models for predicting language and brain recovery.

Finally, the studies discussed in this review article highlight that regions within both the right and left hemispheres are viable candidates for supporting recovery of sentence processing in aphasia following left hemisphere brain damage. Studies in other language domains also have shown a positive relation between treatment outcome and upregulation in right brain regions and/or increased connectivity among nodes within the right hemisphere (Breier, Maher, Novak, & Papanicolaou, 2006; Kiran et al., 2015; Raboyeau et al., 2008). Conversely, findings suggesting a maladaptive role of the right hemisphere have come primarily from studies using repetitive transcranial magnetic stimulation, showing improved language performance following application of inhibitory repetitive transcranial magnetic stimulation to right brain regions, either with (Thiel et al., 2013; Weiduschat et al., 2011) or without (Barwood et al., 2011; P. I. Martin et al., 2009) concomitant language treatment. Notably, this latter work has resulted in often minimal treatment gains (see also Norise & Hamilton, 2017). Findings derived from a few neuroimaging studies also suggest that right hemisphere activation may not reflect improved language, as they show upregulation of the right hemisphere in nonrecovered (vs. recovered) participants (Marcotte et al., 2012), correlations between errors on a picture naming task and right hemisphere activation (Postman-Caucheteux et al., 2010), or a direct association between treatment efficacy and decreased activation (i.e., downregulation) in the right hemisphere (Abel et al., 2015; Baciu et al., 2016; Nardo, Holland, Leff, Price, & Crinion, 2017). However, studies concluding that either right or left hemisphere tissue promotes better or poorer recovery have not completely considered intrinsic and/or extrinsic factors, discussed here, that impact neuroplasticity (also see Hartwigsen & Saur, 2019). To resolve this debate, future studies need to consider these variables.

A major goal for clinical treatment of aphasia is to be able to prescribe treatment and predict its outcome based on the neurocognitive deficit profile of individual patients. Toward this end, future research will require data from large numbers of aphasic participants to account for the inherent heterogeneity in stroke and neurodegenerative disease. Studies exploiting behavioral and neuroimaging as well as treatment outcome data, for example, from databases such as ours, which includes over 100 patients with chronic stroke aphasia, derived from Northwestern University, Boston University, Massachusetts General Hospital, and Johns Hopkins University; within the Center for the Neurobiology of Recovery of Sentence Processing in Aphasia.
of Language Recovery; and from the Predicting Language Outcome and Recovery After Stroke database (Hope et al., 2017, 2013; Seghier et al., 2016), are needed to build models for individualized predictions of behavioral and brain recovery patterns and the variables related to it.

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Summary of studies examining the effects of the Treatment of Underlying Forms (TUF).

| Authors                  | Experimental questions                                                                 | Participants | Overall study outcomes                                                                 | Dependent measures |
|--------------------------|----------------------------------------------------------------------------------------|--------------|----------------------------------------------------------------------------------------|--------------------|
| Thompson et al. (1993)   | Does linguistically based treatment of object *wh*-questions improve production of trained structures? Does generalization to untrained *wh*-questions result from training? Does generalization from more to less complex *wh*-questions result from training? | 2            | • Improved production of trained sentence types (*who*-questions) • Generalization from *who*-questions to *what*-questions in one participant • First observation of generalization from complex to simple structures | Sentence production priming task |
| Thompson & Shapiro (1994)| Does linguistically based treatment improve production of complex, *wh*-movement structures? Does generalization occur across *wh*-question forms? Does generalization occur from complex to simple linguistically related structures? Does generalization occur to unrelated (NP-movement) structures? | 5*           | • Improved production of trained sentence types (object clefts, *who*-questions, *what*-question) • Generalization to linguistically related structures (*who*-questions ➔ *what*-questions, [Study 1]; object clefts ➔ *who*-questions, [Study 2]) • Generalization from complex (object clefts) to simple (object *who*-questions) structures [Study 2] • No generalization from simple (object *who*-questions) to complex (object clefts) structures in all but 1 participant • No generalization to linguistically unrelated structures (object clefts to passives) • First observation of generalization to linguistically related structures, but not unrelated structures • Confirmed generalization from complex to simple structures • Improved production of trained structures (object clefts, passives) • Generalization to untrained, linguistically related structures (object cleft ➔ *who*-questions; passives ➔ subject-raising, subject-raising ➔ passives) • No generalization to linguistically unrelated structures • Confirmed generalization to linguistically related structures • Aspects of sentence production in narrative context improved with treatment | Sentence production priming task Narrative production |
| Thompson et al. (1997)   | Does linguistically based treatment of *wh*- and NP-movement structures result in improved production of trained structures? Does generalization occur from trained to untrained linguistically related and unrelated structures? | 2            | • Improved production of trained structures (object clefts, *who*-questions) • Generalization from complex to simple structures (object clefts ➔ *who*-questions) • No generalization from simple to complex structures (object *wh*-questions ➔ object clefts) • Confirmed generalization to linguistically related structures • Confirmed generalization from complex to simple structures | Sentence production priming task Narrative production |
| Thompson et al. (1998)   | Does linguistically based treatment of syntactically complex *Wh*-movement structures result in generalization to less complex *wh*-movement structures? | 3            | • Improved production of trained structures (object clefts, object *wh*-questions) • Generalization from complex to simple structures (object clefts ➔ *who*-questions) • No generalization from simple to complex structures (object *wh*-questions ➔ object clefts) • Confirmed generalization to linguistically related structures • Confirmed generalization from complex to simple structures | Sentence production priming task Narrative production |
## Summary of studies examining the effects of the Treatment of Underlying Forms (TUF)

| Authors                         | Experimental questions                                                                 | Participants | Overall study outcomes                                                                                                                                                                                                 | Dependent measures                  |
|---------------------------------|----------------------------------------------------------------------------------------|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Ballard & Thompson (1999)       | Does linguistically based treatment improve production of syntactically complex wh-movement structures? Does treatment result in generalization to less complex wh-movement and unrelated structures? | 5            | • Improved production of trained (object clefts) and untrained, linguistically related structures (matrix object wh-questions) for 3/5 participants  
• No generalization to embedded wh-questions, embedded actives, or passive structures  
• Generalization from complex to simple structures  
• Confirmed generalization to linguistically related structures  
• Confirmed generalization from complex to simple structures  
• Three participants showed improvements in spontaneous speech production | Sentence production priming task  
Narrative production |
| Jacobs & Thompson (2000)        | Does cross-modal generalization (from comprehension to production and vice versa) result from linguistically based treatment of complex syntactic structures? | 4            | • Improved comprehension/production of target structures (object clefts, passives)  
• Comprehension treatment resulted in generalization to spoken and written sentence production  
• No generalization from production to comprehension  
• Production treatment (spoken) generalized to written sentence production only  
• Generalization from complex to simpler structures (object clefts ➔ object wh-questions)  
• No generalization from simple to complex structures (object wh-questions ➔ object clefts)  
• Based on results of this and previous studies, the Complexity Account of Treatment Efficacy (CATE) was proposed | Sentence–picture matching task  
Sentence production priming task (oral and written)  
Sentence production priming task |
| Thompson et al. (2003)          | Does training production and comprehension of complex wh-movement structures using linguistically based TUF result in generalization to less complex structures? | 4            | • Generalization from complex to simpler structures (object clefts ➔ object wh-questions)  
• No generalization from simple to complex structures (object wh-questions ➔ object clefts)  
• Based on results of this and previous studies, the Complexity Account of Treatment Efficacy (CATE) was proposed | Sentence–picture matching task  
Sentence production priming task  
Sentence production priming task |
| Dickey & Thompson (2007)        | Does the TUF improve production of wh-movement structures? Does treatment of wh-movement structures improve NP-movement structures? Does training higher nodes in the syntactic tree (i.e., wh-movement) improve lower nodes (i.e., grammatical morphology)? | 1            | • Improved production of wh-movement structures (object relatives, object clefts, object wh-questions)  
• No generalization from wh- to NP-movement structures (passives)  
• No improvement in production of grammatical morphology (tense, agreement, and complementizers)  
• Results support CATE | Sentence production priming task |
| Thompson, Choy, et al. (2010)   | Does Sentactics, an interactive computer system that enables delivery of TUF by a virtual clinician, improve production and comprehension of trained complex wh-movement structures? Does generalization to less complex structures result from treatment? | 6            | • Sentactics significantly improved all participants’ ability to comprehend and produce trained complex sentences (object relatives, object clefts, object wh-questions)  
• Generalization to untrained, linguistically related sentences (object relatives ➔ clefts ➔ object wh-questions)  
• No significant differences between the results of Sentactics and clinician-delivered TUF  
• Results support CATE | Sentence–picture matching task  
Sentence production priming task  
Sentence production priming task |
## Appendix (p. 3 of 3)

Summary of studies examining the effects of the Treatment of Underlying Forms (TUF)

| Authors                  | Experimental questions                                                                 | Participants | Overall study outcomes                                                                 | Dependent measures                                      |
|--------------------------|----------------------------------------------------------------------------------------|--------------|----------------------------------------------------------------------------------------|----------------------------------------------------------|
| Thompson, den Ouden, et al. (2010) | Does TUF focused on complex wh-movement structure production (and comprehension) result in shifts in neural activation using fMRI? | 6            | • Improved production of object-relative structures                                      | Behavioral: sentence production priming task             |
|                          |                                                                                        |              | • Generalization to less complex wh-movement structures (i.e., object clefts and object wh-questions) found in 5/6 participants | Functional neuroimaging: sentence verification task       |
|                          |                                                                                        |              | • The neuroimaging (fMRI) results showed a general shift from left superior temporal to bilateral posterior temporoparietal activation |                                                          |

| Barbieri, Mack, et al. (2019) | Does TUF focused on NP-movement structures improve online and off-line (as tested by eyetracking) sentence processing? Does generalization occur from complex to simple NP-movement structures? Does the TUF result in shifts in neural activation? Are regions within the normal sentence processing and/or dorsal attention networks recruited to support recovery? | 14           | • Improved production and comprehension of trained structures (long passive sentences) | Behavioral: sentence production priming task             |
|                              |                                                                                        |              | • Generalization to untrained syntactically related structures (short passives, actives with unaccusative verbs) | Functional neuroimaging: sentence verification task       |
|                              |                                                                                        |              | • Treatment resulted in a shift toward normal-like eye movements (i.e., emergence of an agent-first strategy) |                                                          |
|                              |                                                                                        |              | • Significant increase in neural activation in both sentence processing and dorsal attention networks |                                                          |
|                              |                                                                                        |              | Results support CATE                                                                   |                                                          |

| Thompson, Barbieri, et al. (under review) | Does TUF improve wh- and NP-movement structures in primary progressive aphasia (PPA)? Does treatment affect online sentence processing during comprehension and production? Does treatment result in shifts in neural (fMRI) activation? | 1            | • Improved ability to comprehend and produce trained (and untrained) structures (passives, object clefts) | Behavioral: sentence—picture matching task               |
|                                          |                                                                                        |              | • Changes in automatic online sentence processing strategies (i.e., normal-like agent-first pattern emerged for comprehension; incremental production emerged for production) | Sentence production priming task                          |
|                                          |                                                                                        |              | • Posttreatment neural activation of neural tissue recruited by healthy people performing the same task | Eyetracking: sentence—picture matching task               |
|                                          |                                                                                        |              | • Results support CATE                                                                  |                                                          |
|                                          |                                                                                        |              | • Results support neural plasticity of sentence processing networks in PPA                 |                                                          |

Note. NP = noun phrase; fMRI = functional magnetic resonance imaging.

*One patient with nonfluent PPA.