The role of executive control in post-stroke aphasia treatment

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4 The role of executive control in post-stroke aphasia treatment

Abstract

Executive control (EC) ability is increasingly emerging as an important predictor of post-stroke aphasia recovery. This study examined whether EC predicted immediate treatment gains, treatment maintenance and generalization after naming therapy in ten adults with mild to severe chronic post-stroke aphasia. Performance on multiple EC tasks allowed for the creation of composite scores for common EC, and the EC processes of shifting, inhibition and working memory (WM) updating. Participants were treated three times a week for five weeks with a phonological naming therapy; difference scores in naming accuracy of treated and untreated words (assessed pre, post, four- and eight-weeks after therapy) served as the primary outcome measures. Results from simple and multiple linear regressions indicate that individuals with better shifting and WM updating abilities demonstrated better maintenance of treated words at four-week follow-up, and those with better common EC demonstrated better maintenance of treated words at both four- and eight-week follow-ups. Better shifting ability also predicted better generalization to untreated words post-therapy. Measures of EC were not indicative of improvements on treated words immediately post-treatment, nor of generalization to untreated words at follow-up. Findings suggest that immediate treatment gains, maintenance and generalization may be supported by different underlying mechanisms.

Keywords: aphasia, anomia, executive control, executive functions, treatment

4.1 Introduction

Aphasia affects roughly one third of stroke survivors, (Flowers, et al., 2016; Dickey, Kagan, Lindsay, Fang, Rowland & Black, 2010; Tsouli, Kyritsis, Tsagalis, Virvidaki & Vemmos, 2009), and leads to difficulties in producing or understanding both spoken and written language. Although reviews of the literature indicate that therapy for aphasia can be beneficial in both the acute and chronic stages of recovery, (Brady, Godwin, Enderby, Kelly, & Campbell, 2016; Cicerone et al., 2011; Faroqi-Shah, Frymark, Mullen, & Wang, 2010; Simmons-Mackie, Raymer, Armstrong, Holland, & Cherney, 2010; Bhogal, Teasell, Foley & Speechley, 2003; Nickels, 2002; Robey & Schultz, 1998), the long-standing clinical and scientific observation that some individuals either do not improve, or do not maintain their improvements after therapy, remains. It is not uncommon for two individuals with comparable aphasia profiles and severities, who are undergoing the same treatment, to have very different responses to therapy (Lazar & Antoniello, 2008; Helm-Estabrooks, 2002). Active investigation into the prognostic indicators of aphasia recovery is therefore an important research avenue, which could aid in allocating treatment and alleviating the burden of care and costs associated with aphasia at the personal, familial and societal levels (e.g., Boehme, Martin-Schild, Marshall, & Lazar, 2016).

4.1.1 What predicts aphasia recovery?

There is evidence both for and against the prognostic value of a variety of factors (e.g., sex, education, lesion size, aphasia type) in aphasia recovery (Kertesz & McCabe, 1977; Pedersen, Stig Jorgensen, Nakayama, Raaschou & Olsen, 1995; Plowman, Hentz & Ellis, 2012; Laska, Hellblom, Murray, Kahan, & Von Arbin, 2001; Lazar, Speizer, Festa, Krakauer, & Marshall, 2008; Lazar & Antoniello, 2008). Among these, age has been identified as a good predictor of aphasia recovery in many studies, whereby younger individuals fare better (Pompon, Bislick, Elliott, Madden, Minkina, Oelke & Kendall, 2017; Knoflach et al., 2012; van de Sandt-Koenderman et al., 2008; El Hachioui, Lingsma, van de Sandt-Keonderman, Dippel, Koudstaal & Visch-Brink, 2013; Laska et al., 2001). However, some studies have also shown that recovery is not necessarily dependent on age (Pedersen et al., 1995; Kertesz & McCabe, 1977; Lazar et al., 2008; Blom-Smink et al., 2017).

In addition, lesion location (Price, Seghier & Leff, 2010; Seghier, Bagdasaryan, Jung, & Price, 2014; Hope, Seghier, Leff & Price, 2013; Plowman et al., 2012; Rjintjes et al., 2006) and aphasia

severity (Godecke, Rai, Ciccone, Armstrong, Granger & Hankey, 2013; Plowman et al., 2012; Lazar, Minzer, Antoniello, Festa, Krakauer & Marshall, 2010) have emerged as promising indicators of language recovery. More severe aphasia at stroke onset has been associated with smaller improvements in the acute stage (Laska et al., 2001), and with poorer outcomes and greater language impairment in the chronic stage (Pedersen, Vinter, & Olsen, 2004). However, some studies have demonstrated that individuals with severe aphasia can benefit from treatment and show significant gains in language ability in both the acute (Godecke, Hird, Lalor, Rai & Phillips, 2012; Robey, 1998) and chronic (Persad, Wozniak & Kostopoulos, 2013) stages of recovery.

Though informative, many agree that such predictors are often not adequate in determining the differential patterns of recovery seen in individuals with aphasia (Lazar & Antoniello, 2008; Lazar, et al., 2008; Pompon, et al., 2017; Pedersen, et al., 1995), nor are they always good indicators of overall clinical improvement and generalization to everyday communication settings (Fridriksson, Nettles, Davis, Morrow, & Montgomery, 2006; Purdy, 2002; Ramsberger, 2005; Kiran, 2016; Persad et al., 2013). It remains difficult to predict how a particular individual with aphasia will fare after treatment (Nickels, 2002), and additional factors must be considered.

It has been hypothesized that residual non-linguistic cognitive abilities play an important role in rehabilitation after acquired brain injury, with Robertson and Murre (1999) suggesting that self-awareness of deficits and strong executive control (EC) systems are key predictors of successful recovery. Indeed, EC was identified as the most robust cognitive predictor of post-stroke functional recovery at one-year follow-up in one study (Lesniak, Bak Czepiel, Seniow & Czlonkowska, 2008). As a result, EC and related cognitive abilities are increasingly being considered as potentially important predictors of language recovery in post-stroke aphasia as well.

4.1.2 What is executive control?

EC has traditionally been a difficult construct to define and measure, and as a result, the literature investigating EC is fraught with both conceptual and methodological issues (Snyder, Miyake & Hankin, 2015). EC is conceptualized as a director of goal-oriented behavior and lower-level verbal and visuospatial systems (Baddeley, 2012; Cowan, 2005); a supervisory attentional system, primarily activated during novel tasks (Norman & Shallice, 1986; Stuss,

2011; Stuss & Alexander, 2000; Sohlberg & Mateer, 2001; McCabe, Roediger, McDaniel, Balota & Hambrick, 2010). The nature of EC is often debated: while some view it as a unitary, undifferentiated director of behavior, others view it as a diverse collection of separable cognitive processes (Snyder et al., 2015; McCabe et al., 2010; Diamond, 2013; Stuss, 2011; Miyake, Friedman, Emerson, Witzki, Howerter & Wager, 2000; Baddeley, 2012; Hull, Martin, Beier, Lane & Hamilton, 2008). In a seminal study, Miyake et al. (2000) found that specific EC processes were distinguishable and separable (i.e., EC diversity), but nevertheless shared a common underlying EC factor (i.e., EC unity). This unity/diversity framework is supported by several different models of EC and by current best evidence (Snyder et al., 2015).

The specific EC processes measured by Miyake and colleagues (2000), were: inhibition, the ability to control one's attention, thoughts and behaviours in the face of internal and external distractors; WM updating, the ability to mentally manipulate information such that new, relevant information is incorporated into thoughts and action plans, while irrelevant information is discarded; and shifting (also described as cognitive flexibility), the ability to divide one's attention, shift between tasks or mental sets, and adjust to changing conditions (Diamond, 2013; Miyake et al., 2000). These have been described as three core EC processes (Diamond, 2013): they interact in various combinations and contribute differentially to broader, more complex EC abilities, such as planning and sequencing thoughts and behaviours, problem-solving, and reasoning (Miyake et al., 2000; Stuss, 2011; Diamond, 2013; Chan, Shum, Toulopoulou & Chen, 2008).

However, traditional and commonly used tests of EC, such as the Wisconsin Card Sorting Test (WCST) and the Tower of Hanoi (TOH) task, are often broad and complex measures that tend to correlate poorly (e.g., Miyake et al., 2000). Because the very nature of EC is to control or act upon other cognitive processes in order to accomplish task demands, it follows that tasks used to measure EC also tap into various other (non-EC) abilities (Snyder et al., 2015). It is also unclear whether performance on any given task is driven by a process-specific ability or by the common EC factor (Miyake et al., 2000; Snyder et al., 2015). As a result, EC data are inherently noisy. This is known as the task impurity problem, and makes developing psychometrically stable tasks a challenge. The task impurity problem can be addressed with careful task selection, and by using multiple, specific tasks to measure each process of interest; the shared variance across tasks can then be extracted to represent a purer measure of the EC process in question (Miyake et

al., 2000; Snyder et al., 2015). Taken together, the conceptual and methodological issues discussed lead to difficulties in interpreting EC data.

4.1.3 Why is EC important in aphasia recovery?

Domain-general cognitive control networks, which are widely distributed brain regions implicated in EC processing, play an important role in healthy language functioning (Fedorenko, 2014; Fedorenko & Thompson-Schill, 2014). This relationship has also been demonstrated in aphasia (Geranmayeh, Chau, Wise, Leech & Hampshire, 2017; Geranmayeh, Brownsett & Wise, 2014), and as a result, individuals with greater impairments in language processing may rely more heavily on domain-general cognitive control networks when completing language tasks. Furthermore, studies have shown that individuals with aphasia often have concomitant neuropsychological deficits (Murray, 2012; Ramsberger, 2005; Glosser & Goodglass, 1990), which can be independent of their language disorder (Brownsett, Warren, Geranmayeh, Woodhead, Leech & Wise, 2014; Glosser & Goodglass, 1990). Thus, differences in EC ability may lead to differential language therapy outcomes.

Indeed, aspects of EC appear to have important predictive value in both structured and individualized treatment programs targeting various language areas. For example, better visuospatial working memory (Seniow et al., 2009) and higher cognitive composite scores (Des Roches et al., 2015) have been associated with better language outcomes following individually-tailored aphasia treatments administered both in person (Seniow, Litwin & Lesniak, 2009) and via iPad (Des Roches, Balachandran, Ascenso, Tripodis & Kiran, 2015). In addition, divided attention (Lambon-Ralph, Snell, Fillingham, Conroy & Sage, 2010), visuospatial working memory (Harnish & Lundine, 2015; Conroy, Sage & Lambon-Ralph, 2009a, 2009b; Lambon-Ralph et al., 2010), verbal short-term memory (Dignam, Copland, O'Brien, Burfein, Khan & Rodriguez, 2017), self-monitoring, and nonverbal problem solving (Fillingham, Sage & Lambon-Ralph, 2006) have been shown to be predictive of improvements in naming accuracy after treatment for anomia. Verbal short-term memory (Dignam et al., 2017) and inhibitory control (Yeung, Law & Yau, 2009) have also emerged as predictors of treatment generalization following naming therapy.

In addition, non-linguistic measures of EC have been linked to better recovery from acute (El Hachioui, et al., 2014) and severe (Van de Sandt-Koenderman et al., 2008) aphasia, as well as

more effective communication strategy use (Purdy & Koch, 2006), better overall functional communication (Fridriksson et al., 2006) and conversational skills (Frankel, Penn & Ormond-Brown, 2007). EC ability also appears to be necessary in the successful use of assistive communication devices by individuals with severe aphasia (Nicholas, Sinotte & Helm-Estabrooks, 2011; Nicholas & Connor, 2017; Van de Sandt-Koenderman, Wiegers, Wielaert, Duivenvoorden & Ribbers, 2007).

However, as with the majority of prognostic indicators (Lazar & Antoniello, 2008), the exact role and predictive value of EC in aphasia recovery remains unclear. Some studies have failed to demonstrate a relationship between purported measures of EC and language recovery (Babbitt, Worrall & Cherney, 2016; Rose, Attard, Mok, Lanyon & Foster, 2013), and others have even demonstrated the opposite relationship, whereby better EC ability has been associated with smaller treatment effect sizes (e.g., Rohter, 2014). Furthermore, the methodological issues associated with measuring EC in general (Snyder et al., 2015) are mirrored in studies examining the role of EC in aphasia in particular (Simic, Rochon, Greco & Martino, 2017). Very few studies have employed a theoretically-motivated framework of EC when assessing its role in aphasia. Fewer still have addressed the task impurity problem, often administering a single complex or non-specific task, such as the WCST (which may in fact be a measure of phonological processing when administered to individuals with aphasia; Baldo, Dronkers, Wilkins, Ludy, Raskin & Kim, 2005; Allen, Martin & Martin, 2012).

As it stands, the current literature lacks consensus on the optimal methods by which to measure EC in post-stroke aphasia, and the studies that have measured this relationship are highly variable in terms of the language treatments administered and the EC abilities assessed (Simic et al., 2017). Nevertheless, researchers agree that linguistic profiles alone are insufficient in predicting aphasia treatment outcomes: successful aphasia recovery appears to be dependent, at least in part, on the integrity of top-down control processes.

4.1.4 Objectives and Hypotheses

The goal of the present study is to measure the prognostic value of EC in language recovery following a structured treatment approach for anomia. Building upon previous work, this study addresses the aforementioned limitations in the literature by applying a robust, theoretically-driven approach (i.e., based on Miyake et al., 2000) to EC task selection and analysis in order to

achieve this goal. Thus, the primary objective of this study was to determine whether the common EC factor and the three core EC processes (i.e., inhibition, WM updating, and shifting) would be good predictors of a) improvement in accuracy of naming treated words following therapy, b) maintenance of these improvements and c) generalization, or improvements in naming accuracy on untreated words. Based on the literature suggesting a role for EC in aphasia recovery, we hypothesized that better EC task performance would predict better immediate and long-term treatment gains and generalization.

4.2 Methods

4.2.1 Participants

Participants were recruited from multiple referral sites in the Greater Toronto Area, and were included in the study if they were primarily English-speaking, premorbidly right-handed adults (aged 18 and over), with chronic aphasia (i.e., at least 6 months post-onset) due to a single left-hemisphere stroke. The primary inclusion criterion was the presence of moderate anomia, defined as 10-75% naming accuracy on the Boston Naming Test (BNT; Kaplan, Goodglass & Weintraub, 2001). All participants had corrected normal vision and hearing (i.e., perceived 40 dB at .5, 1 and 2 kHz in at least one ear). Those who did not pass screening for hearing loss and those with visual perceptual deficits or severe motor speech disorders were excluded from the study. Participants were also excluded if they were receiving speech-language therapy services at the time of recruitment or had a known history of drug or alcohol abuse, neurological disorder, or major psychiatric disorder.

Ten individuals with aphasia participated in this study. Participants were predominantly males (9/10), between 35 to 79 years of age (Mean (M) = 55.50; SD = 15.04), ranging from six to 74 months post-onset of stroke (M = 18.10; SD = 20.06). Individuals in our sample had between 14 and 20 years of education (M = 16.70; SD = 2.21) and presented with mild to severe aphasia of various types, as defined by the Western Aphasia Battery (Kertesz, 2006) Aphasia Quotient (WAB AQ; range = 39.60 - 85.20, M = 67.84; SD = 13.91). Table 4.1 provides individual participant characteristics.

Table 4.1. Individual participant characteristics.

Pt	Sex	Age	Handedness*	Education (years)	МРО	Etiology	Stroke Type	Lesion Location	WAB AQ	Aphasia Severity	Aphasia Type
P1	М	58	L	16	13	L MCA CVA	ischemic	fronto-parietal, temporal, insula	61.80	Moderate	Broca's
P2	М	35	L	17	8	L MCA CVA	ischemic + CP hemorrhage	large portion of MCA territory, basal ganglia	58.10	Moderate	Broca's
Р3	М	75	R	20	12	L MCA CVA	ischemic	frontal, posterior parietal, insula	77.20	Mild	Anomic
P4	F	35	L	15	18	L MCA CVA	subarachnoid hemorrhage	sylvian fissure, temporal sulci, intrahemispheric fissure	39.60	Severe	Broca's
Р6	М	56	L	17	12	L MCA CVA	ischemic	mass effect in frontal horn of lateral ventricle	64.90	Moderate	Broca's
P7	М	64	R	18	6	L MCA CVA	ischemic	temporo-parietal	78.60	Mild	Conduction
P8	М	55	L	14	10	L CVA	hemorrhagic	basal ganglia	66.80	Moderate	Broca's
Р9	М	42	L	19	9	L MCA & ACA CVA	Ischemic + hemorrhagic transformation	frontal, temporal, insula	62.10	Moderate	Broca's
P10	М	79	R	13	74	L CVA	hemorrhagic	frontal	84.10	Mild	Anomic
P11	М	56	L	18	19	L MCA CVA	ischemic + CP hemorrhage	frontal, caudate, basal ganglia, internal and external capsules + occipital involvement	85.20	Mild	Anomic
Mean		55.50		16.70	18.10				67.84		
Median		56.00		17.00	12.00				65.85		
SD		15.04		2.21	20.06				13.91		

^{*}Refers to currently dominant hand

All participants passed visuoperceptual and hearing screening.

ACA - Anterior Cerebral Artery; CP - Cortical Petechial; CVA - Cerebrovascular Accident; L - Left; MCA - Middle Cerebral Artery; MPO - Months Post-Onset; Pt – Participant; R - Right; WAB AQ - Western Aphasia Battery Aphasia Quotient

4.2.2 Language Assessment

A battery of assessments was administered prior to treatment, in order to characterize participants' language abilities. In addition to the WAB, which provided information on aphasia type and severity, we identified anomia severity using the BNT (M = 18.60; SD = 8.57; range = 7/60 - 34/60), and semantic and phonological processing, repetition and reading abilities using the Pyramids and Palm Trees Test (PPTT; Howard & Patterson, 1992), and various subtests of the Psycholinguistic Assessments of Language Processing in Aphasia (PALPA; Kay, Lesser & Coltheart, 1992). Assessment measures which required verbal output by the participant were audio recorded to facilitate offline scoring by an independent rater blind to the purposes of the study. Language assessment measures and corresponding participant raw scores are shown in Table 4.2.

4.2.3 EC Assessment

We administered multiple, simple tasks to measure the three core EC processes of inhibition, WM updating, and shifting (Miyake et al., 2000). The tasks, thought to primarily tap each EC process separately, were selected based on previous research with both healthy younger adults (Miyake et al., 2000), and older adults with aphasia (Allen, et al., 2012). We administered 14 EC tasks in total: five measuring inhibition, five measuring WM updating, and four measuring shifting. Three tasks, the *Cued Shifting*, *Stop-Signal*, and *Keep-Track* tasks were excluded from the analysis due to experimental software error, floor, and ceiling effects, respectively. Therefore, four inhibition tasks (*Spatial Stroop*, *Flanker*, *Go No-Go*, and *Recent Negatives*), four WM updating tasks (*Verbal* and *Auditory 1-* and *2-backs*), and three shifting tasks (*Plus-Minus 1* and *3*, *Trail Making*) were used in the final analysis.

The dependent variables within each group of tasks were similar in nature and directionality: the dependent variable for WM updating tasks was accuracy (better performance → greater accuracy), and for shifting tasks, it was shift cost in seconds (better performance → smaller shift cost). Given that both accuracy and reaction time (RT) data were collected for the inhibition tasks, there were two dependent variables measured: the RT interference effect, and the effect of interference on accuracy. In both cases, smaller interference effects indicated better (i.e., faster, or more accurate) performance in the face of distractors. For conciseness, detailed task descriptions and corresponding dependent variables are presented in Table 4.3.

Table 4.2. Individual participant raw scores on the language assessment battery administered pre-treatment.

Area	Assessment Measure						ı	Partici	pant (raw so	cores)			
		Total	P1	P2	P3	P4	P6	P7	P8	P9	P10	P11	Mean	SD
	PPTT - 3 Pictures	/52	46	44	40	47	48	50	44	51	48	46	46.40	3.20
	PPTT - 1 Spoken word/2 pictures	/52	47	43	31	44	48	46	39	46	42	47	43.30	5.12
Semantic	PALPA 47 Spoken Word-Picture Match	/39	38	35	30	35	36	38	33	<i>37</i>	38	36	35.60	2.55
Processing	PALPA 48 Written Word-Picture Match	/39	39	36	29	30	35	39	34	38	37	37	35.40	3.50
	PALPA 49 Auditory Synonym Judgment	/60	55	29	39	49	55	24	52	46	38	*	43.00	11.25
	PALPA 50 Written Synonym Judgment	/60	49	53	48	36	33	<i>57</i>	56	53	47	56	48.80	8.32
	PALPA 1 Nonword Minimal Pairs	/65	62	60	46	56	55	51	65	63	52	64	57.40	6.40
	PALPA 5 Auditory Lexical Decision - Real													
	Words	/80	78	74	70	73	77	55	79	74	72	79	73.10	7.06
	PALPA 5 Auditory Lexical Decision -	/00	73	76	77	60	72	59	67	52	55	73	67.20	0.01
	Nonwords PALPA 7 Syllable Length Repotition	/80		_	• •	69 16			<i>67</i>	_			67.30	8.91
Phonological	PALPA 7 Syllable Length Repetition	/24	21	23	18	16	21	14	24	23	19	21	20.00	3.23
Processing	PALPA 8 Auditory Nonword Repetition	/30	24	23	12	13	16	0	19	19	9	24	15.90	7.64
	PALPA 9 Auditory Word Repetition	/80	69	<i>78</i>	59	54	61	28	<i>75</i>	<i>75</i>	56	74	62.90	15.07
	PALPA 14 Rhyming Judgment	/38	26	22	13	23	21	21	3	12	16	22	17.90	6.90
	PALPA 15 Auditory Rhyme Judgment	/58	52	<i>57</i>	34	41	<i>57</i>	54	55	53	40	54	49.70	8.19
	PALPA 31 Oral Reading	/80	54	43	76	24	38	<i>57</i>	67	40	71	73	54.30	17.59
	PAL 08 - Picture Homophone Matching	/32	23	21	18	16	20	29	18	21	26	23	21.50	3.92
Naming	Boston Naming Test (BNT)	/60	14	29	12	7	16	34	19	10	21	24	18.60	8.57

^{*}Test not administered

PAL - Psycholinguistic Assessment of Language (Caplan, 1993); PALPA - Psycholinguistic Assessments of Language Processing in Aphasia (Kay, Lesser & Coltheart, 1992); PPTT - Pyramids and Palm Trees Test (Howard & Patterson, 1992).

Table 4.3. EC task descriptions and corresponding dependent variables, grouped by EC process, for all EC assessments conducted prior to treatment.

EC Process	Task	Modality	Description	Dependent Variable	# Trials
	Plus Minus 11,	Paper and Pencil	Participants are presented with three lists (L1, L2, L3), each comprised of 30 two-digit numbers (ranging from 10-99, pre-randomized) on a single sheet of paper. Participants must add one to each number in L1, subtract one from each number in L2, and alternate between adding and subtracting one to/from each number in L3. Participants are timed using a stopwatch for each list. Errors are identified by the examiner and corrected by the participant immediately, adding to task completion time.	Shift cost [L3 - Mean L1 + L2 (seconds)]	90 (30 per list)
g	Plus Minus 31,	Paper and Pencil	As above, except participants add, subract, or alternate between adding and subtracting <i>three</i> to/from each number in each respective list.	Shift cost [L3 - Mean L1 + L2 (seconds)]	90 (30 per list)
SHIFTING	Trails A&B	Paper and Pencil	Participants are timed using a stopwatch as they complete two tasks: Trails A entails connecting a series of numbered dots $(1-15)$ in numerical order and Trails B, connecting an alternating series of dots in both numerical and alphabetical order simultaneously (e.g., 1-A, 2-B, 3-C, 4-D). No time limit was imposed. Errors are identified by the examiner and corrected by the participant immediately, adding to task completion time.	Shift cost [Trails B - Trials A (seconds)]	n/a
	Cued Shifting ₂	Psyscope X B51	Participants are cued with a written word (SHAPE or COLOUR) presented on the screen (in black font, for 650 ms), and must categorize the stimulus that follows the cue according to either its SHAPE (triangle or square) or COLOUR (blue or yellow). Participants complete three blocks: two pure blocks (i.e., SHAPE only; COLOUR only), and one mixed block (i.e., 4 SHAPE trials, 4 COLOUR trials, 4 SHAPE trials, etc). Participants are told in advance that the target cue will change every four trials in the mixed block.	Global shift cost [Mixed block (mean RT) - Pure Blocks (mean RT)]	384 (128 per block)
INHIBITION	Flanker3	E-Prime 2.0	Participants are instructed to respond as quickly and accurately as possible to a red left or right pointing arrow, surrounded by black congruent (<<<><) or incongruent (<<>><) flanking arrows. In the neutral condition, the target arrow appears alone without flankers.	Interference effect RT [Incongruent – Neutral Trials (msec)] Accuracy [(Congruent+Neutral) – (Incongruent+Neutral) Trials (%)]	96 (24 neutral; 36 each congruent and incongruent)

EC Process	Task	Modality	Description	Dependent Variable	# Trials
	Spatial Stroop2	Psyscope X B51	Participants view a single left- or right-pointing arrow appearing on the left, middle or right sides of the screen and must respond to the direction of the arrow, while ignoring its location. The task has three conditions: congruent (e.g., left-pointing arrow on left side of screen), neutral (e.g., left-pointing arrow in middle of screen) or incongruent (e.g., left-pointing arrow on right side of screen).	Interference effect RT [Incongruent – Neutral Trials (msec)] Accuracy [(Congruent+Neutral) – (Incongruent+Neutral) Trials (%)]	240 (80 per condition)
	Recent Negatives ₂	Psyscope X B77	Participants hear three words, followed by a fourth probe word. They must indicate via yes or no button presses whether or not the probe is one of the three words just presented. This task has three conditions: positive (probe presented in current <i>n</i> list), non-recent negative (NRN; probe presented at least <i>n-5</i> lists earlier), and recent negative (RN; probe presented in immediately preceding <i>n-1</i> list). On positive trials, "yes" was the correct response. On RN and NRN trials, a "no" response was the correct answer.	Interference effect RT [RN - Positive trials (msec)] Accuracy [(NRN+Positive) – (RN+Positive) trials (%)]	84 (43 positive; 41 negative: 20 recent, 21 non- recent)
	Go No-Go3	E-Prime 2.0	Participants respond as quickly and accurately as possible to the direction of a left- or right-pointing red arrow. In the "Go" condition, the arrow is flanked by diamonds. In the "No Go" condition, the arrow is flanked by Xs, and participants are instructed to withhold their responses.	Commission errors [% responses on "No Go" trials]	72 (36 Go; 36 No Go)
	Stop Signal ₃	E-Prime 2.0	Participants must press the letters A and D as quickly and accurately as possible in response to corresponding letters presented on the screen ("Go" trials). On 25% of trials, participants receive an auditory stop signal and must withhold their response on these trials. The stop signal has three onset delays based on each individual's mean RT (mean RT - 100 ms; mean RT - 250 ms; mean RT - 375 ms).	Commision errors [% responses on stop trials]	192 (48 stop trials; 16 at each onset delay)
	Verbal 1- back ₂	Psyscope X B51	Participants view a continuous string of individually presented letters, and must indicate with a button press when the current letter is the same as the letter presented immediately $(n-1)$ before it. No response is required on remaining trials.	Accuracy [% hits + correct rejections]	60 (5 blocks x 12 stimuli)
TING	Verbal 2- back ₂	Psyscope X B51	As above, except participants must indicate when the current letter is the same as the letter presented two letters $(n - 2)$ before it. No response is required on remaining trials.	Accuracy [% hits + correct rejections]	60 (5 blocks x 12 stimuli)
WM UPDATING	Auditory 1- back ₂	Psyscope X B51	Participants hear a continuous string of individually presented tones (5 tones in total: 334Hz, 375Hz, 420Hz, 472Hz and 500Hz). Once familiarized with the different tones, participants are asked to indicate whether the current tone is exactly the same as the tone presented immediately $(n-1)$ before it. No response is required on remaining trials.	Accuracy [% hits + correct rejections]	60 (5 blocks x 12 stimuli)
	Auditory 2- back ₂	Psyscope X B51	As above, except participants must indicate whether the current tone is the same as the tone presented two tones $(n - 2)$ before it. No response is required on remaining trials.	Accuracy [% hits + correct rejections]	60 (5 blocks x 12 stimuli)

EC Process	Task	Modality	Description	Dependent Variable	# Trials
	Keep Track ₂	Psyscope X B77	Participants view a series of square colour patches (red, blue, yellow or green) appear consecutively in one of four locations on the screen. They must compare each patch to a target colour (presented in a circle at the bottom of the screen). On each trial, the participant sees 16 colour patches, and must keep track of the last location in which the target colour appeared.	Accuracy [% correct responses]	40

¹Adapted from Miyake et al., 2000

²Adapted from Allen et al., 2012

³Obtained from the Hasher Laboratory, Department of Psychology, University of Toronto

Shaded rows indicate tasks that were excluded from the analysis. *Cued Shifting:* Due to a glitch in the experimental software, data for 4 participants were not adequately captured. As a result, this task could not be included in the Shifting composite score for all participants and was therefore removed from the analysis altogether. *Stop Signal:* Due to floor effects, this task was removed from the analysis.

Each EC measure was administered in the same modality for each participant. Namely, the *Trail Making*, *Plus-Minus 1* and *3* were paper-and-pencil tasks, while the *Flanker*, *Go No-Go* and *Stop Signal* tasks were administered using *E-Prime version 2.0* software, on a 15.6-inch *Dell Latitude E6530* laptop. All other EC measures were administered using the *PsyScope X Software* (*versions B51* or *B77*) on a 15-inch *MacBook Pro*. Participants were seated approximately 40 cm from the computer screen and were instructed to use the index and middle fingers of their currently dominant hand to make button-press responses on either the laptop keyboard, or an attached button pad. Where auditory stimuli were used, participants wore *LTB True 5.1 Surround Sound* headphones, set to a comfortable volume. All computerized tasks were preceded by practice trials, and the order of task administration was pseudo-randomized, such that participants never completed more than two consecutive tasks measuring the same EC process. Raw EC data are presented in Table 4.4.

All assessment measures were completed either at the University of Toronto or in participants' homes, in quiet, well-lit conditions, with the examiner (TS) present. Communication strategies (i.e., picture and written supports) were used in explaining task instructions to all participants, and comprehension was verified and confirmed prior to task administration. Together, the language and EC assessment batteries were completed within an average of nine sessions, each of which lasted approximately two hours. Fatigue levels were frequently monitored, and sessions were discontinued if fatigue was reported.

4.2.3.1 Data Preparation

Raw RT and speed data (i.e., from inhibition and shifting tasks, respectively) were assessed for outliers, which were defined as responses beyond three standard deviations (SDs) from the mean for a given task. Only RTs from correct response trials were used. The data were assessed for outliers using a two-step procedure: first, overall between-subject (group) data were reviewed and outliers were replaced with the value equal to the mean plus/minus three SDs for the task in question; subsequently, the same procedure was performed at the individual, within-subject level. For the *Plus-Minus* and *Trails* tasks, individual level analyses were not possible, as only a single response time was collected per condition. Overall, 3.69% of the RT (i.e., inhibition) data were replaced and only 1.25% of the speed (i.e., shifting) data were replaced. No outliers were

found in the inhibition accuracy data, nor in the accuracy data obtained from the WM updating tasks.

4.2.3.2 Composite Scores

We developed composite scores for each EC process of interest. Raw data for each task were transformed into standardized scores, and these were subsequently averaged across all tasks measuring a single EC process. This approach has been used in previous research (e.g., Allen et al., 2012, El Hachioui et al., 2014), and has been recommended by Snyder and colleagues (2015) for analyzing EC in small samples. Standardized scores for the *Plus/Minus 1* and *3*, and *Trails* tasks were averaged to create a shifting composite for each participant. Averaged standardized scores of the *Verbal* and *Auditory 1-* and *2-back* tasks generated the WM updating composite score. The inhibition accuracy composite score was comprised of standardized scores from the *Flanker*, *Spatial Stroop*, *Recent Negatives* and *Go No-Go* tasks. Finally, the inhibition RT composite was created using standardized scores from the *Flanker*, *Spatial Stroop* and *Recent Negatives* tasks (i.e., tasks where RT data were available).

Smaller shifting, inhibition accuracy and inhibition RT composite scores reflect better performance (i.e., overall smaller shift costs and interference effects). For ease of interpretation in the figures, the signs of the standardized WM updating scores were reversed to match the directionality of the shifting and inhibition measures, such that smaller WM updating composite scores also reflect better performance (i.e., higher accuracy). A single, composite score of EC (which we have termed common EC), was also obtained by averaging the standardized scores of all EC tasks administered, excluding RT data for the inhibition tasks. These data were excluded as a subset of participants used their non-dominant hand to make button-press responses, which may have impacted the RT data, but was not expected to impact the accuracy data. Smaller common EC composite scores reflect overall better EC processing (see Table 4.4).

5We created a common EC composite score which included inhibition RT data in addition to inhibition accuracy, shifting and WM updating measures. Main regression findings show the same patterns when inhibition RT measures were added to the common EC composite score. However, in order to give equal weight to each EC process of interest, we opted to use the common EC composite score which did not include measures of inhibition RT.

Table 4.4. Individual participant EC task raw scores and EC composite scores.

EC Process	Task	P1	P2	Р3	P4	P6	P7	Р8	Р9	P10	P11	Mean	SD
SHIFTING (sec) ²	Plus Minus 1	47.00	58.50	37.00	256.20	41.14	22.97	259.54	25.83	109.80	169.92	102.79	93.19
FTII Sec.)	Plus Minus 3	-10.99	76.00	77.00	158.50	72.75	1.48	456.17	-47.63	183.29	231.09	119.77	147.63
HS)	Trails A&B	168.60	83.18	55.31	306.34	153.35	59.92	411.19	81.69	357.95	110.82	178.84	131.53
ON (2)	Flanker	223.85	156.56	253.08	342.78	150.18	149.99	321.92	251.07	228.47	362.94	244.08	78.91
INHIBITION (RT, msec) ²	Spatial Stroop	88.66	141.65	-10.78	333.01	146.82	67.03	167.06	202.53	95.62	198.90	143.05	93.09
R (R	Recent Negatives	273.96	778.11	644.64	120.29	93.88	-32.73	992.84	471.89	1575.04	186.68	510.46	498.75
	Flanker	0.00	0.00	-5.00	3.33	0.00	0.00	10.00	-1.67	3.33	8.33	1.83	4.54
INHIBITION (Accuracy) ²	Spatial Stroop	1.88	0.00	2.50	6.88	0.63	1.25	2.50	0.00	0.63	4.38	2.06	2.17
HIB	Recent Negatives	1.71	-1.17	6.67	1.98	6.42	1.91	14.48	7.99	0.60	-1.49	3.91	4.95
<u>z</u> &	Go No-Go	2.78	0.00	11.11	5.56	0.00	2.78	2.78	2.78	5.56	0.00	3.33	3.41
چ [.] ت	Verbal 1-back	98.33	98.33	91.67	95.00	98.33	95.00	98.33	100.00	83.33	100.00	95.83	5.11
WM UPDATING (% Accuracy)³	Verbal 2-back	78.33	86.67	83.33	78.33	90.00	95.00	90.00	88.33	73.33	73.33	83.67	7.53
PDA Acc	Auditory 1-back	100.00	93.33	61.67	83.33	100.00	98.33	98.33	98.33	93.33	100.00	92.67	12.05
	Auditory 2-back	98.33	73.33	60.00	63.33	85.00	86.67	80.00	90.00	56.67	91.67	78.50	14.48
				Co	mposite	Scores						_	
	Shifting ₂	-0.52	-0.50	-0.64	0.96	-0.39	-0.85	1.91	-0.90	0.62	0.32	-	
	Inhibition (RT) ₂	-0.44	-0.20	-0.42	0.84	-0.66	-1.03	0.74	0.22	0.48	0.49		
	Inhibition (Accuracy) ₂	-0.27	-0.85	0.38	0.69	-0.38	-0.32	0.99	-0.27	-0.09	0.12		
	WM Updating₃	-0.44	-0.15	1.18	0.67	-0.60	-0.59	-0.48	-0.68	1.32	-0.24		
	Common EC _{2,4}	-0.40	-0.50	0.39	0.76	-0.46	-0.57	0.71	-0.59	0.62	0.04		

₁Composite scores were calculated by averaging standardized (z) scores of the raw data for each EC process.

²Higher scores indicate worse performance.

³Signs of the WM Updating composite were reversed to match the directionality of the shifting and inhibition composites; higher scores indicate worse performance.

⁴Inhibition accuracy, WM updating and shifting scores were used to calculate the common EC composite.

4.2.4 Treatment

4.2.4.1 Treatment Protocol

All participants were treated for their word-finding deficits using the Phonological Components Analysis (PCA) therapy, a structured treatment protocol with demonstrated efficacy for improving naming impairments in individuals with post-stroke aphasia, and inducing changes in brain activation (Marcotte, et al., 2018; Leonard et al., 2015; Rochon et al., 2010; Leonard, Rochon & Laird, 2008; Van Hees, McMahon, Angwin, de Zubicaray & Copland, 2014; Van Hees, Angwin, McMahon & Copland, 2013). PCA required participants to name a picture stimulus (e.g., sweater), and to provide five phonological components associated with that stimulus: a rhyme word (e.g., letter), the first and last sounds (i.e., /s/, /er/), the number of syllables (i.e., 2) and another word starting with the same sound (e.g., seat). Participants were given three naming attempts, and heard the examiner say each target a total of two times per trial. The order of stimulus presentation was randomized for every session.

4.2.4.2 Stimulus Selection

Treatment stimuli were selected according to baseline naming performance on a battery of 198 coloured photographs of nouns, administered on three separate sessions. Nouns named incorrectly during two or three baseline sessions were selected as potential stimuli, and two lists of approximately 30 words each, matching in terms of semantic category, frequency and syllable length, were created for each participant. Treatment was administered on one of these lists, while the other served as a matched, within-subject untreated list. Treatment lists were matched within-but not between-participants.

4.2.4.3 Treatment schedule

Participants were treated either in their homes, or in a quiet room at the University of Toronto, by a research associate trained in PCA therapy. Participants received two sessions of treatment per day (i.e., 15 words per session), three days a week, for five weeks, totaling 30 sessions6. A

6Three participants (P1, P2 & P3) were part of a concurrent study and received the PCA treatment protocol on slightly different schedules: P2 and P3 (3 sessions per day, 4 days a week for 2.5 weeks); P1 (1 session per day, 3 days a week for 10 weeks). All participants received a total of 30 sessions of therapy. No differences were noted in average session duration, total treatment hours, or in treatment performance as a function of treatment schedule, thus these participants were included in the present analysis.

five-minute break was given between the same-day sessions, which were considered complete once all 30 words were treated. As a result, session times varied according to the pace of the participant, and the stage of treatment (i.e., sessions became shorter as treatment progressed, due to increased familiarity with the protocol). Mean session length was 42.09 minutes (SD = 10.77) and participants received an average of 21.05 hours of treatment (SD = 3.35).

4.2.5 Primary Outcome Measure

Our primary outcome measure for the treatment data was naming accuracy on an overt picturenaming task, using coloured photographs of the treated and untreated stimuli. Outcomes were
measured at four time points (pre-treatment, post-treatment, and four-, and eight-weeks posttreatment), and the order of stimuli was randomized at each presentation. The post-treatment
outcome measure was taken within one week following the completion of therapy, but never on
the same day as the final therapy session. These sessions were audio recorded and later
transcribed and scored by an independent rater who was blinded to assessment time, word list
(i.e., treated versus untreated), and study objectives. Outcome data were scored according to
specific scoring instructions, which included both coding for naming accuracy and naming
errors, and followed the detailed procedures outlined by Roach and colleagues (1996) for the
Philadelphia Naming Test (PNT; Roach, Schwartz, Martin, Grewal & Brecher, 1996). Only
naming accuracy data were used in the present study.

4.2.5.1 Reliability of Outcomes

An independent rater who was blind to time point (i.e., pre-, post-treatment, four- and eight-week follow-up) transcribed and scored a random selection of 20% of the data, in order to ascertain the reliability of both the transcription and scoring of outcomes. Point-to-point agreement among the raters was 96.67% for transcription, and 90.34% for scoring, indicating excellent inter-rater reliability.

4.2.6 Statistical Analyses

Given that the primary objective of this study was to determine the prognostic value of EC in naming improvements seen after treatment, we discuss treatment outcomes only as difference scores which can be seen in Table 4.5. Participants improved their naming accuracy after treatment by an average of 36% (range: 16 - 73%). We discuss treatment outcomes more

extensively in a separate paper (Simic et al., in preparation). All statistical procedures were conducted using IBM SPSS Statistics Software Version 24.

Table 4.5. Individual participant differences in naming accuracy (%) immediately following therapy (post - pre), and at four- (4W - post) and eight-week (8W - post) follow-ups, for treated and untreated words.

		TREATED			UNTREATED	
	Treatment	Mainto	enance	G	eneralization	1
					4W -	
Participant	Post - Pre	4W - Post	8W - Post	Post - Pre	Post	8W - Post
P1	16.67	3.33	6.67	0.00	10.00	10.00
P2	26.67	0.00	0.00	10.00	0.00	3.33
P3	33.33	-16.67	-23.33	6.67	13.33	10.00
P4	33.33	-20.00	-33.33	-6.67	13.33	6.67
P6	23.33	-6.67	13.33	-6.67	-6.67	-3.33
P7	65.52	0.00	-6.90	10.34	17.24	6.90
P8	73.33	-16.67	-20.00	13.33	33.33	26.67
P9	20.00	0.00	-3.33	10.00	-13.33	-6.67
P10	41.67	-20.83	-25.00	0.00	4.35	8.70
P11	31.03	-6.90	-20.69	-14.29	14.29	7.14
Average	36.49	-8.44	-11.26	2.27	8.59	6.94

⁴W - Four week follow-up; 8W - Eight week follow-up

4.2.6.1 Correlations

We analyzed relationships among EC task raw scores, and general trends in the data using Spearman's rho correlation coefficients. Variables significantly associated with the dependent variables (i.e., naming accuracy difference scores) were to be included as predictors in our regression models (this approach can also be seen in Dignam et al., 2017 and Murray, 2012). The variables of interest were age, pre-treatment aphasia severity (i.e., WAB AQ scores), naming (i.e., BNT scores), semantic, and phonological processing abilities. Due to our large battery of language assessment measures (listed in Table 4.2), composite scores for semantic (comprised of two PPTT subtests, and the PALPA 47, 48, 49 and 50 subtests) and phonological processing (comprised of the PAL 08, PALPAs 1, 5, 7, 8, 9, 14, 15 and 31) were derived in the same way as

Positive values indicate gains in naming accuracy, while negative values indicate drop-offs in naming accuracy.

described above for the EC predictors. We chose to assess the predictive value of pre-treatment naming ability separately as this was the target of our treatment protocol.

4.2.6.2 Regressions

Our analyses evaluated the predictive value of common EC and the individual EC processes, using both simple and multiple linear regressions, respectively. Multiple regression analyses were conducted using the forced entry method. For each EC model, treatment and maintenance phases were assessed separately, as was generalization to untreated items. In total, twelve regression models were conducted to examine the predictive value of a) common EC and b) the individual EC processes in two conditions (i.e., treated and untreated words) across three time periods (i.e., pre to post treatment, post to four-week follow-up, and post to eight-week follow-up). To control for false discovery rate (FDR), we adjusted for multiple comparisons using the Benjamini-Hochberg procedure (FDR was set at q = .05; Benjamini & Hochberg, 1995).

Detailed residual analyses were conducted to ensure that model assumptions were met, especially given the small sample size; outliers and influential data points were assessed through careful evaluation of residual plots and diagnostic statistics (i.e., Cook's distance, Mahalanobis distance, standardized DFFit and DFBeta values, leverage values and covariance ratios); cut-off criteria were obtained from the literature (Field, 2009; Stevens, 2002; Verran & Ferketich, 1987; Barnett & Lewis, 1978). Assumptions of linearity, normality, independence of errors, homoscedasticity and multicollinearity were met in each analysis reported. Model stability was assessed using adjusted *R*² (Field, 2009; Prescott, 1987).

4.2.6.2.1 Dependent Variables

The dependent variables in each regression analysis were the differences in naming accuracy from a) pre- to post-treatment, b) post-treatment to four-week follow-up, and c) post-treatment to eight-week follow-up. A reciprocal transformation was performed on the pre- to post-treatment data (for treated words) only, to reduce the influence of two outliers in the regression models using this dependent variable. Generalization was assessed using difference scores in naming accuracy on untreated items (obtained in the same way described above). Individual difference scores (i.e., dependent variables) are shown in Table 4.5.

4.2.6.2.2 Independent Variables

The independent (predictor) variables were composite scores for each EC process of interest, namely, inhibition RT, inhibition accuracy, WM updating and shifting (see Table 4.4). Predictor variables were assessed for multicollinearity using variance inflation factors (VIFs), and eigenvalues (Field, 2009; Stevens, 2002); inhibition RT and inhibition accuracy were assessed in separate models, and both were found to be collinear with shifting (average VIF > 2), indicating that tasks used to measure the processes of inhibition and shifting tapped into a common underlying EC factor. According to Miyake and Friedman (2012), unlike measures of shifting and updating, which are separable EC processes, inhibition varies together with, and is thus not separable from the common EC factor. Therefore, to control for multicollinearity, inhibition measures (both RT and accuracy) were removed as predictors from the multiple linear regression models. The final model consisted of two predictor variables: shifting and WM updating. The predictor variable for simple linear regression models was common EC, a single composite score of all EC tasks (including WM updating, shifting and inhibition accuracy scores as described above).

4.3 Results

4.3.1 Correlations

We first examined correlations among EC task raw scores and EC composite scores (presented in Table 4.6). Significant correlations emerged among the individual shifting tasks, and also among the individual WM updating tasks. The inhibition RT and inhibition accuracy raw scores were more variable; individual inhibition tasks were not significantly correlated. Among the predictor variables, significant correlations were found between the shifting and inhibition RT composite scores, and the inhibition accuracy and inhibition RT composite scores. Not surprisingly, common EC was also significantly correlated with the WM updating, shifting, inhibition accuracy, and inhibition RT composites. No significant correlations were found between any of the EC composite scores and age (range of r = -.439 to .280, ns), aphasia severity (range of r = -.079 to .115, ns), anomia severity (range of r = -.442 to .006, ns), semantic processing (range of r = -.600 to -.297, ns), or phonological processing (range of r = -.152 to .188, ns).

Table 4.6. Spearman's rho (r_s) correlation coefficients for individual EC task raw scores and EC composite scores.

			SI	HIFTING			INHIBIT	TION (RT	Γ)		INHI	BITION	(Accuracy	Δ		W	/M UPDAT	ING	
		1	2	3	Composite	4	5	6	Comp osite	7	8	9	10	Composite	11	12	13	14	Comp osite
1	Plus Minus 1	-																	
2	Plus Minus 3	.82**	-																
3	Trails A&B	.81**	.53	-															
	Shifting Composite	.94**	.84**	.86**	-														
4	Flanker	.65*	.64*	.29	.49	-													
5	Spatial Stroop	.50	.21	.39	.42	.55	-												
6	Recent Negatives	.38	.41	.33	.29	.25	09	-											
	Inhibition (RT) Composite	.83**	.70*	.58	.71*	.86**	.71*	.42	-										
7	Flanker	.86**	.78**	.78**	.87**	.46	.45	.15	.66*	-									
8	Spatial Stroop	.52	.57	.25	.49	.70*	.17	23	.47	.47	-								
9	Recent Negatives	15	12	.01	08	.09	.13	.06	.04	24	.02	-							
10	Go No-Go Inhibition	02	.11	.04	.02	.27	25	.27	.21	18	.32	.36	-						
	(Accuracy) Composite	.58	.66*	.38	.53	.86**	.31	.29	.75*	.45	.75*	.39	.59	-					
11	Verbal 1-back	.04	20	06	15	.18	.55	17	.09	.08	15	01	74*	18	-				
12	Verbal 2-back	45	36	28	32	54	13	31	48	27	34	.59	24	30	.12	-			
13	Auditory 1- back	06	22	.15	06	19	.14	39	29	.21	09	16	71*	34	.68*	.13	-		
14	Auditory 2- back	24	46	15	37	09	.15	48	29	03	02	12	58	29	.77**	.14	.85**	-	
	WM Updating Composite ¹	.42	.54	.18	.39	.35	25	.47	.37	.18	.34	42	.53	.35	66*	71*	66*	70*	
	Common EC Composite	.79**	.79**	.66*	.83**	.65*	.18	.32	.69*	.61	.73*	.08	.51	.79**	45	47	37	53	.65*

Shaded rows highlight EC composite score correlations.

1Signs of the WM Updating composite were reversed to match the directionality of the shifting and inhibition composites.

^{**} Correlation is significant at the 0.01 level (2-tailed).

^{*} Correlation is significant at the 0.05 level (2-tailed).

Better EC ability was associated with better maintenance of improvements in naming accuracy (see Table 4.7). No significant correlations were found between EC measures and naming accuracy difference scores immediately post-treatment for the treated words. However, naming accuracy difference scores for treated words were significantly correlated with all EC composite scores at four-week follow-up, and with all EC composite scores (apart from shifting) at eightweek follow-up. No significant correlations emerged between EC measures and naming accuracy difference scores for untreated words at any time point. Finally, results of correlational analyses reveal that age, aphasia severity, naming on the BNT, phonological and semantic processing did not demonstrate significant associations with naming accuracy difference scores for treated or untreated items at any time-point (see Table 4.7). Consequently, these variables were not included as predictors in the regression models.

Table 4.7. Spearman's rho (r_s) correlation coefficients demonstrating associations between naming accuracy difference scores (for treated and untreated words) and age, language and EC variables of interest.

		TREATED			UNTREATED	
	Treatment	Mainto	enance		Generalizatio	n
	Post - Pre	4W - Post	8W - Post	Post - Pre	4W - Post	8W - Post
Age	.254	167	159	040	.187	.502
WAB-AQ	.456	295	285	055	.395	.359
BNT	.347	.197	.188	.251	.298	.085
Phonological						
Processing	486	.351	.455	239	109	.140
Semantic Processing	389	.591	.430	.061	207	201
WM Updating ¹	.316	628*	697*	281	.170	.432
Shifting ²	.444	689*	430	281	.359	.353
Inhibition (RT) ²	.298	640*	661*	171	.237	.170
Inhibition (Accuracy) ²	.511	695*	<i>7</i> 58*	037	.571	.565
Common EC ²	.498	819**	<i>709</i> *	281	.474	.602

¹Signs of WM Updating composite are reversed such that smaller EC scores indicate better performance.

²Smaller EC scores indicate better performance.

^{*}Correlation is significant at the 0.05 level (2-tailed).

^{**}Correlation is significant at the 0.01 level (2-tailed).

4.3.2 Regression Models: Immediate treatment gains and maintenance

Regression analyses were conducted to assess whether EC predicted the acquisition and maintenance of treated items. Relationships (i.e., raw scores) between individual predictors and naming accuracy difference scores for the treated words are presented in Figure 4.1.

4.3.2.1 Common EC

Simple linear regressions were conducted to assess whether common EC predicted difference scores in naming accuracy of treated items (post – pre, four weeks – post, and eight weeks – post; see Table 4.8 for detailed statistics). Immediate treatment gains (i.e., naming accuracy difference scores post – pre-treatment) were not predicted by the regression model. Visual analysis of residual plots and diagnostic statistics revealed that two individuals made substantially larger gains pre- to post-treatment (P7 and P8) than the rest of the group; P7 was among the best in terms of overall EC performance, whereas P8 was among the worst. When these data points were removed, the remaining data show a significant trend mirroring the pattern seen in P8, and indicating that worse EC ability is associated with greater improvements in naming immediately post-treatment ($R_2 = .738$, adjusted $R_2 = .695$; F(I,7) = 16.929; p = .006). In contrast, common EC was a significant predictor of four- and eight-week treatment maintenance scores (see Table 4.8 and scatterplots in Figure 4.1). Individuals with more efficient EC processing maintained improvements on treated words more successfully.

4.3.2.2 Individual EC processes

The parameters entered into the multiple regression analysis were WM updating and shifting (see Table 4.8 for detailed statistics). The model did not predict treatment gains immediately post-treatment. As noted above, there were two individuals (P7 and P8) with very large gains pre- to post-treatment; while they both had above average WM updating abilities relative to the sample, P8 demonstrated poor shifting ability, while P7 demonstrated the opposite. As with the common EC model, trends among the remaining eight participants appear to indicate, contrary to our hypotheses, that those with worse shifting and WM updating abilities made greater gains pre- to post-treatment.

At four-week follow-up, the regression model accounted for 88.1% of the variance in naming accuracy difference scores; both shifting and WM updating parameters were significant

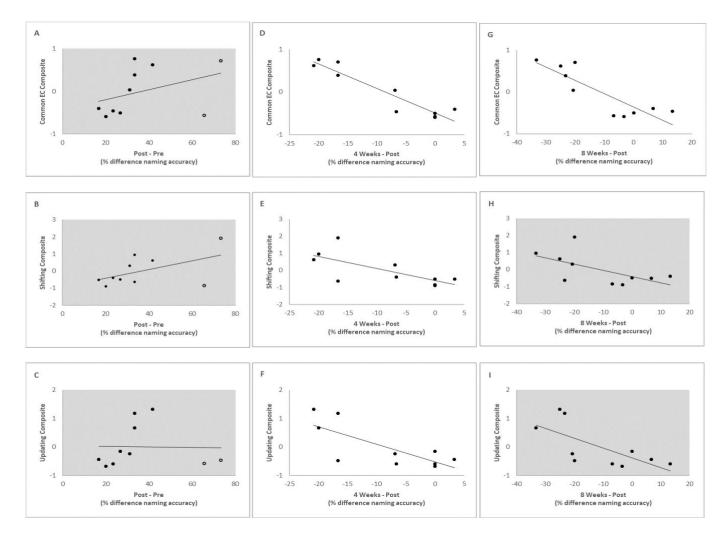


Figure 4.1. Scatterplots demonstrating the relationship between difference scores in naming accuracy of *treated words* and common EC, shifting and WM updating composite scores i) pre to post treatment (A, B, C), ii) post to four-week follow-up (D, E, F) and iii) post to eight-week follow-up (G, H, I). Smaller EC composite scores indicate better performance. Open circles are influential data points. Plots with white backgrounds indicate significant relationships; plots shaded grey indicate non-significant findings. Plots H and I approached significance. Note that a reciprocal transformation was performed on the pre- to post-treatment data (A, B, C) for regression analyses, to account for the influential data points indicated.

predictors of treatment maintenance, such that individuals with better shifting and WM updating performance better maintained treatment gains. Similarly, at eight-week follow-up the regression model was significant, accounting for 69.5% of the variance in naming accuracy. At this second follow-up stage, however, the individual shifting and WM updating parameters approached but did not reach significance. Detailed statistics are presented in Table 4.8 (also see scatterplots in Figure 4.1).

Table 4.8. Simple (common EC) and multiple (individual EC processes) linear regression model summaries for *treated words*.

							Model Summary
	Immediate Treatment gains ¹	В	SE B	β	t	p	$R_2 = .292,$
	Constant	0.034	0.004		8.138	0.000	Adjusted R ₂ = .204; F(1,8) = 3.307; p =
	Common EC	-0.014	0.008	-0.541	-1.818	0.106	.106
Ä	Maintenance (4 Weeks)						$R_2 = .890,$
δ	Constant	-8.440	1.038		-8.132	0.000	Adjusted R ₂ = .876;
COMMON EC	Common EC	-15.473	1.927	-0.943	-8.028	0.000*	F(1,8) = 64.449; p < .001*
•	Maintenance (8 Weeks)						$R_2 = .748,$
	Constant	-11.258	2.587		-4.351	0.002	Adjusted R ₂ = .716;
	Common EC	-23.388	4.804	-0.865	-4.868	0.001*	F(1,8) = 23.697; p = .001 *
	Immediate Treatment gains ¹	В	SE B	β	t	p	$R_2 = .304,$
	Constant	0.034	0.004		7.678	0.000	Adjusted R ₂ = .106;
SES	Shifting	-0.008	0.005	-0.491	-1.522	0.172	F(2,7) = 1.532; p =
CES	WM Updating	-0.003	0.006	-0.166	-0.516	0.622	.281
Š	Maintenance (4 Weeks)						R ₂ = .881,
EC P	Constant	-8.440	1.154		-7.313	0.000	Adjusted R ₂ = .846;
AL	Shifting	-5.718	1.349	-0.567	-4.240	0.004*	F(2,7) = 25.798; p
INDIVIDUAL EC PROCESSES	WM Updating	-7.745	1.632	-0.635	-4.745	0.002*	= .001*
<u> </u>	Maintenance (8 Weeks)						$R_2 = .695,$
Z	Constant	-11.258	3.043		-3.700	0.008	Adjusted R ₂ = .607;
	Shifting	-7.919	3.556	-0.477	-2.227	0.061	F(2,7) = 7.958; p =
	WM Updating	-11.837	4.304	-0.588	-2.750	0.028^	.016*

In all analyses, N = 10.

^{*}significant (with Benjamini-Hochberg adjustment)

[^]approaching significance

¹Reciprocal transformation performed on the dependent variable (i.e., post-pre difference scores in naming accuracy) to account for impact of two influential data points.

4.3.3 Regression Models: Generalization

Additional regression analyses were conducted to assess whether EC predicted generalization to untreated items. Relationships (i.e., raw scores) between individual predictors and naming accuracy difference scores for the untreated words are presented in Figure 4.2.

4.3.3.1 Common EC

With common EC as the only predictor, the regression model was not significant in predicting immediate gains on untreated words pre- to post-therapy. Simple linear regressions did not reach significance at four-week follow-up but approached significance at the eight-week follow-up stage, suggesting a trend for those with poorer EC performance to make the greatest improvements in naming untreated items eight-weeks following therapy (see Table 4.9 and scatterplots in Figure 4.2).

4.3.3.2 Individual EC processes

Naming improvements pre- to post-therapy on untreated words were not predicted by the multiple linear regression model with shifting and WM updating as parameters. Diagnostic statistics, however, revealed an influential data point (P8) on the shifting parameter. When this data point was removed, the model explained 63.3% of the variance in naming accuracy on untreated words pre- to post-therapy (see Table 4.9 and scatterplots in Figure 4.2). Individual parameter estimates indicate that those with better shifting performance tended to improve more on untreated words immediately following therapy. Though better than the original model, diagnostic statistics indicate an overall poor fit of the model to these data. As such, we also conducted a simple linear regression for the shifting parameter; shifting explained 48.6% of the variance in naming improvements pre- to post-therapy on untreated words ($R_2 = .486$, adjusted $R_2 = .414$; F(1,7) = 6.623; p = .037) when P8 was removed.

At four-week follow-up, the regression model with shifting and WM updating as parameters was not significant. In fact, the parameter coefficient for shifting suggests that individuals with greater improvements on untreated words at four-week follow-up tended to have poorer shifting skills. Likewise, at eight-week follow-up, the regression model was not significant, even after an influential data point (P8) was removed (see Table 4.9 and scatterplots in Figure 4.2).

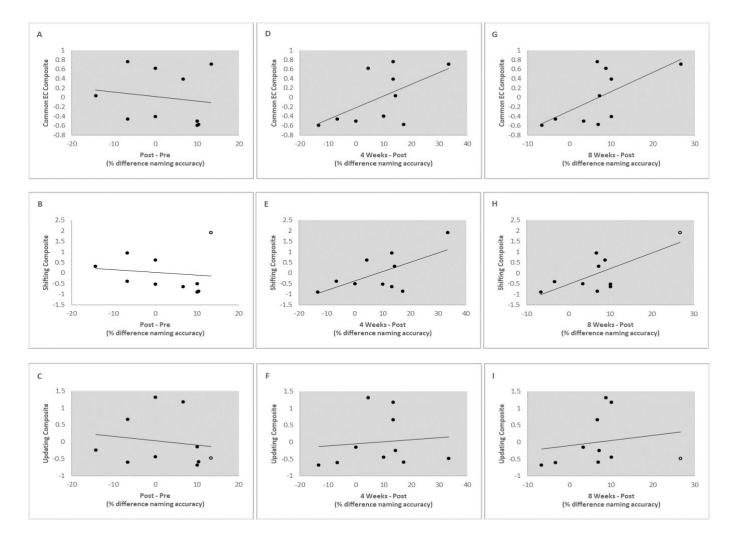


Figure 4.2. Scatterplots demonstrating the relationship between difference scores in naming accuracy of *untreated words* and common EC, shifting and WM updating composite scores i) pre to post treatment (A, B, C), ii) post to four-week follow-up (D, E, F) and iii) post to eight-week follow-up (G, H, I). Smaller EC composite scores indicate better performance. Open circles are influential data points. Plots with white backgrounds indicate significant relationships; plots shaded grey indicate non-significant findings. Plot G approached significance.

Table 4.9. Simple (common EC) and multiple (individual EC processes) linear regression model summaries for untreated words.

							Model Summary
	Therapy Period	В	SE B	β	t	p	R2 = .153, adjusted
	Constant	2.273	3.067		0.741	0.480	R2 = .023; F(1,8) =
ပ္ပ	Common EC	-2.493	5.695	-0.153	-0.438	0.673	.192; p = .673
N	Four-week follow-up						R ₂ = .341, Adjusted
Σ	Constant	8.587	3.599		2.386	0.044	R ₂ = .258; F(1,8) =
COMMON EC	Common EC	13.588	6.683	0.584	2.033	0.076	4.133; p = .076
0	Eight-week follow-up						R ₂ = .417, Adjusted
	Constant	6.941	2.282		3.042	0.016	R ₂ = .345; F(1,8) =
	Common EC	10.145	4.237	0.646	2.394	0.044^	5.733; p = .044^
	Therapy Period1	В	SE B	β	t	p	
	Constant	-1.912	2.283		-0.837	0.435	R2 = .633, adjusted
							D2 = E10. E(2.6) =
SES	Shifting	-12.632	3.945	-0.956	-3.202	0.019*	R2 = .510; F(2,6) = 5.170: p = .050^
CESSES	Shifting WM Updating	-12.632 5.210	3.945 3.365	-0.956 0.462	-3.202 1.548	0.019* 0.173	R2 = .510; F(2,6) = 5.170; p = .050^
ROCESSES	, ,						5.170; p = .050^
EC PROCESSES	WM Updating						5.170; p = .050^ R ₂ = .404, Adjusted
AL EC PROCESSES	WM Updating Four-week follow-up	5.210	3.365		1.548	0.173	5.170; p = .050^ R ₂ = .404, Adjusted R ₂ = .234; F(2,7) =
IDUAL EC PROCESSES	WM Updating Four-week follow-up Constant	5.210 8.587	3.365	0.462	1.548 2.348	0.173	5.170; p = .050^ R ₂ = .404, Adjusted
DIVIDUAL EC PROCESSES	WM Updating Four-week follow-up Constant Shifting	5.210 8.587 9.189	3.365 3.657 4.274	0.462	1.548 2.348 2.150	0.173 0.051 0.069	5.170; p = .050^ R ₂ = .404, Adjusted R ₂ = .234; F(2,7) = 2.375; p = .163
INDIVIDUAL EC PROCESSES	WM Updating Four-week follow-up Constant Shifting WM Updating	5.210 8.587 9.189	3.365 3.657 4.274	0.462	1.548 2.348 2.150	0.173 0.051 0.069	5.170; p = .050^ R ₂ = .404, Adjusted R ₂ = .234; F(2,7) = 2.375; p = .163 R ₂ = .322, adjusted
INDIVIDUAL EC PROCESSES	WM Updating Four-week follow-up Constant Shifting WM Updating Eight-week follow-up1	5.210 8.587 9.189 -0.603	3.365 3.657 4.274 5.173	0.462	2.348 2.150 -0.116	0.173 0.051 0.069 0.911	5.170; p = .050^ R ₂ = .404, Adjusted R ₂ = .234; F(2,7) = 2.375; p = .163

 $_{1}$ One extreme outlier (P8) removed (n = 9). In all other analyses, N = 10.

4.3.4 Generalizability of models

Adjusted R₂ was used to assess model stability, as it provides an unbiased estimate of shrinkage (i.e., decreases in predictive performance) of a model when it is applied to the population. Shrinkage estimates were calculated by subtracting adjusted R₂ values from R₂. Overall, shrinkage estimates are smaller (indicating more robust findings) for the simple- (range = 1.4% - 13.0% shrinkage), compared to the multiple regression models (range = 3.5% - 22.5% shrinkage) due to the smaller number of predictors relative to the sample size. Models predicting the maintenance of treated words were found to be quite robust, whereas models assessing immediate treatment effects on treated and untreated words and long-term generalization to untreated items appeared to be less so.

^{*} significant (with Benjamini-Hochberg adjustment)

[^]approaching significance

4.4 Discussion

It is of theoretical and clinical importance to determine the best predictors of aphasia recovery. Though this question has received much attention, the optimal combination of factors needed for successful treatment outcomes in aphasia remains somewhat unclear. Recent evidence points to neuropsychological factors, such as EC, as potentially important predictors of treatment success. The purpose of this study was to use a theoretically-driven approach to the selection and analysis of EC tasks (based on Miyake et al., 2000; Miyake & Friedman, 2012) to determine whether EC could predict short- and long-term treatment gains and generalization after a structured treatment for anomia.

Our results suggest three important findings, namely: 1) in line with our hypotheses, common EC, shifting, and WM updating were strong positive predictors of treatment maintenance up to eight weeks following therapy, 2) better shifting ability predicted better generalization to untreated items immediately following therapy, and 3) contrary to our hypotheses, neither individual EC processes nor common EC predicted immediate treatment gains for trained items or long-term generalization to untrained items. These findings will be discussed in turn below, in addition to the nature of the EC tasks used, and the relationship of language variables to treatment outcomes.

4.4.1 EC as a predictor of aphasia recovery

4.4.1.1 Treatment maintenance

Outcomes taken some time after the end of treatment (i.e., in the maintenance phase) likely reflect more robust, real-life changes in underlying lexical representations. Both common EC and separable EC processes were found to be strong and robust predictors of treatment maintenance. Smaller decays in naming accuracy four and/or eight weeks following the end of treatment (i.e., better maintenance) were seen in individuals with better shifting, WM updating, and common EC. WM updating emerged as a somewhat stronger predictor of this effect over time. Good WM updating may allow individuals to actively maintain task-related goals during therapy, which may in turn lead to better encoding and consolidation of the items learned in treatment. Furthermore, individuals who are better able to flexibly shift tasks may have greater flexibility in applying learned words to new contexts outside of therapy, which may also promote treatment

maintenance. Therefore, specific EC processes as well as common EC may be critical in organizing and encoding to-be-learned material in such a way that it is more successfully retrieved in the long-term, complementing research that highlights the crucial role of top-down EC processing in learning and consolidating new material (Diamond, 2013; Lambon-Ralph & Fillingham, 2007; Robertson & Murre, 1999).

4.4.1.2 Immediate treatment gains

Research has shown that the same top-down EC abilities that aid in new learning are seldom recruited during well-learned tasks and can even hinder performance on such tasks (Diamond, 2013). In the present study, individuals received five weeks of consistent training, and as such, were very well-versed in the picture-naming task at post-treatment assessment. This might partially explain why neither common EC nor specific EC processes were good indicators of immediate treatment gains, given the relative automaticity of naming the treated words shortly after the completion of therapy. These findings suggest that different mechanisms are recruited at different stages of recovery. While EC ability seems to be important in treatment maintenance, immediate treatment gains may be mediated by other factors. Previous work indicates that measures of facilitation (e.g., cue effectiveness), may perhaps hold predictive value as indicators of immediate treatment gains (Hickin et al., 2002; Leonard et al, 2008). It may be that in the case of phonological treatments such as the PCA, the facilitative effect of a phonological component (e.g., the first sound or a rhyme word) in eliciting the target word could be a more appropriate predictor of immediate pre to post treatment improvements.

4.4.1.3 Treatment generalization

Based on the view that top-down EC processes are recruited during learning of novel tasks, we might expect EC to be a positive predictor of generalization to novel, untrained items. Indeed, verbal short-term memory (Dignam et al., 2017) and inhibitory control (Yeung et al., 2009) have been identified as positive indicators of generalization to untrained items, and better working memory has been positively correlated with generalization to untrained tasks (Harnish, Blackett, Zezinka, Lundine & Pan, 2018). Although the changes noted pre- to post-treatment on untrained items were relatively small, our data are in line with these findings, indicating that better shifting ability is predictive of improvements on untreated items pre- to post-therapy. Individuals with

better shifting ability, or greater flexibility, may be better able to transfer what they've learned in treatment to a set of untrained words.

Contrary to this finding and to our hypotheses, long-term improvements on untrained items were not predicted by EC performance. In addition, we noted a trend for individuals with worse common EC performance at baseline to show greater improvements on untreated items post-treatment to eight-week follow-up. Interpreting such trends is highly speculative and it is likely that they would not hold in a larger sample. Nevertheless, we offer some possible explanations below.

Previous work (Miyake et al., 2012) suggests that common EC and shifting-specific processes, when associated with other measures, can show opposing correlations. One explanation for this may lie in the dual nature of shifting, which requires a dynamic balance between two conflicting states: stability and flexibility (Goschke, 2000; Gruber & Goschke, 2004). Actively maintaining multiple, potentially relevant goals in mind may promote flexible shifting among tasks, but may also result in poorer maintenance (i.e., stability) of any single task (Gruber & Goschke, 2004). Another possible explanation comes from studies showing that while stronger top-down EC processing supports learning and consolidation (which is upheld by our treatment maintenance data), it may in fact limit *transfer* of learning, especially in older adults (Mosha & Robertson, 2016; Weeks & Hasher, 2014; Amer & Hasher, 2014; Biss, Ngo, Hasher, Campbell & Rowe, 2013). Although contrary to expectations, these findings nevertheless support our claim that immediate treatment gains, maintenance and generalization may be mediated by different underlying mechanisms.

4.4.2 EC task selection

The majority of existing studies characterize EC ability using either a single, complex task or a composite score comprised of a range of cognitive abilities (including, but not limited to EC). As discussed above, this approach can be problematic for interpreting results. In the present study we addressed some of the limitations concerning the accurate and precise measurement of EC found in previous work (Simic et al., 2017). The creation of composite scores based on multiple, process-specific tasks mitigated the impact of non-EC factors on the data. This approach, however, was not without its difficulties.

The EC tasks used to measure each EC process were relatively similar in terms of their stimuli and task requirements. For example, shifting tasks all contained number stimuli, and multiple inhibition tasks required a left/right decision. Likewise, the *Plus-Minus 1* and *3*, *Verbal 1-* and *2-back*, and *Auditory 1-* and *2-back* tasks, respectively, were similar pairs of tasks with differing levels of difficulty; ideally, task selection should be more broad (Miyake et al., 2000). The common EC composite score, however, was comprised of a broader range of tasks; in contrast to previous studies, the selection of these tasks was more theoretically-driven (Miyake et al., 2000; Miyake, Emerson & Friedman, 2000; Miyake & Friedman, 2012; Snyder et al., 2015). The fact that this broader EC measure demonstrated relationships with our language outcomes that paralleled those seen with the individual EC processes is encouraging. This also highlights the advantage and importance of using a theoretical framework to measure EC.

However, despite the similarity of the EC tasks administered, correlations among individual tasks were variable. For example, inhibition tasks correlated poorly with one another in our sample, as did the *1*- and *2-back* versions of the *Verbal* (and *Auditory*) n-back tasks. It is possible that the correlations observed would show different patterns in a larger sample; for this reason we opted to aggregate individual EC tasks based on a-priori theoretical assumptions. However, data from a larger sample would allow for the use of more robust statistical techniques, such as latent variable analysis, to tease apart the individual contributions of each EC task on a given EC process.

The presence of aphasia further complicated EC task selection, somewhat narrowing the range of EC tasks that could be administered. Thus, EC tasks were selected not only according to their specificity in tapping the desired EC process, but also according to their verbal requirements. Despite our best efforts to minimize the verbal requirements of each task, the extent to which linguistic strategies (such as subvocal rehearsal) were employed to complete EC tasks remains unclear. Indeed, previous studies have demonstrated that language ability (e.g., phonology) plays a role in EC task performance (Baldo, et al., 2005; Allen, et al., 2012). Although based on a small sample, language abilities (i.e., aphasia and anomia severity, semantic and phonological processing) were not correlated with EC in the present study. In addition, we found significant correlations between verbal (e.g., Trail Making, Verbal 1-back) and nonverbal EC tasks (e.g., Plus Minus 1, Auditory 1-back, respectively), suggesting that these tasks measured similar EC abilities. However, the recent negatives task, which perhaps was the most linguistically taxing,

did not correlate with any other EC tasks administered. This calls into question the appropriateness of this task in individuals with language deficits.

In addition, it remains unclear to what extent the structure of EC in aphasia resembles that of neurotypical individuals. Although most participants demonstrated typical response patterns within the EC tasks, one individual (P3) did not show considerably better performance in less-, compared to more demanding task conditions (e.g., the congruent condition of the Flanker task; see Appendix 4-A). Replication in a larger sample may help to determine whether this is a common pattern in this population, or an anomalous finding. Thus, the impact that language and/or aphasia might have on EC is an important question to consider in this, and future studies.

4.4.3 The relationship between language measures and treatment outcomes

In contrast to the significant correlations found between EC measures and long-term improvements in the naming accuracy of treated words, initial aphasia severity (i.e., WAB AQ score) was not significantly correlated with short- or long-term improvements in naming accuracy for treated or untreated words. Similarly, other measures of language performance (i.e., anomia severity, semantic and phonological processing) were not significantly correlated with naming outcomes at any stage of recovery for treated or untreated words. This finding could also be a result of the small sample size, especially given that aphasia severity has been highlighted as an important predictor of aphasia recovery in previous research (e.g., Godecke et al., 2013; Plowman et al., 2012; Lazar, et al., 2010; Laska, et al., 2001; Pederson, et al., 2004). However, our data comply with studies which show that predicting treatment outcome based solely on aphasia or anomia severity may not be adequate, and that other factors must be considered (Lazar & Antoniello, 2008; Lazar et al., 2010; van de Sandt-Koenderman et al., 2008). Data from large scale studies will help to further elucidate these important questions.

4.4.4 Limitations

The primary limitation of this study is the small sample size, which precludes the generalization of our correlational and regression findings beyond the present sample, and which may have prevented significant relationships in the data from being detected. Replication of our design and analyses in a larger sample would provide a basis for more robust interpretation. In addition, although steps were taken to mitigate the impact of task impurity on our assessment of EC, this is

an ever-present issue in our study, as in the broader EC literature, and it is further complicated by the presence of aphasia. The EC tasks used to measure each EC process were relatively similar in terms of their basic processing characteristics; future studies must administer a broader spectrum of tasks to measure any given EC process. Here too, a larger sample would have allowed for the use of more robust statistical techniques to tease apart the differential contributions of individual EC tasks, separable EC processes and common EC on language recovery. Finally, it remains unclear to what extent some of the EC tasks used called upon linguistic ability (e.g., subvocal rehearsal) for their successful completion. Future research must determine the optimal EC tasks for the specific and precise measurement of this construct in individuals with aphasia.

4.4.5 Conclusions

Like many of the prognostic indicators of aphasia recovery, the role of EC is not straightforward. However, our findings suggest that EC is an important variable to consider when predicting aphasia therapy outcomes. Common EC, shifting and WM updating seem to play a particularly important role in the consolidation of treated items over time. The role of EC in immediate treatment gains and in short- and long-term generalization was not as clear in our data, however better shifting ability appears to be associated with better generalization to untreated items immediately following therapy. Neither common EC nor specific EC processes were good indicators of short-term treatment gains, nor of long-term treatment generalization, suggesting that other factors may be at play at these stages of recovery.

Taken together, our findings suggest that immediate treatment gains, treatment maintenance and treatment generalization following naming therapy may be mediated by different underlying mechanisms. This is a crucial consideration not only in evaluating the efficacy of aphasia therapy, but also in evaluating potential predictors of treatment success. Future work must tease apart not only *which* factors are predictive of language recovery, but also at which *stages of recovery* such factors come into play.