12-14-2017

The Association Between Structured Sequence Processing and Grammatical Language Processing: The Neurocognitive Mechanisms and the Potential to Enhance Them

Gretchen NL Smith

Follow this and additional works at: https://scholarworks.gsu.edu/psych_diss

Recommended Citation
Smith, Gretchen NL, "The Association Between Structured Sequence Processing and Grammatical Language Processing: The Neurocognitive Mechanisms and the Potential to Enhance Them."
Dissertation, Georgia State University, 2017.
doi: https://doi.org/10.57709/11104349

This Dissertation is brought to you for free and open access by the Department of Psychology at ScholarWorks @ Georgia State University. It has been accepted for inclusion in Psychology Dissertations by an authorized administrator of ScholarWorks @ Georgia State University. For more information, please contact scholarworks@gsu.edu.
Structured Sequence Processing (SSP) is a fundamental, general-purpose neurocognitive mechanism used to learn patterns of information in the environment over time. SSP helps us make predictions about upcoming events and is vital for grammatical language processing. The primary aim of my doctoral research is using cognitive training techniques with brain imaging to better understand and to improve attention and learning mechanisms that support (and could, in turn, enhance) language. The focus has been on SSP and grammatical/predictive language processing. To summarize main findings across three studies, 1) the results from a mediation
analysis (N=60) demonstrate that computerized SSP training has an underlying effect on predictive language processing by way of its effect on SSP, 2) the results from source localization of electrophysiological activity in the brain (N=32) suggest the neurocognitive mechanisms recruited for a non-linguistic SSP task and a grammatical language processing task share marked overlap in the left anterior superior temporal gyrus, and 3) the preliminary findings of a second computerized SSP training study with EEG/ERP recording (N=51) establish the feasibility of improving SSP as a way to improve language, possibly modulated by changes to attention and working memory. These outcomes inform future investigations of how SSP and language mechanisms can be enhanced in individuals with atypical SSP and language processing, either developmental or acquired. This approach could lead to collaborative opportunities for exploring the potential to improve SSP and language by functionally reorganizing their shared neural circuitry.

INDEX WORDS: Structured Sequence Processing, Grammatical Language Processing, Computerized Cognitive Training, Event-Related Potentials, P300, P600
THE ASSOCIATION BETWEEN STRUCTURED SEQUENCE PROCESSING AND GRAMMATICAL LANGUAGE PROCESSING: THE NEUROCOGNITIVE MECHANISMS AND THE POTENTIAL TO ENHANCE THEM

by

GRETCHEL SMITH

A Dissertation Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy in the College of Arts and Sciences Georgia State University 2017
THE ASSOCIATION BETWEEN STRUCTURED SEQUENCE PROCESSING AND
GRAMMATICAL LANGUAGE PROCESSING: THE NEUROCOGNITIVE MECHANISMS
AND THE POTENTIAL TO ENHANCE THEM

by

GRETCHEL SMITH

Committee Chair:  Chris Conway

Committee:  Rose Sevcik

David Washburn

Samuel Fernandez-Carriba

Electronic Version Approved:

Office of Graduate Studies
College of Arts and Sciences
Georgia State University
December 2017
DEDICATION

This dissertation is dedicated to my mom and dad, who are the finest examples of ethical behavior in the pursuit of education in art and science I have ever known. You are my inspiration to learn, grow, and achieve while holding true to myself.

My hero has been with me encouraging and supporting me my whole life. That hero is my mom who is one of the strongest, most logical, and most genuine humans I know. You are a woman who, at a time decades ago and with zero financial advantages gifted to you, achieved a college degree that preceded a successful career in one of the most important, if not the most important, occupational positions there are—an elementary school teacher. You are a true “first” who paved my way toward another “first” in our family. We women of the tens stick together.

To my brother, I salute you and everyone else out there whose job it is to figure out what we in academia know and what our arguments are…and then to systematically rip them to shreds. Keep us in the hot seat. It’s a good thing.

To my dad, have a good one.
ACKNOWLEDGEMENTS

Thank you to my committee: Chris Conway, Rose Sevcik, David Washburn, and Samuel Fernandez-Carriba, the Language & Literacy Initiative, and the research team “ALIENS”—Juan Galvis, Rocky Haynes, Elizabeth Hilvert, Sanjay Pardasani, Pooja Parupalli, Grace Signiski, Ryan Town, Gerardo Valdez and Kate Winderman— for your contributions to my dissertation studies. To J.D. Purdy, Anne Walk, Michelle Gremp, Sonia Singh, Ben Rickles, my friends from SLU, my friends from GSU, and my friends from Marcus Autism Center: thank you for your support, encouragement, insights, and camaraderie. Funding: This work was supported by the National Institutes of Health R01DC012037 awarded to Dr. Christopher M. Conway.
TABLE OF CONTENTS

ACKNOWLEDGEMENTS ....................................................................................................... V

LIST OF FIGURES ................................................................................................................. 4

1 BACKGROUND AND OUTLINE ....................................................................................... 5

2 CHAPTER 1: GENERAL INTRODUCTION ....................................................................... 8

2.1 Structured Sequence Processing ................................................................................. 8

2.2 Structured Sequence Processing and Language ......................................................... 8

2.3 Cognitive Training Effects ......................................................................................... 10

2.3.1 WM training studies ............................................................................................... 11

2.4 Moving Beyond the Kitchen Sink Approach To More Targeted Computerized Training ......................................................................................................................................................................................... 13

2.5 Do Non-Trained Tasks of SSP Measure SSP? .............................................................. 15

2.5.1 The AGL paradigm ................................................................................................. 15

2.5.2 The standard AGL task .......................................................................................... 16

2.5.3 Debate about knowledge learned in the AGL paradigm. .................................... 17

2.5.4 The combined AGL/WM paradigm ....................................................................... 19

2.6 What is the Neural Basis of Training-Related Transfer? ........................................... 21

2.6.1 Prefrontal cortex ..................................................................................................... 22

2.6.2 Neural mechanisms recruited for SSP as measured by the AGL paradigm. ......... 23
2.7 How Can Potential Individual Differences Better Factor into the Training Regimen? .................................................................................................................................................................................. 25

3 CHAPTER 2: CAN WE ENHANCE STRUCTURED SEQUENCE PROCESSING? EXPLORING THE DIRECT AND INDIRECT EFFECTS OF COMPUTERIZED TRAINING USING A MEDIATIONAL MODEL........................................ 29

4 CHAPTER 3: HOW THE BRAIN PROCESSES LINGUISTIC AND NONLINGUISTIC STRUCTURE: THE ANTERIOR SUPERIOR TEMPORAL GYRUS AS A GENERAL-PURPOSE PATTERN PROCESSOR .......................................................... 29

5 CHAPTER 4: INVESTIGATING BEHAVIORAL AND ELECTROPHYSIOLOGICAL CHANGES TO STRUCTURED SEQUENCE PROCESSING AND LANGUAGE FOLLOWING TRAINING ......................................................... 31

6 GENERAL DISCUSSION ........................................................................................................................................................................................................................................ 32

6.1 Summary of Main Findings ...................................................................................................................................................................................................... 32

6.1 Career Relevance and General Relevance of the Findings ................................................................................................................................. 32

6.2 The Findings Under the Microscope of the WM Training Researchers and Critics ........................................................................................................................................................................................................................................ 36

6.3 Next Steps for this Emerging Program of Research ........................................................................................................................................ 38

6.3.1 Clarifications to my broader research goals .................................................................................................................................................... 38

6.4 SSP Training to Enhance SSP and Grammatical Language Processing in Children with ASD .................................................................................................................................................................................................................. 41
6.5 SSP Training to Enhance SSP and Grammatical Language Processing in Children with Cochlear Implants ................................................................. 45

REFERENCES........................................................................................................... 47
LIST OF FIGURES

Figure 1 Artificial Grammar Learning Paradigm (Reber, 1967). Strings of letters, or exemplars, generated by entering the grammar from the leftmost side of the model and moving from node to node until the rightmost side is reached............................................................... 15

Figure 2 Finite state probabilistic artificial grammar used first in Meulemanns & van der Linden (1997) and then in Poletiek & Schijndel (2009). ........................................................................................................ 16

Figure 3 The language network diagram from Friederici, 2011, p.1359.................................................. 25

Figure 4 Conceptual model of adaptive intervention components from Nahum-Shani et al., 2012, p.6.................................................................................................................................................. 27
1 BACKGROUND AND OUTLINE

My primary career research interest is developing cognitive training interventions used with brain imaging to attempt to improve foundational attention and learning mechanisms that support (and could, in turn, improve) language and motor functions. I am especially interested in 1) better understanding these mechanisms and how they interact and 2) developing training techniques for individuals with atypical language and motor development [e.g., Autism Spectrum Disorder (ASD), children with cochlear implants] and with injury to the brain resulting in difficulty with language and motor sequencing (e.g., aphasia). The aim of my doctoral work reflects my primary interests and is intended to help build an emerging career program of research. The focus has been on Structured Sequence Processing (SSP)—a core mechanism used to learn patterns of information from the environment over time—and grammatical language processing. Two research questions that guide my dissertation studies are as follows: 1) Are there similarities between the neurocognitive mechanisms underlying SSP and grammatical language processing and 2) Can we enhance grammatical language processing by way of improving SSP?

Included in the dissertation are a Chapter 1 general introduction framing the above research questions, three chapters reflecting manuscripts, and a Chapter 5 general discussion.

The Chapter 1 general introduction is framed around the scientific question of if the neurocognitive mechanisms recruited for grammatical language processing can be improved by way of improving the neurocognitive mechanisms recruited for SSP. As mentioned, my longer-term interest is in using cognitive training techniques to improve language in clinical populations, including children with ASD, children with cochlear implants and adults with agrammatism. The dissertation general introduction will focus more broadly on the viability of
using computerized cognitive training to enhance SSP and grammatical language processing at
the neurocognitive level, to introduce some initial general considerations toward this endeavor,
with the longer-term goal of developing effective training regimens to improve SSP and
grammatical language processing in the clinical populations mentioned above

Chapter 2 has been published as a manuscript and includes the reference for the
publication. The manuscript is included in the dissertation Appendix. Chapter 3 has been
published as a peer-reviewed conference proceedings paper and submitted as an extended
manuscript to the journal *Cognition*. The chapter includes the references for the conference
proceedings publication, the reference for the extended manuscript, and the full manuscript as
submitted to the journal *Cognition*. The first version of this chapter, published as a peer-reviewed
conference proceedings paper is included in the dissertation Appendix in final format. Chapter 4
has been submitted as a manuscript to the journal *Neuropsychologia*. The chapter includes the
references for the submitted manuscript and the full manuscript as submitted to the journal
*Neuropsychologia*.

The 3 manuscript chapters in the dissertation report findings from three studies reflecting
doctoral work, with me as first author. Study 1 is a computerized cognitive training study
examining if behavioral improvement to SSP mediates the effect of SSP training on language
processing. Study 2 is a within-subject investigation of the electrophysiological responses
elicited during an SSP task and a grammatical language processing task, and the source
localization of each component. Study 3 is a second, separate computerized cognitive training
study in conjunction with electroencephalography/event-related potential (EEG/ERP) recording,
to investigate both the neural and behavioral outcomes following computerized cognitive
training.
The Chapter 5 general discussion will address how the three dissertation studies fit together in a program of research, how the three studies fit into the field of computerized cognitive training interventions for clinical populations, and the future directions for that program of research.
CHAPTER 1: GENERAL INTRODUCTION

2.1 Structured Sequence Processing

When we observe and carry out daily social and communication activities such as eating dinner at a restaurant, walking through a park, or having a conversation, we use structured sequence processing (SSP). Structured sequence processing (SSP), related to the constructs implicit statistical learning and sequential learning, is a general-purpose neurocognitive mechanism used to learn patterns of information in the environment over time. SSP is largely automatic and implicit (Cleeremans, Destrebecqz, & Boyer, 1998), although explicit processing can occur in parallel with implicit SSP (Batterink, Reber, Neville, & Paller, 2015; Sun, Slusarz, & Terry, 2005). SSP involves learning a complex pattern in which each item that occurs next is generated probabilistically based on what item or items occurred previously, versus learning a simpler pattern such as a fixed, repeating sequence or a sequence generated deterministically (Conway & Christiansen, 2001). SSP is hierarchical, where nonadjacent/local dependencies as well as adjacent/long-distance dependencies can occur among elements (Conway, 2012; Lashley, 1951). Crucially, SSP helps us make predictions about which events will occur next in a sequence (Christiansen, Conway, & Onnis, 2012). The ability to predict upcoming events and to detect when events deviate from their most likely succession promotes processing efficiency that is generally beneficial our everyday functioning (Bar, 2007).

2.2 Structured Sequence Processing and Language

Intuitively, SSP appears vital for the development and use of sequential, hierarchical, structure-rich grammatical language processing. Behavioral evidence does suggest that SSP is used to perceive, extract, and encode the structure inherent in word order (Conway et al., 2010), phonology (Saffran, 2003), and morphology and syntax (Ullman, 2004). Furthermore, atypical
SSP has been observed in several language and communication disorders including ASD (Klinger, Klinger, & Pohlig, 2007), dyslexia (Vicari, Marotta, Menghini, Molinari, & Petrosini, 2003), specific language impairment (Tomblin, Mainela-Arnold, & Zhang, 2007), hearing loss (Conway, Pisoni, Anaya, Karpicke, & Henning, 2011), and agrammatic aphasia (Christiansen, Louis Kelly, Shillcock, & Greenfield, 2010). When individual differences in SSP are observed, they tend to be associated with individual differences in language ability (Conway, Karpicke, & Pisoni, 2007; Conway, Pisoni, Anaya, Karpicke, & Henning, 2011; Evans, Saffran, & Robe-Torres, 2009; Grunow, Spaulding, Gómez, & Plante, 2006; Howard, Howard, Japiske, & Eden, 2006; Misyak, Christiansen, & Tomblin, 2010; Plante, Gómez, & Gerken, 2002).

Despite the behavioral evidence showing links between SSP and aspects of grammatical language processing, empirical studies are only beginning to examine the putative underlying process by which SSP shares an association with grammatical language processing. For example in a recent study, implicit statistical learning training was successfully used with typically-developing adults to modulate behavioral preference for using either forward or backward transitional probabilities to process sequences of phonemes, suggesting that experience with underlying structural regularities is a process by which SSP can be modulated (Onnis, Lou-Magnuson, Yun, & Thiessen, 2015). This early behavioral training study shows that implicit statistical learning—a construct closely related to SSP—can be modified with experience through training. This result lends support for the malleable nature of SSP and implicit statistical learning throughout the lifespan, not just early in development. An immediate next step would be to directly test if the neural mechanisms underlying SSP and grammatical language processing can be modified by training, with the longer-term goal of examining if this neural modulation of SSP would result in stronger and longer-lasting improvements to behavioral assessments.
measuring grammatical language processing than have been observed from explicitly-taught, language-specific interventions.

In summary, if the neural mechanisms recruited for foundational SSP support or show similar activation with the neural mechanisms recruited for grammatical language, then it might be beneficial to try to enhance both SSP and grammatical language processing at the neurocognitive level, by targeting their shared neural circuitry. This technique would utilize the potential for brain plasticity (Kleim & Jones, 2008; van Praag, Kempermann, & Gage, 2000) functionally to reorganize shared neural circuitry in a way that information about structure and patterns is processed more efficiently. This type of intervention approach might be particularly effective in cases where both SSP and grammatical language processing show atypicalities or inefficiencies, such as the clinical populations previously mentioned. However, the basis for such an approach has not been specified, leaving unanswered the critical question, “Can we enhance the neurocognitive mechanisms recruited for SSP to enhance both SSP and grammatical language processing?” Subsequently, the rest of the review aims to lay initial groundwork for which experimental controls might maximize the potential to enhance the neural mechanisms recruited for SSP and grammatical language processing. The CogMed WM training approach (CWMT; Stockholm, Sweden) will be used as example for how a computerized training regimen could be used to enhance SSP and grammatical language processing. The focus will address to build an SSP training regimen that moves beyond the prevalent core-training, “kitchen sink” approach to cognitive training interventions, such as CWMT (Morrison & Chein, 2011).

2.3 Cognitive Training Effects

Numerous studies have demonstrated promising results using computerized cognitive training techniques to improve aspects of neurocognition. This type of cognitive training strategy
has roots in Hebb’s (1949) theory of learning based on neural synaptic strengthening. In Hebbian theory, cellular mechanisms of learning include 1) structural changes to neurons, in which synapses can be eliminated or generated and 2) functional changes within existing neuronal structures, in which synapses can be strengthened or weakened. In essence, if two adjacent neurons fire simultaneously, then the connection between them is strengthened. This strengthening of synapses facilitates the formation of a network of interconnected neurons. In terms of the rationale behind cognitive training techniques, if a given regimen can strengthen the network disrupting the cognitive domain of interest, then that domain might show enhancement (with stronger and more lasting effects usually occurring over time through experience).

2.3.1 WM training studies.

One cognitive domain that has been prevalent in the training literature is WM. WM refers to the capacity-limited, “temporary storage and manipulation of information necessary for complex cognitive tasks” (Baddeley, 1992, p. 556). The general goal of the early WM training studies was to investigate if WM training could improve WM capacity, show “near” transfer to non-trained WM tasks, and “far” transfer to tasks measuring other cognitive domains that rely on WM (e.g., Verhaeghen, Cerella, & Basak, 2004; Westerberg et al., 2007). In one of the seminal studies out of the CWMT research group, Klingberg and colleagues (2002; 2005) designed a computerized WM training task that was first used with children with ADHD (Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005). Participants performed visuospatial and/or verbal WM tasks over a period of 5 weeks (for details see Klingberg et al., 2005). Difficulty level of the tasks was adjusted to match each subject’s WM ability by frequently modifying the number of elements that had to be recalled. It was hypothesized that the adjustment of difficulty level to continually match performance was a critical manipulation that
would lead to improvement in WM capacity over time, keeping the subject engaged at a level that was not so easy it was boring and not so difficult it was too frustrating. A control group performed the same tasks but the length of items to recall remained fixed rather than adaptively increasing and decreasing. At post-training sessions both 5-to-6 weeks and 3 months following the baseline measures, participants showed significant improvement in non-trained WM ability compared to the control group, as measured by the visuospatial Span Board task. Additionally, participants showed improvement on non-trained executive functioning tasks including the Stroop task, and Raven’s Matrices.

The results from the CWMT studies suggest that WM is not a fixed ability, but can be improved through adaptive training. One overall implication from the CWMT studies is that training on an adaptive WM task seems to generalize to non-trained tasks of WM and may also generalize to other cognitive functions. For example, evidence from studies using versions of CWMT suggest that enhancement of visuospatial WM improves verbal WM (Holmes et al. 2009; Thorell et al. 2009), inhibition (Klingberg et al. 2002; Klingberg et al. 2005; Olesen, Westerberg, & Klingberg, 2004), and attention (Westerberg et al. 2007).

Recently the effectiveness of WM training has been under dispute, with critique from meta-analyses of the WM training literature pointing mainly to methodological issues such as the validity of how WM was being measured (e.g., with simple span tasks) and the omission of “active” or “contact” control groups that experience the same level of task difficulty and feedback and the experimental group, along with questions about the reliability and validity of some of the far transfer findings (e.g., Harrison, Shipstead, Hambrick, Hicks, Redick, & Engle, 2013; Klingberg, 2010; Melby-Lervåg & Hulme, 2013; Morrison & Chein, 2011; Redick et al., 2013; Shipstead, Hicks, & Engle, 2012; Shipstead, Redick, & Engle, 2010; 2012). Still, a portion of the
WM training results raise the possibility that WM and other aspects of cognition are modifiable by training.

2.4 Moving Beyond the Kitchen Sink Approach To More Targeted Computerized Training

Numerous meta-analyses of the WM training literature have been informative about the relative strengths and areas of improvement for WM training regimens, (e.g., Au, Sheehan, Tsai, Duncan, Buschkuehl, & Jaeggi, 2014; Diamond & Lee, 2011; Harrison, Shipstead, Hambrick, Hicks, Redick, & Engle, 2013; Karbach & Verhaeghen, 2014; Klingberg, 2010; Melby-Lervåg & Hulme, 2013; McLaughlin, 2016; Morrison & Chein, 2011; Shipstead, Hicks, & Engle, 2012; Shipstead, Redick, & Engle, 2010; 2012; Soveri, Antfolk, Karlsson, Salo, & Laine, 2017). One broad lesson from the WM “core training” studies such as CWMT that have taken a “kitchen sink approach” to intervention (Morrison & Chein, 2011), is that attempting to enhance a cognitive construct by taxing it in the most intensive way possible (e.g., with a barrage of different tasks, using different types of stimuli, over a range of several weeks) might be an imprecise approach to treatment. Although initially something about the intensive CWMT programs seemed to work, the exact aspect of the regimen driving the training-related gains was not distinguishable. One contribution of the ever-growing body of meta-analyses examining the methodology and effectiveness of WM training is that this body of work can help identify specific guidelines for what types of experimental controls lead to meaningful training-related gains.

Thus, criticism centered on portions of CWMT methodology can be utilized a priori to better streamline a neural-mechanistic approach toward designing computerized cognitive training paradigms aimed to enhance SSP and grammatical language processing. Three of the
major areas of concern from the WM training meta-analyses (and from direct reports from numerous CWMT studies themselves) are as follows. First, the tasks used to demonstrate near-transfer of WM training to non-trained WM do not measure the construct WM (e.g., Melby-Lervåg & Hulme, 2013; Morrison & Chein, 2011; Shipstead, Redick, & Engle, 2010; 2012). Second, the putative far-transfer effects to other, non-WM domains have not been reliably empirically supported (e.g., Egeland, Aarlien, & Saunes, 2013; Karbach & Verhaeghen, 2014; Liu, Lishak, Tannock, & Woltering, 2017; Melby-Lervåg & Hulme, 2013; Morrison & Chein, 2011; Sala & Gobet, 2017; Schwaighofer, Fischer, & Bühner, 2015). Third, individual differences in baseline WM capacity, motivation, dosage requirements, and other dynamics intrinsic to the subject could impact the efficacy of WM training, yet typically not even one of these types of variables are factored into the training regimens (e.g., Foster, Harrison, Hicks, Draheim, Redick, & Engle, 2017; Jaeggi, Buschkuehl, Shah, & Jonides, 2014; Söderqvist, Matsson, Peyrard-Janvid, Kere, & Klingberg, 2013).

All three of these main criticisms of the CWMT studies could be viewed as hindrances to near and far transfer effects, which are two of the main objectives of computerized cognitive training. In addition, addressing these three areas of improvement takes some degree of critical thought, versus the “failing to use an active control group” criticism that can be more readily solved simply by including an active control group in the paradigm. Therefore, the above three potential constraints will be addressed in terms their relevance to prospective training approaches aimed to enhance SSP and grammatical language processing.
2.5 Do Non-Trained Tasks of SSP Measure SSP?

The most prevalent paradigm used to measure SSP is the Artificial Grammar Learning (AGL; Reber, 1967) paradigm. More recently, the AGL paradigm has been combined with adaptations of WM paradigms to measure SSP.

2.5.1 The AGL paradigm.

Variations of the AGL paradigm have been used extensively to operationalize SSP. In the AGL paradigm, strings (or sequences) of stimuli (e.g., letters, shapes, tones) are generated by a finite state Markovian grammar. In this type of grammar, a network with paths and nodes transitions from one node to the next to produce full strings of elements, or exemplars (See Figure 1 below). For example, one transition through the nodes of Figure 1 generates the grammatical exemplar VXRRM.

![Figure 1 Artificial Grammar Learning Paradigm (Reber, 1967). Strings of letters, or exemplars, generated by entering the grammar from the leftmost side of the model and moving from node to node until the rightmost side is reached.](image)

To incorporate the probabilistic nature of a finite state grammar associated with SSP, transition probabilities are quantified for the paths moving from node to node (see Figure 2 below for an example taken from previous studies Meulemanns & van der Linden, 1997; Poletiek & Schijndel, 2009). For any given grammar, the transition probabilities can be varied to
make grammatical structures suitable to the aims of the experiment, including grammars incorporating long-distance dependencies between elements (e.g., Misyak, Christiansen, & Tomblin, 2010). The probability of the complete exemplar equals the product of its transition probabilities (Poletiek, 2006; Poletiek & Chater, 2006), and the summed probabilities of all possible exemplars generated by the grammar equals 1 (Poletiek & Schijndel, 2009).

![Finite state probabilistic artificial grammar](image)

*Figure 2 Finite state probabilistic artificial grammar used first in Meulemanns & van der Linden (1997) and then in Poletiek & Schijndel (2009).*

### 2.5.2 The standard AGL task.

The standard AGL task (Reber, 1967) consists of a learning phase and a test phase. In the learning phase, participants are exposed to exemplars of stimuli that covertly conform to the rules of the artificial grammar and are asked to memorize them. In the test phase, they are then informed that the previous exemplars followed rules of an artificial grammar and are asked to classify new exemplars as either “grammatical” if they follow the rules or “ungrammatical” if they do not follow the rules. The widely replicated finding is that participants perform better than chance at classifying grammatical and ungrammatical exemplars, despite being unable to explicitly describe the rules of the grammar (Pothos, 2007; Reber, 1993).
2.5.3 Debate about knowledge learned in the AGL paradigm.

Investigators generally agree that participants learn some type of information about the grammatical exemplars in the AGL paradigm that gets transferred to correct classification of grammatical and ungrammatical exemplars at test. However, a great deal of debate centers on precisely what the learned information entails. A critical question relevant to the use of the AGL task in an SSP training study is, does the AGL task measure SSP?

The classic disagreement concerning the AGL paradigm is if new exemplars are consistently correctly classified because the underlying abstract rules of the artificial grammar have been learned or because similarities between certain surface features of the learning exemplars and test exemplars have been perceived.

2.5.3.1 Abstractionist view.

Based on findings from his seminal AGL studies, Reber (1967; 1969; 1989; Reber & Lewis 1977) maintained that participants learn the abstract rules that are whole or partial representations of the artificial grammar, which has been referred to as knowledge of the “deep structure” of the grammar (Whittlesea & Dorken, 1993). Much of the empirical support for Reber’s abstractionist stance has come from “transfer experiments” in which the learning and test exemplars contain different surface features yet maintain the same underlying abstract rules (Redington & Chater, 1996).

2.5.3.2 Similarity view.

One similarity account is that participants store whole exemplars and compare those exemplars directly to new test items (Brooks, 1978; Brooks & Vokey, 1991; Vokey & Brooks, 1992). Other more popular similarity accounts state that learning exemplars are processed as smaller portions of the whole, either as successive fragments (e.g., bigrams and trigrams) that are
familiar in the test exemplars (Perruchet & Pacteau, 1990) or are processed as “chunks” that compete for so-called associative “chunk strength” with the grammatical category (Knowlton & Squire, 1994, p.79; Servan-Schreiber & Anderson, 1990, p. 607).

2.5.3.3 **Reconciling the abstractionist and similarity views.**

Some investigations attempt to reconcile the contribution of grammaticality versus similarity to responses on the AGL paradigm. Generally, findings from these studies suggest that training with a large set of exemplars improves grammaticality judgments of test items, whereas training with a small set of exemplars promotes the learning of fragments/chunks or the memory for whole exemplars (McAndrews & Moscovitch, 1985; Meulemans & Van der Linden, 1997; Vokey & Brooks, 1992).

2.5.3.4 **Does the AGL paradigm measure SSP?**

Although the aforementioned debate does help clarify the type of knowledge learned in the AGL paradigm, it does not completely capture if the AGL paradigm measures knowledge and use of the *statistical regularities of a probabilistically generated pattern*, which is a characterizing component of SSP (for a similar view see Conway et al., 2010 discussion of the Botvinick & Plaut, 2006 neural network model of short-term memory for serial order). Using a novel analytic approach, Politiek and van Schijndel (2009) calculated the “statistical coverage” (SC) of the exemplars in their finite-state artificial grammar, defined as how much a sample of exemplars statistically comprises the underlying structure. SC was mathematically operationalized as the summed probabilities of the sample’s exemplars, which would vary not only as a function of each exemplar’s length, but also of the values quantified for its transition probabilities. With exemplar length balanced across grammatical and ungrammatical conditions, the results indicated that performance on the AGL classification task was modulated solely by
the amount of SC in the input, rather than by set size (Politiek & van Schijndel, 2009). These findings provide empirical evidence that the performance AGL paradigm does rely heavily on sensitivity to the transitional probabilities between elements of the grammar (i.e., SSP), giving credence to its construct validity as a measure of SSP.

2.5.4 The combined AGL/WM paradigm.

Some contemporary studies combine the AGL and WM paradigms to measure SSP, by embedding an artificial grammar into a WM span task (e.g., Conway, Bauernschmidt, Huang, & Pisoni, 2010; Conway, Karpicke, Pisoni, 2007; Karpicke & Pisoni, 2004). One of the original combined AGL/WM paradigms (Karpicke & Pisoni, 2004) was developed to assess individual differences in implicit learning, based on the premise that the grammaticality classification task in AGL may not adequately assess variability in this ability among individuals. The paradigm was modeled after an earlier study by Miller (1958), in which participants were first asked to learn lists of letter strings and then to recall them. One list included randomly generated letter strings, and a second list include letter strings generated by an artificial grammar. Miller’s findings suggested that participants learned the list of grammatical letter strings faster than the list of random letter strings. Then Karpicke and Pisoni (2004) combined AGL/WM paradigm consisted of a learning phase and a test phase. In the learning phase, participants were presented with sequences of stimuli covertly generated by an artificial grammar and were asked to immediately reproduce the sequence in the correct order using a response box. During the test phase, half of the sequences presented were new sequences generated by the artificial grammar used in the learning phase, and the other half of the sequences were new sequences generated by a different artificial grammar to which participants had not been previously exposed. The results showed that immediate memory span for sequences generated by the artificial grammar to which
participants had been previously exposed was significantly higher than immediate memory span for sequences generated by a different grammar to which the participants had not been previously exposed. Furthermore, individual performance during the learning phase of the AGL/WM task was significantly positively correlated with individual performance during the test phase of the task.

The combined AGL/WM task initially designed by Karpicke and Pisoni (2004) has been modified to utilize more complex patterns associated with SSP. In this version, a probabilistic finite state artificial grammar was embedded into sequences consisting of colored or non-colored squares (e.g., Conway et al., 2007; 2010). The primary aim of the study was to examine if variability in SSP was associated with language ability. Similar with the robust findings from standard AGL studies, the Conway et al. (2007; 2010) results indicated that participants generally performed better on grammatical sequences versus ungrammatical sequences, suggesting learning occurred. In addition, scores on the measures of SSP were correlated with scores on the measures of language.

An advantage of the combined AGL/WM task used in the Conway et al. (2007; 2010) studies is that the non-colored stimuli, at least, are not language-like, as are stimuli used in many other AGL-based tasks measuring SSP. Thus, this approach may be a purer way of measuring fundamental, general-purpose SSP than using stimuli that are readily verbalizable or easily mapped onto vocalizations (i.e., that might tap the phonological loop of WM, Baddeley & Hitch, 1974). The characteristic of being non-linguistic helps make the AGL/WM task particularly suitable for a training study investigating if improvement to SSP will transfer in a domain-general manner to a non-trained measure of grammatical language processing.
In conclusion, both the standard AGL task and the combined AGL/WM task seem to measure SSP and, critically, can be adapted to tap knowledge and use of statistical regularities of a sequence by quantifying the transitional probabilities from one sequence element to the next. Additionally, the combined AGL/WM task may be a purer measure of SSP, as it is more fundamentally non-linguistic.

2.6 What is the Neural Basis of Training-Related Transfer?

One prominent hypothesis from the WM training literature is that far-transfer should occur only when the trained and transfer tasks recruit overlapping neural regions (Jonides, 2004; Morrison & Chein, 2011; Olesen, Westerberg, & Klingberg, 2004). However, few WM studies have empirically investigated the neural mechanisms of far-transfer from the trained WM tasks to untrained measures of WM or other non-trained aspects of cognition, such as executive control or fluid intelligence. Numerous researchers have examined the neural changes resulting from WM training itself and have suggested that the dorsolateral prefrontal cortex (DLPFC), along with parietal regions, are associated with training-related enhancements to WM (Brehmer et al., 2009; Curtis & D’Esposito, 2003; Dahlin, Backman, Neely, & Nyberg, 2009; Hempel et al., 2004; McNab et al., 2009; Morrison & Chein, 2011; Olesen et al., 2004; Takeuchi et al., 2010; Westerberg & Klingberg, 2007). The relatively small number findings from studies investigating the effects of far-transfer from WM training to improvements in executive control (as measured by the Stroop task) showed that training-related gains to non-trained WM tasks and to the Stroop task were associated with increased activation in DLPFC (Jonides, 2004; Olesen et al., 2004).
2.6.1 Prefrontal cortex.

Taken together, evidence from the WM training studies suggest that increases in prefrontal and parietal cortical activity during or following WM training is an indicator of training-related plasticity of the neural mechanisms recruited for WM and executive functions (Brehmer et al., 2009; Curtis & D’Esposito, 2003; Dahlin et al., 2009; Hempel et al., 2004; Jonides, 2004; Klingberg, 2010; McNab et al., 2009; Olesen et al., 2004; Takeuchi et al., 2010; Westerberg & Klingberg, 2007). Studies involving control of attention have shown activation in the PFC similar with that in visuospatial WM tasks (Hopfinger, Buonocore, & Mangun, 2000; Kastner, Pinsk, De Weerd, Desimone, & Ungerleider, 1999). In these types of attention tasks, the subject searches for a particular target or is cued to the location of a future target or. Klingberg et al. (2002) pointed out that the subject may need to keep a representation of the target or its location in WM, in a similar way that information is kept online in WM tasks. Therefore, tasks aimed at measuring control of attention could be measuring, at least in part, WM. However, Engle (2002) argued that although greater WM capacity does mean that more items can be maintained as active, this result is due to greater ability to control attention, not to a larger memory store. At the very least, there appears to be some degree of overlap in the underlying neural mechanisms recruited for control of attention and WM.

One possibility as to why the “recruit overlapping neural regions” premise of the CWMT studies (Jonides, 2004; Morrison & Chein, 2011; Olesen, Westerberg, & Klingberg, 2004) has not yet translated into reliable, empirical far-transfer gains may be the non-specificity of the neural recruitment the types of tasks used in CWMT studies elicit. The PFC (and the sub-region DLPFC) as part of a frontal/parietal network is associated with many facets of cognition, including subcomponents of attention, memory, cognitive control, intelligence, and language...
(Kobayashi, 2009; Siddiqui, Chatterjee, Kumar, Siddiqui, & Goyal, 2008). Going back to the “kitchen sink approach” (Morrison & Chein, 2011), the fact that WM plays a role in such a wide range of higher-order and executive functions was precisely the rationale for why CWMT researchers thought boosting WM capacity would transfer to so many other abilities. Instead of trying to investigate shared neural regions as a way to bring about far-transfer effects from one cognitive domain to another, it may be of utility to investigate shared neural circuitry. In other words, it may be of value to take a mechanistic approach toward clarifying training-related gains and consider the process by which the entire network is active for each type of task (e.g., where do the regions project, how do the regions interact as a circuit). Therefore, the shared neural circuitry between SSP and grammatical language processing that are most likely involved in any training-related gains will be outlined.

2.6.2 Neural mechanisms recruited for SSP as measured by the AGL paradigm.

Broca’s area [Brodmann’s area (BA) 44/45] has long been thought to play a critical role in human syntactic natural language processing as part of the so-called “language network” (Friederici, 2004; 2011), and has been suggested to be particularly involved in processing dependency relationships in syntactic structure (Grodzinsky & Friederici, 2006). Evidence from behavioral lesion studies and from imaging studies using the AGL paradigm suggest that activity in Broca’s area, which has largely been associated with language-specific abilities, may be associated with performance on general-purpose SSP tasks (e.g., Forkstam, Hagoort, & Fernández, 2006; Petersson, Folia, & Hagoort, 2012). Furthermore, in an investigation of a putative causal relation between activity in Broca’s area and SSP, Uddén et al. (2008) found that offline repetitive transcranial magnetic stimulation (rTMS) to left BA 44/45 enhanced grammaticality classification in an AGL-based SSP task. According to Ullman (2001; 2008), the
neurocognitive mechanisms supporting the acquisition of a range of sequentially or hierarchically organized rule-based cognitive and motor skills involve basal ganglia thalamocortical circuitry projecting to and looping back from posterior/dorsal regions of frontal cortex in Broca’s area corresponding to BA 44/45. Collectively, there is a growing body of empirical support indicating Broca’s area may be associated with global rule-based SSP, rather than with learning that is specialized for language.

2.6.2.1 **The neural circuitry including Broca’s area.**

The above evidence suggesting activity in Broca’s area may be involved with general-purpose SSP as well as natural syntactic language operations of the language network (Friederici, 2011). Given this, it might seem a straightforward presumption that SSP training would lead to successful transfer to non-trained tasks of SSP and grammatical language processing because of Hebbian learning represented by shared neural activity in Broca’s region, similar with PFC involvement observed in WM training studies. However, Broca’s involvement in any training-related transfer to non-trained SSP and grammatical language processing might not be so simply explained. In terms of the language network (see Figure 3 below for the language network as illustrated in Friederici, 2011, p. 1359), Broca’s area encompassing BA 44/45 and the deep frontal operculum (FOP) connects with the superior temporal gyrus (STG) via the ventral pathway (Anwander, Tittgemeyer, von Cramon, Friederici, & Knösche, 2007; Friederici, 2011; 2012).
Findings from recent imaging studies suggest computation of sequences with adjacent dependencies activate FOP and anterior STG, whereas computation of sequences with non-adjacent dependencies activate FOP and Broca’s area (Friederici, Bahlmann, Heim, Schubotz & Anwander, 2006; Grodzinsky & Friederici 2006). The anterior STG is recruited for early processing of adjacent syntactic dependencies (Friederici, Wang, Herrmann, Maess, & Oertel, 2000), and Broca’s area is only additionally recruited when non-adjacent dependencies need to be processed, possibly modulated by the additional load on WM (Friederici et al., 2006). Therefore, to maximize transfer effects to SSP and grammatical language processing, which are both hierarchically structured, the SSP training task arguably would need to elicit neural overlap in the network encompassing Broca’s area, as well as FOP and anterior STG.

2.7 How Can Potential Individual Differences Better Factor into the Training Regimen?

In general, the one-regimen-fits-all, “kitchen sink” approach of the CWMT regimens did not take into account individual differences in variables such as baseline WM capacity, dosage requirements, and motivation at the outset of or in response to treatment. Adaptive interventions have the potential to help better customize computerized training regimens to the individual (e.g., Nahum-Shani et al., 2016). Adaptive interventions are designed under the view that treatments
should be individualized and adjusted over time to individual outcomes in order to be most effective (Lei, Nahum-Shani, Lynch, Oslin, & Murphy, 2012). Apart from correlational evidence that individual differences in SSP are associated with atypical development and language disorders (e.g., Arciuli & Simpson, 2012; Christiansen, Kelly, Shillcock, & Greenfield, 2010; Conway et al., 2010; Conway, Evans, Saffran, & Robe-Torres, 2009; Grunow, Spaulding, Gómez, & Plante, 2006; Hsu, Tomblin, & Christiansen, 2009; Karpicke, & Pisoni, 2007; Kidd, 2012; Misyak, Christiansen & Tomblin, 2010, 2014; Plante, Gómez, & Gerken, 2002; Spencer, Kaschak, Jones, & Lonigan, 2014), little is known about individual differences in SSP ability. Still, even when individual differences are under-specified prior to treatment, a version of the adaptive intervention design could be used to develop individualized SSP training interventions that factor in intervention parameters (Nahum-Shani et al., 2012), like dosage requirement, task difficulty/type, and motivation as the training regimen progresses, which can greatly impact treatment outcomes. The adaptive feature simply utilizes ongoing information about the participant’s progress, which can be viewed as a “tailoring variable” (Nahum-Shani et al., 2012, p.6) to adapt the intervention options in a way that maximizes gains for that individual (Collins, Murphy, & Bierman, 2004; for full details on the scientific motivation for and design components of adaptive interventions, see examples Murphy, 2005; Nahum-Shani et al., 2012; for a conceptualization of the adaptive intervention design, see Figure 4 below from Nahum-Shani et al., 2012, p.6).
Using a recent SSP training study in an approximate example of how an adaptive intervention design could be used to help individualize the SSP training regimen, consider “type of task” as one of the intervention options. Smith and Conway (under review) used a visual-spatial computerized SSP training regimen with ERP recording to enhance SSP and grammatical language processing in typically-developing adults. The findings indicated training-related improvements to non-trained computerized measures of SSP and grammatical language processing. The SSP training regimen is currently being modified for use with children with ASD. One suggestion to our group from a session at the International Meeting for Autism Research (IMFAR) 2014 conference in Atlanta was to bolster the visually-presented SSP stimuli by adding a different corresponding auditory tone onto to each individual visual stimulus. To keep it simple, assume the intervention options related to task type have already been theoretically motivated and include 1) a visual-spatial task or 2) a visual-spatial task with auditory tones. Again, the CWMT approach would administer to all participants several different types of SSP stimuli, presented in all the different combinations of modality types. However, given the hypothetical intervention choice between a visual-spatial task or a visual-spatial task
with tones, an adaptive intervention could be developed similar with the one used in Kasari et al. (2014) to enhance social communication outcomes in minimally-verbal children with ASD. For example, one training regimen could begin with visual-spatial SSP training and intensified visual-spatial training for nonresponders. A second training regimen could begin with visual-spatial SSP training and visual-spatial SSP training bolstered with auditory tones for nonresponders. A third training intervention could begin with visual-spatial SSP training bolstered with auditory tones and intensified visual-spatial SSP training with auditory tones for nonresponders. Like Kasari et al. (2014), the effect of each adaptive intervention during Phase 1 could be assessed at pre-determined time points and success rate determined by % improvement in accuracy, reaction time, or standardized assessments. Nonresponders would then be moved up in training dosage to the intensified level, and the study would move forward to Phase 2, and so forth. This hypothetical example above is just one way the adaptive intervention design could be incorporated into a computerized SSP training study to start to develop more effective, more individualized, and more evaluable treatments with gains lasting for longer periods of time.

In conclusion, training approaches that target the neurocognitive mechanisms recruited for SSP and grammatical language processing could be a promising way to use the brain’s potential for plasticity (Kleim & Jones, 2008; van Praag, Kempermann, & Gage, 2000). Meta-analysis-based critique of CWMT studies can be used as an a priori guideline for developing effective training regimens to enhance SSP and grammatical language processing, by focusing on the three main areas of concern discussed above.
3 CHAPTER 2: CAN WE ENHANCE STRUCTURED SEQUENCE PROCESSING?
EXPLORING THE DIRECT AND INDIRECT EFFECTS OF COMPUTERIZED
TRAINING USING A MEDIATIONAL MODEL

This chapter has been published as the following manuscript, which is included in the Appendix:


4 CHAPTER 3: HOW THE BRAIN PROCESSES LINGUISTIC AND NONLINGUISTIC STRUCTURE: THE ANTERIOR SUPERIOR TEMPORAL GYRUS AS A GENERAL-PURPOSE PATTERN PROCESSOR

This chapter was first published as peer-reviewed conference proceedings paper, which is included in the Appendix:

Then, the peer-reviewed conference proceeding publication was extended into the following manuscript submitted to the journal *Cognition*. This manuscript is included in the Appendix.

5 CHAPTER 4: INVESTIGATING BEHAVIORAL AND ELECTROPHYSIOLOGICAL CHANGES TO STRUCTURED SEQUENCE PROCESSING AND LANGUAGE FOLLOWING TRAINING

The following included manuscript will be submitted for publication to Neuropsychologia. The manuscript is included in the Appendix

6 GENERAL DISCUSSION

1.1 Summary of Main Findings

The studies described in this proposal compose my developing program of research and are intended to contribute to my career goal of developing cognitive training interventions used with brain imaging to improve foundational attention and learning mechanisms that support (and could, in turn, improve) language and motor functions. My primary interests moving toward my long-term goals are 1) better understanding these attention, learning, and language mechanisms and how they interact and 2) developing effective training techniques for individuals with atypical language and motor development (e.g., children with ASD, children with cochlear implants] and with acquired difficulty with language and motor sequencing (e.g., adults with aphasia). It is these motivations that drive the direction of my research. To summarize the findings across the 3 dissertation studies, 1) the results from the mediation analysis included in Chapter 1 demonstrate that computerized SSP training has an underlying impact on predictive language processing by way of its effect on SSP, 2) the results from the source localization analysis included in Chapter 2 suggest the neurocognitive mechanisms recruited for a non-linguistic SSP task and for grammatical language processing task share marked similarities, and 3) the results of a computerized training study with ERP included in Chapter 3 establish the viability of improving SSP as a way to improve grammatical language processing, possibly mediated by changes to attention and WM.

6.1 Career Relevance and General Relevance of the Findings

It is constructive to give context to these three initial studies that have been done thus far. The crux of this dissertation is the same, in terms of the way the studies fit with my career research goals and also within broader scope of using cognitive-based training effectively with
individuals with atypical language processing share. As a whole, the 3 studies demonstrate the feasibility of enhancing the neurocognitive mechanisms recruited for SSP as a way to enhance grammatical language processing. The feasibility of this approach has been supported through a succession of information gleaned across 3 studies. This succession will be summarized in chronological order as presented in the dissertation chapters.

First, SSP can be modulated though training and then causally impact modulation of predictive, structure-based language process. Although the relation among SSP training, modulation of SSP, and modulation of predictive language processing is complex, these variables do appear to interact with one another in a causal way. Our first training study suggested some direct early interference effects from training with visual-spatial, adaptive, structured, sequences to performance on using structure to predict elements in a spoken sentence that dampened the mediating effect of enhancement of SSP to enhancement of predictive language processing. However, this adverse effect can be ameliorated with experimental controls, including manipulations as straightforward as increasing the duration of training (i.e., ultimately adding more trials/more experience). The main point being, now that we have evidence there is an underlying association between enhancement of SSP and enhancement of predictive, structured language processing, we can start making testable predictions about what experimental parameters will lead to stronger training gains.

Second, the neurocognitive mechanisms recruited for SSP and grammatical language processing share overlap not just in a brain region, but in a specific network involving connections and projections that have been specified and can be used as a map for where to target synaptic plasticity in order maximize processing efficiency of the entire circuit. For example, enhancing processing of only Broca’s area would not seem optimal, as Broca’s area
may be more involved with later stage processing of the network. Remember, the anterior STG seems to be recruited for early processing of adjacent syntactic dependencies (Friederici et al., 2000), and Broca’s area is only additionally recruited when non-adjacent dependencies need to be processed (Friederici et al., 2006). Therefore, processing in Broca’s could be optimized, but if processing in anterior STG is left diminished then the net result could still be negligible gain to the network that supports both SSP and grammatical language processing. In fact, if training were to target one region more central to the SSP and language network, it might be anterior STG rather than Broca’s area. Keep in mind that SSP and grammatical language processing are hierarchically-structured, and processing associated with anterior STG likely operates at a level precursor to that of processing associated with Broca’s area. My dissertation research adds some support to this notion, with findings from the source localization analysis suggesting that anterior STG, as part of what traditionally has been considered the language network, connects with Broca’s area encompassing BA 44/45 and the deep frontal operculum (Anwander et al., 2007; Friederici, 2011; 2012) and may modulate SSP and language processing in a more network-based, domain-general manner. Therefore, now that we have evidence of a neural network that is recruited for both SSP and grammatical language processing, we can start making testable predictions about where in this network could be the optimal place to target synaptic strengthening following computerized training.

Third, it is possible to enhance the neurocognitive mechanisms recruited for SSP, and observe transfer of those gains to the neurocognitive mechanisms recruited for grammatical language processing. It is worth mention that in terms of enrollment, this study completed with no attrition. Thus, we were also able to demonstrate that it is possible to recruit, retain, and bring into the lab healthy participants for 14 separate training-related sessions. This outcome shows
promise for similar feasibility for enrollment and retention for individuals with atypical SSP and language processing. Overall, now that we have evidence that participants can complete the training regimen and that the regimen does seem to enhance SSP and grammatical language processing in healthy adults, we can start making testable predictions for how to modify the training regimen for use with individuals with atypical language processing, including children with ASD, children with cochlear implants, and adults with agrammatic aphasia.

In summary, my dissertation studies have been a succession of steps toward two shorter-term goals that directly relate to my primary research interests. 1) Using a neural mechanistic approach, I am beginning to better understand the process by which SSP interacts with grammatical language processing at the level of the network. Discovering this process is an ongoing endeavor that can be directly applied toward designing more effective training paradigms. 2) Using an SSP training study with ERP, I have shown that it is possible to enhance grammatical language processing by way of enhancing SSP. This finding is a promising start for my longer-term goals of developing effective training regimens for individuals with atypical language processing, and fulfilled one of my main goals for my dissertation work.

Both of these outcomes, both related to a demonstration of feasibility, do need to be put into perspective. My dissertation studies were all conducted with typically-developing adults, all enrolled at a university at time of testing. Yes, this sample was partially chosen for convenience. It was also chosen because these three initial studies were more of a testing phase to see if this type of training work targeting the neurocognitive mechanisms recruited for SSP and grammatical language processing even had viability, which now seems to be the case. This type of exploratory research is not, at least at first, an ideal way to utilize clinical samples from special populations that are known to be difficult to recruit and retain over longer periods of time
(e.g., children with ASD, children with cochlear implants, adults with agrammatic aphasia). Now that my overall approach to training intervention seems viable, I am more comfortable taking the next steps, which are first demonstrating the feasibility of using this type of training regimen with the previously mentioned clinical samples of individuals with atypical language processing.

### 6.2 The Findings Under the Microscope of the WM Training Researchers and Critics

Although the SSP training paradigm used in two of the dissertation studies was inspired by the CWMT adaptive sequence reproduction task, I spent a large portion of the introduction chapter not only pointing out some of the heavy criticism of the CWMT studies, but also agreeing with the criticism and suggesting a better strategy for SSP training that would move beyond the CWMT kitchen-sink approach. First, I made an argument that the non-trained measure of SSP used in my dissertation does measure the construct SSP. Second, I proposed that far-transfer effects were more likely to result from our SSP paradigm than CWMT paradigms because the neural mechanisms recruited for both SSP and grammatical language processing shared specific circuitry encompassing the language network, rather than one under-specified region such as PFC.

My guess is that the CWMT researchers would not take issue with my approach. SSP is not the same construct as WM, and my reasons for modifying the SSP tasks and for predicting they overlap greatly in a specific network were supported in literature. I also think the CWMT researchers and critics would understand that my dissertation studies demonstrate feasibility of my approach and would have the perspective this is the start of an iterative program of research. Having said that, I do think both the CWMT researchers and the CWMT critics would, at this point, be skeptical that the findings from my dissertation studies are any more encouraging than the CWMT studies. One of the less disputed findings from the CWMT studies is that
improvement to WM can lead to near-transfer to non-trained tasks of WM for at least one session occurring in the relative short-term. Looking at the training-related SSP findings from the behavioral mediation analysis in Chapter 1 and from the behavioral results in Chapter 3, my findings suggest that improvement to SSP can lead to near-transfer to non-trained tasks of SSP for at least one session occurring in the relative short-term. The SSP ERP findings from the Chapter 3 training study were more modest than I had hoped and do not unequivocally support or refute the SSP behavioral findings. Therefore, my SSP near-transfer findings seem roughly equivalent to the CWMT near-transfer findings.

Most of the doubt has centered on the CWMT far-transfer findings, not the near-transfer findings. Many of the CWMT critics have concluded that, as of yet, there is not enough evidence supporting the claim that improvement to WM can show far-transfer to other cognitive domains other than WM. At best, the CWMT far-transfer findings seem mixed and suggest transfer from one domain to another is a difficult goal to attain. The SSP findings from the mediation analysis in Chapter 1 suggested a complex relation between SSP and grammatical language processing involving competitive mediation and far-transfer that was also mixed. Furthermore, the ceiling-level behavioral performance on the Chapter 3 measure of grammatical language processing was the equivalent of no behavioral demonstration of far-transfer. The ERP results elicited by the measure of grammatical language processing were more remarkable in terms of showing neural evidence indicative of far-transfer, but without supporting behavioral evidence I am in a position similar with the CWMT researchers. Essentially, I have made a case that I am still striving toward a more convincing demonstration of far-transfer and have not decidedly shown that I cannot achieve that research aim.
I do think the CWMT critics such as Shipstead, Redick, Engle would appreciate that I am trying to take their suggestions and tighten some of the experimental controls in my SSP training paradigm, and at least strive to use their critique to make my regimens more and more effective. I also think they might give me some credit for trying to not generally over-state my training findings toward grander claims of efficacy when I only believe I have made a case for feasibility. However, I would expect that these very CWMT critics would want me to clarify the contributions of constructs such as attention and WM to what I am describing as SSP training related gains and would certainly have examples from their research group how to use confirmatory factor analysis (e.g., Shipstead, Redick, Hicks, & Engle, 2012; Shipstead Yonehiro, 2016) to help achieve this goal.

One important difference between my SSP training studies conducted thus far and CWMT studies is that I have not yet attempted to use a version of my regimen with a clinical population showing atypicalities to SSP and grammatical language processing; whereas, versions of the CWMT paradigm have been widely used with numerous clinical populations. Given that CWMT researchers have repeatedly unconvincingly suggested far-transfer to clinical populations—their main focus—there is a great deal more empirical evidence that the current CWMT approach may be ultimately ineffective. Until I have had a chance to use my approach to SSP training with children with autism, children with cochlear implants, and adults with agrammatism, I will not concede to the same fate.

6.3 Next Steps for this Emerging Program of Research

6.3.1 Clarifications to my broader research goals.

My focus is using a neural mechanistic approach to better understand and try to improve disrupted circuitry recruited for SSP and grammatical language processing. During my doctoral
work at various conferences and presentations, I have been asked on more than one occasion if I had considered using this type of training approach to try to enhance SSP and grammatical language processing for everyone, not just certain clinical populations I have identified. The answer to that question is no. My primary research interest is not to try to enhance the neurocognitive mechanisms recruited for SSP and grammatical language processing in individuals who are already showing functional-to-ceiling level behavior in those domains.

Ultimately, my approach to enhance the neurocognitive mechanisms recruited for SSP and grammatical language processing is in pursuit of behavioral change on standardized assessments measuring these cognitive constructs. I am pursuing this SSP-based neural mechanistic approach because it is my prediction that it will lead to longer-lasting, more successful outcomes than explicit remediation targeting only the language domain, especially in the beginning stages of intervention when it is critical to get the neurons in the SSP/language network firing together in the first place. Once that first level of treatment has taken place, it is my supposition that interventions aimed at maintaining and/or enhancing efficiency of the circuit could be more effectively introduced. These types of longer-term interventions, including cognitive training regimens, would be a necessary component to maximize gains and maintain them over time.

Subsequently, one question that needs to be explored is how to get the neurons in a disrupted circuit recruited for SSP and grammatical language processing firing together in the first place. Possibilities will be discussed further below within the framework of what the considerations might be for accomplishing this first step with children with autism and children with cochlear implants. Before delving into that discussion, I want to make it clear that, whereas enhancing the neurocognitive mechanisms recruited for SSP and grammatical language
processing would be an exciting and informative part of my research, it is not the end game. In terms of my vision for developing an effective training regimen for use with individuals with atypical SSP and language processing, is to discover how to implement a paradigm that will result in behavioral enhancements as measured by standardized assessments of SSP and language and/or standardized quality of life assessments. This is where collaborations will be crucial to the success of my research program, as attempting this ultimate goal is beyond the scope of what I could, or would want to do on my own.

In fact, a part of each of the three dissertation studies, including all of the analytic work, was done while I was a Language & Literacy Fellow. Being part of this area of focus, I was able to work toward my scholarly pursuits among students and faculty across numerous concentrations including education, linguistics, developmental psychology, speech-language pathology, statistics, early childhood intervention, adult intervention, neuroscience, and cognitive science. Therefore, throughout all of my doctoral studies, I have consulted with and been given good advice from numerous faculty and students affiliated with L&L, numerous faculty and students affiliated with my own concentration in Cognitive Sciences, as well as being mentored by Dr. Conway, my advisor.

It is my aim to continue my program of research in this spirit of collaboration. Dr. Conway and I have fostered connections with scholars at other universities and hospitals in order to collaborate with them on projects that will extend this line of research to clinical populations who may benefit from our approach. Our immediate next steps include collecting baseline measures of SSP and grammatical language processing in individuals with autism spectrum disorder (in collaboration with Dr. Larry Scahill and Dr. Toby Amoss at Marcus Autism Center in Atlanta and supported by an L&L seed grant awarded to Dr. Conway), We will follow this
study with a training pilot study with ASD children as well as adults. Additionally, Dr. Conway and I will be collaborating closely over the next several years with Dr. Bill Kronenberger and Dr. David Pisoni at Indiana University School of Medicine, Riley Hospital, DeVault Research Lab, to use a version of our computerized training to attempt to enhance SSP, executive functions, and language processing in children with cochlear implants. Further down the road, but still in our research pipeline, Dr. Conway and I will be working with Dr. Eric Wasserman at the NIH to develop a version of our training regimen with fMRI-guided repetitive transcranial magnetic stimulation (rTMS). We will first test and pilot this approach with the participant pool of typically-developing adults already available at the NIH. After that, we plan to collaborate off-site with hospitals who can access patients with agrammatic aphasia. Therefore, steps have been taken by Dr. Conway and me to help ensure this program of research continues in the direction of my primary research interests and toward my long-term goals. Given that our collaborative efforts toward using versions of our training approach with children with ASD and children with cochlear implants are either currently underway (training with children with ASD) or are on the immediate horizon (training with children with cochlear implants), potential ways in which these 2 research directions could be implemented will be briefly discussed. More focus will be on training with children with ASD, as we are further along trying to develop this line of research.

6.4 SSP Training to Enhance SSP and Grammatical Language Processing in Children with ASD

Our SSP training approach with ERP recording could be a novel and effective intervention for use with individuals with ASD who show atypicalities to SSP (Mostofsky et al., 2000), grammatical language processing (Walenski et al., 2006) and attentional control (Courchesne et al. 1994) that may underlie core difficulties with social and linguistic functioning.
Considering the complex symptomatology that characterizes the ASD, it may make sense to first more directly tap the lower-level cognitive processing that may underlie the higher-order processing in communication and social interaction. In one illustration of this possibility, Grynszpan (2008) discussed how he and colleagues developed a computerized cognitive training software for training pragmatics and used it with both typically-developing children and children with ASD. A series of social scenarios were displayed as written dialogues between two characters. Dialogues contained semantically ambiguous phrases that could be understood only by taking into account the context. Pragmatic ambiguities relied on irony or metaphors. The children were required to select one of three “assertions” about each dialogue. Their responses were scored as either a contextually correct interpretation of the pragmatic ambiguity, an out of context literal interpretation of the ambiguity, or an invalid non-literal interpretation. To examine the impact of emotional facial expressions as pragmatic cues, an associated facial expression was displayed along with the phrases to help the participant indicate if there was a contrast between what the characters said literally and what they were actually feeling. Qualitative observations and quantitative analysis indicated that the participants with autism had difficulty navigating the software and using the facial expressions appropriately precisely because it required them to manipulate controlled attention. The author noted the autistic participants were unable to perform the task designed to train pragmatics because of impairments to attentional control and gave a word of caution that researchers utilizing cognitive training techniques “need to take into account the particular cognitive impairments attributed to a disorder when designing training software intended for this disorder” (Grynszpan, 2008).

If the next step for our research team is a pilot study using the SSP training with children with ASD the advice of Grynszpan (2008) is astute. It is also important to consider the structural
atypicalities present in the brain of children with ASD, especially those to frontal lobes. For example, Courchesne and Pierce (2005) suggest that frontal cortex of individuals with ASD “talks with itself but fails to hear and respond to other brain systems.” Their fundamental argument is that there are too many local connections within the frontal lobe and that there are too few long-distance connections between frontal cortex and other areas of the brain, which causes frontal cortex to function much less efficiently and prevents communication with and control over lower-level systems (Courchesne & Pierce, 2005). Their review further outlined how the structural and functional integrity of frontal cortex is greatly compromised (Courchesne & Pierce, 2005). With this information in mind, is it reasonable to try this training approach with children with autism and would the same kinds of effects be observed? The answers appears to be yes, it seems both reasonable this training approach could be modified to be more engaging and appropriate for children with autism and that the possibility exists promising results would be observed with this population as well. Recent findings suggest structural training-related changes to gray matter in older adults (Boyke, Driemeyer, Gaser, Büchel, & May, 2008), a population for whom these types of changes would have once seemed improbable. Given results such as these indicating that we have only begun to witness what the brain can do in terms of plasticity, it seems worthwhile to attempt to utilize a version of the training regimen with children with ASD who show atypicalities to SSP (e.g., Gordon & Stark, 2007; Klinger & Klinger, 2007) and to grammatical language processing (e.g. Ullman, 2008). A better understanding would be gained of what, if any, neural changes the training regimen might induce in this population and how the approach could be made more effective as a treatment for their specific core impairments to language and social communication. Pursuing this goal brings us back to the question of how to get the neurons in the SSP/language network firing together to
begin with, especially if the frontal cortex of children with ASD has too many connections and
is, thus, generating a lot of noise right in proximity to the SSP/language network.

In the next section discussing directions for using training with children with cochlear
implants, I will make the argument that it may be useful to use longer-term computerized
cognitive training techniques with neural stimulation. This is one possibility for promoting the
adjacent firing of neurons in a network that are disrupted or firing inefficiently, and brief details
are outlined below. Electrical stimulation of neurons has been safely used with children with
ASD (e.g., Amatachaya et al., 2014; Hupfeld & Ketchum, 2016). One important consideration
for using this type of stimulation to enhance neural activity in the SSP/language network
involving Broca’s area, aSTG, and FOP, is this circuitry is either directly positioned in the over-
connected frontal lobe in the ASD brain or in close proximity. It seems possible, if not likely,
stimulating an already noisy region of that has isolated itself with too many local connection and
too few long-distance connections to other parts of the brain would just create more noise right
within the network where we would be trying to enhance signal. Findings from a recent study
using a mouse model suggests that it may be possible to chemically induce pruning of synapses
that are over-connected (Tang et al, 2014). The mice used in this study were programmed to
develop social behaviors characteristic of ASD in humans. In these mice a protein labeled mTOR
was hyperactive, which stopped the brain’s ability to prune unnecessary, over-connected
synapses. The mice were administered the drug rapamycin, which suppressed activity of the
protein mTOR and restored synaptic pruning. As a result, atypical social behaviors ceased in
these mice. Conceptually, and if these early findings hold up, this might be one way to first clear
away the overly-abundant local connections with the frontal lobes prior using neural stimulation
and computerized training approaches to build up connections that are either too sparse or operate inefficiently.

6.5 SSP Training to Enhance SSP and Grammatical Language Processing in Children with Cochlear Implants

These findings from my three dissertation studies have relevance toward future studies intended to help determine why children with hearing aids and cochlear implants show wide variability in SSP, executive functions, and language processing (e.g., Pisoni & Cleary, 2004; Pisoni et al., 2016) and toward future studies investigating how these mechanisms can be improved in deaf or hard of hearing children who have trouble with these crucial aspects of cognitive processing. For example, one promising avenue is to utilize electrical neural stimulation—an approach that has been used safely and effectively in special populations with children (e.g., Amatachaya et al., 2014; Hupfeld & Ketchum, 2016)—to not only clarify the neurocognitive mechanisms recruited for executive processing and for language processing, but also to boost their enhancement if used in conjunction with longer-term computerized cognitive training approaches (e.g., Rabey et al., 2013). Evidence from behavioral and imaging studies suggest that activity in inferior frontal cortex (IFC) [Brodmann areas (BA) 44/45, or Broca’s area], which has largely been associated with language-specific abilities, may be associated with performance on general-purpose SSP tasks (e.g., Peterson et al., 2004; 2012). My dissertation research suggests that one way to enhance function in Broca’s area would be to stimulate anterior STG, which as part of what has been traditionally thought of as the language network connects with Broca’s area encompassing BA44/45 and the deep frontal operculum (Anwander et al., 2007; Friederici, 2011; 2012) and may modulate SSP and language processing in a more network-based, domain-general manner. And SSP training study with ERP recording and neural
stimulation would be a novel and innovative way utilizing brain plasticity within the neural consequences of disrupted SSP and executive functioning following deprivation of sound and spoken language (Conway et al., 2009), especially in terms of the possible training-related benefits of functionally reorganizing their shared network.
REFERENCES


learning and motivation: Advances in research and theory*. (Vol. 8, pp. 47–89). New


B.B. Lloyd (Eds.), *Cognition and categorization* (pp. 169-211). Hillsdale, NJ: Lawrence
Erlbaum Associates, Inc.

Reber (1989) and Mathews et al. (1989). *Journal of Experimental Psychology: General,
120*, 316-323.

and sequential learning: Evidence from event-related brain potentials. *Language and
Cognitive Processes, 27*, 231-256.

Christiansen, M.H., Louise Kelly, M., Shillcock, R.C., & Greenfield, K. (2010). Impaired


Appendix A
Can We Improve Structured Sequence Processing? Exploring the Direct and Indirect Effects of Computerized Training Using a Mediation Model

Gretchen N. L. Smith¹*, Christopher M. Conway¹, Althea Bauernschmidt², David B. Pisoni³

¹ Department of Psychology, Georgia State University, Atlanta, GA, United States of America, ² Department of Psychology, St. Bonaventure University, St. Bonaventure, NY, United States of America, ³ Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, United States of America

* gsmith77924@gmail.com

Abstract

Recent research suggests that language acquisition may rely on domain-general learning abilities, such as structured sequence processing, which is the ability to extract, encode, and represent structured patterns in a temporal sequence. If structured sequence processing supports language, then it may be possible to improve language function by enhancing this foundational learning ability. The goal of the present study was to use a novel computerized training task as a means to better understand the relationship between structured sequence processing and language function. Participants first were assessed on pre-training tasks to provide baseline behavioral measures of structured sequence processing and language abilities. Participants were then quasi-randomly assigned to either a treatment group involving adaptive structured visuospatial sequence training, a treatment group involving adaptive non-structured visuospatial sequence training, or a control group. Following four days of sequence training, all participants were assessed with the same pre-training measures. Overall comparison of the post-training means revealed no group differences. However, in order to examine the potential relations between sequence training, structured sequence processing, and language ability, we used a mediation analysis that showed two competing effects. In the indirect effect, adaptive sequence training with structural regularities had a positive impact on structured sequence processing performance, which in turn had a positive impact on language processing. This finding not only identifies a potential novel intervention to treat language impairments but also may be the first demonstration that structured sequence processing can be improved and that this, in turn, has an impact on language processing. However, in the direct effect, adaptive sequence training with structural regularities had a direct negative impact on language processing. This unexpected finding suggests that adaptive training with structural regularities might potentially interfere with language processing. Taken together, these findings underscore the importance of pursuing designs that promote a better understanding of the mechanisms underlying...
training-related changes, so that regimens can be developed that help reduce these types of negative effects while simultaneously maximizing the benefits to outcome measures of interest.

**Introduction**

The acquisition of natural language may be one of the more formidable tasks facing human beings, and yet we are exceptionally proficient at it. Understanding the core mechanisms responsible for the ability to learn language has been a particular challenge in cognitive neuroscience. One long-standing, prominent argument has been that humans have dedicated domain-specific neural mechanisms that evolved specifically for language acquisition [1]. An alternative hypothesis is that language acquisition may rely heavily on domain-general learning and processing abilities that allow the learner to utilize the structure inherent in language [2], [3]. One such domain-general mechanism that may support language acquisition has been referred to as structured sequence processing (SSP), or the ability to extract, encode, and represent structured patterns occurring in a temporal sequence [4], [5], [6]. If SSP supports language, then it may be possible to improve language function by enhancing this basic learning ability, similar to the way that computerized working memory (WM) training has been demonstrated to transfer to non-trained tasks of executive function, attention, and other aspects of cognition [7], [8], [9], [10], [11]. The possibility of improving SSP through adaptive training, with improvements generalizing to aspects of language processing, has both clinical and theoretical ramifications as it would not only identify a novel intervention to treat language impairments but would also identify a more direct relationship between SSP and language.

In this paper, we will first review recent evidence that SSP may underlie language learning, underscoring the scarcity of literature using experimental manipulations to investigate the two processes. We will then review relevant findings from the WM training literature, which served as inspiration for the structure-based sequence training regimen used in the present study. This background will then lead to a description of our study using a novel computerized sequence training task and a mediational analysis to explore the relationship between SSP and language function.

**Previous Evidence Linking SSP to Language**

SSP, sometimes referred to as sequential learning or statistical learning, allows people to learn about structured patterns of information in the environment in a relatively automatic and unconscious fashion [12], [13], [6]. Importantly, SSP abilities may be especially crucial for the development of social and linguistic knowledge [14], [5]. SSP allows the language learner to detect and to utilize the structure inherent in phonology [13], syntax [15], and word order [5]. Furthermore, impairments in SSP may contribute to a number of communication disorders, including dyslexia [16], specific language impairment [17], and language delays observed in hearing impairment [18].

Research findings have indicated that individual differences in performance on non-linguistic sequential learning tasks are significantly correlated with how healthy typically-developing adults perform on a degraded speech perception task, in which participants must use preceding context to predict upcoming units of speech [5], [19], see also [20]. Furthermore, Christiansen et al. [21] provided a within-subject comparison of the neural mechanisms supporting visual sequence learning and language processing using event-related potentials (ERPs). The key
finding was that sequences containing structural irregularities in the SSP task elicited a P600-like component that was statistically identical to the P600 elicited by syntactic violations in the natural language task. This outcome suggests that the same neural mechanisms may be recruited for both SSP and language processing, a finding that is also substantiated by other neuroimaging studies showing that Broca’s area is active in both language and non-language SSP tasks e.g., [22], [23]; for reviews, see [24], [6].

Although these studies are highly promising, more direct evidence of a link between SSP and language is needed. One particularly striking void in the type of approach used thus far is the pursuit of designs that incorporate experimental manipulations designed to improve SSP, as a way to help demonstrate an underlying link between SSP and language. Even a first step in this direction could have potential implications for how to improve language functioning in typical and atypical development.

Cognitive Training

If language development relies, at least in part, on SSP, then it may be beneficial to improve language function by enhancing SSP itself. One strategy for this might be to stimulate neural regions, such as Broca’s area, that are thought to underlie SSP using magnetic or electrical stimulation e.g., [25]. Another possibility would be to use computerized neurocognitive training techniques to improve SSP. One cognitive domain that has received much interest in the cognitive training literature and may be relevant to the current endeavor is WM. WM refers to the temporary storage and manipulation of information necessary for complex cognitive tasks [26]. While the training tasks and populations have varied, the general goal of a number of recent studies has been to determine whether WM training tasks could improve WM capacity and show transfer to non-trained tasks of spatial and verbal WM, attention, and other cognitive functions. Sometimes this distinction is referred to as “near transfer” (transfer effects to constructs closely related to the training technique itself) and “far transfer” (transfer effects to other constructs thought to have a theoretical link with what is being trained). For example, Klingberg et al. [7], [8] used a WM training task (Cogmed Systems, Stockholm, Sweden) with children with ADHD. The children performed visuospatial and/or verbal WM tasks over a period of 5 weeks. The visuospatial task involved remembering the position of objects on a 4 x 4 grid, and the verbal task involved remembering phonemes, letters or digits [8]. Importantly, difficulty level of the tasks was adjusted to match each child’s WM ability by changing the number of elements that had to be recalled. A control group performed the same tasks except the length of items to recall stayed fixed rather than being adaptively adjusted. At post training sessions both 5 to 6 weeks and 3 months following the pre measures, children showed significant improvement to performance on WM and executive functions (as measured by a visuospatial Span board task, digit span, Stroop task, and Raven’s matrices) compared to a control group.

Overall, the results from a number of recent WM training studies suggest that WM can be improved through adaptive training [27], [28], [29]. Furthermore, training on an adaptive visuospatial task can also transfer in a domain-general manner to nontrained tasks of WM (demonstrating near transfer) but also to other cognitive functions such as inhibition [7], [8], [9], attention [11], and verbal WM [10] (demonstrating far transfer).

Although there have been some questions about the effectiveness of WM training [30], [31], and especially in relation to the far transfer results, these findings raise the possibility that WM and other aspects of cognition, perhaps even SSP, can be modifiable by intensive training. The difference between the standard WM task and SSP is that WM involves recalling a series of stimuli that have no structural relationship to each other; that is, the stimuli are presented in a
random order. On the other hand, many of our interactions with the world involve encoding, storing, and processing structural regularities, in which SSP is recruited. For this reason, we propose that to target and train SSP it is necessary to embed structured rather than random sequences into the training protocol.

To summarize, the previous evidence suggests that language functions may rely, at least in part, on SSP. Furthermore, recent findings from the WM training literature are promising because they offer the possibility that SSP could be improved, which if successful, could possibly lead to improvements to language processing. Finally, it may be beneficial to use the results from this type of intervention design in conjunction with process modeling techniques to provide more insight about the putative underlying relations among the constructs. We will now describe the present study, which combines all of these elements to specifically test whether adaptive training with structural regularities has a contributory impact on language via the mediation of SSP.

The Present Study

The goal of the present study was to investigate the putative underlying relationship between domain-general structure-based learning mechanisms (i.e., SSP) and language functions by exploring the effect of adaptive sequence training with structural regularities (SSP training) versus adaptive sequence training without structural regularities (WM training), relative to a control or reference group. Participants in the SSP training group engaged in a 4-day computerized sequence training regimen that involved viewing and then reproducing visual-spatial structured sequences. This type of training is similar to previous WM training studies; however, our novel manipulation for this group was the introduction of sequences containing structural regularities. Thus, rather than having those participants trained with random sequences (as in the case of all previous WM training studies), they were trained with non-random, structured patterns. For the second group, which we refer to as the WM training group, these participants engaged in the same computerized sequence training task but instead of using structured sequences, the sequences contained no structure, consistent with all other previous WM training studies.

Participants received a battery of cognitive tests on the first day, then four days of either the SSP training condition, the WM training condition, or the control condition (which, similar to the control groups used in previous WM training studies, consisted of a non-adaptive computerized training that is not expected to result in cognitive improvements). On the sixth day participants received the same battery of cognitive tests that were administered on the first day in order to measure changes to non-trained tasks. The group of participants engaging in the adaptive sequence training with structural regularities (SSP training, Group 1) and the group of participants engaging in the adaptive sequence training without structural regularities (WM training, Group 2) were both compared to a control group that engaged in nonadaptive, unstructured sequences (Group 3).

1. Thus, the first hypothesis for this study was simply that only the SSP training would result in improvements to both a non-trained SSP task and a language processing task. This hypothesis was examined through the use of multivariate analysis of variance (MANOVA) comparing group means of SSP and language processing.

However, regardless as to the results of the MANOVA, there is a second and perhaps more useful way to analyze these data. Whereas all of the previous WM training studies used as their primary analyses a comparison of the means on non-trained task from pre- to post-training, the present study also used a mediation model. This analysis approach has the ability to explore...
the core mechanisms or processes underlying any such relation between cognitive training and language processing by investigating whether there exists a mediating relationship among the variables. It can also help tease apart the separate influences relating to near and far transfer effects, and help explain why one or the other might be present. With the mediation model technique, we may be better able to understand the effects of cognitive training on SSP and language processing. A MANOVA or other regression technique does not allow for the identification of mediating variables and, thus, is unable to help clarify the nature of the relations among training, SSP, and language processing.

A mediation analysis allows one to explain the mechanism by which one variable influences, or has an effect, on another [32], [33]. Both "direct" and "indirect" effects can be tested [32], [33]. Direct effects are when the independent variable (IV) directly impacts the dependent variable (DV). Indirect effects are when the IV impacts the DV through the mediation of a third variable, called the mediator (M). Hayes and Preacher [33] introduced a technique for conducting a mediation analysis when the IV is multicategorical, as in the case of the present study comparing two experimental groups to a control group. Since the effects of being in one of the experimental groups are in comparison to the effects of being in a reference group, they suggest using the terms "relative direct effects" and "relative indirect effects" [33]. In the present study, the IV is training type [i.e., whether participants receive SSP training (Group 1), or WM training (Group 2), with both compared to the control participants (Group 3). The DV is language processing (measured at post-training). The M is SSP ability (also measured at post-training). Thus, our aim is to test the relative direct and indirect effects through which cognitive training might affect language processing. Specifically, does cognitive training have a relative direct impact on language processing? And, does cognitive training have a relative indirect effect on language processing by impacting SSP ability?

The untested model is presented in Fig 1. For both experimental training groups (i.e., Group 1 and Group 2), path $a \times b$ represents the relative indirect effect of the IV (training type) on the DV (language) via the mediator, M (SSP) (relative to the reference group, Group 3). Path $a$ represents the effect of the IV on M, whereas path $b$ represents the effect of M on the DV. On the other hand, path $c'$ represents the relative direct effect of the IV on the DV (relative to the reference group, Group 3). The relative total effect (path $c$, not depicted in the untested model) would represent the sum of the direct and indirect effects (compared to the reference group). Again, our focus was testing, for Group 1 and Group 2, the relative indirect and relative direct effects, represented by path $a \times b$ and path $c'$, respectively. Additionally for both groups, we tested the individual components of the relative indirect effect, represented by path $a$ and path $b$. We did not make an a priori hypothesis about the relative total effect for both groups, represented by path $c$.

Thus, in association with the mediation model, we assessed the following hypotheses:

1. We predicted that there would be a significant relative indirect effect (path $a \times b$) only for the SSP training group (Group 1). That is, we predicted that adaptive sequence training with structural regularities would have an underlying impact on language processing by way of the mediating variable, SSP. In terms of the individual components of this indirect path, we predicted a significant (positive) effect of path $a$; that is, adaptive sequence training with structural regularities would have a significant positive impact on SSP. We also predicted a significant (positive) effect of path $b$; that is, SSP would have a significant positive impact on language processing.

2. We also predicted that there would be a significant relative direct effect (path $c'$) only for the SSP group (Group 1). That is, we predicted that adaptive sequence training with structural regularities would have a positive effect overall on language processing.
Method

Ethics Statement

The study was approved by the Indiana University Institutional Review Board. Participants provided written consent prior to participation.

Participants

Sixty-six participants (38 males and 28 females, ages 18–30) were recruited at Indiana University to participate in this study for monetary compensation. All participants were native speakers of English and reported no history of a hearing loss, speech impairment, or other cognitive/perceptual/motor impairments at the time of testing.

Materials

All visual stimuli/sequences were presented using a Magic Touch touch-sensitive monitor and a Macintosh Power PC G4. Responses were made on the Magic Touch touch-sensitive monitor. For the measure of language, the auditory stimuli were presented using Beyer dynamic DT100 headphones. All experimental tasks for this experiment took place in a sound-attenuated booth (Industrial Acoustics Company).
Procedure

Participants took part in the experiment for 6 days, with no more than 2 intervening days between sessions. On Day 1 they were assessed on several measures, two of which we focus on in the present manuscript: a measure of SSP and a measure of language (speech recognition in noise). During the next 4 days participants received either adaptive sequence training with structural regularities (Group 1, SSP training), adaptive sequence training without structural regularities (Group 2, WM training), or the control condition of non-adaptive unstructured sequences (Group 3, reference group)). On Day 6 participants were re-assessed on the same measures as Day 1. An overview of the study design is given in Table 1.

Pre-training measures. Although several other pre-training measures were administered as part of a separate study reported in Conway et al. [5], in the present analysis we focus on only the measures of SSP and language. Participants in each of the three groups completed the measure of SSP first, the measure of language second, and the other cognitive assessments last. Below we briefly describe each measure; further details are provided in Conway et al. [5].

Measure of structured sequence processing. The measure of SSP was identical to the “Simon” visual statistical-sequential learning task used in previously published work, see [5], [34] for full details. Performance on this task has been shown to be significantly correlated with language processing skills in healthy adults [5] and in language-delayed children [18]. In this task, participants viewed a series of 4 colored squares that light up on the touchscreen and were asked to reproduce each sequence they had just observed by touching the appropriate color.

The task consisted of two phases, a learning phase and a test phase. In both phases, the participant’s task was the same: to reproduce each sequence immediately following presentation by touching the colored squares displayed on the touch-sensitive monitor in the correct order. No feedback was given. However, unbeknownst to participants, the phases differed in terms of the types of temporal sequences that were presented. In the learning phase, the sequences were not random but rather were generated according to an underlying artificial grammar that specified the probability of a particular element in a sequence occurring given the preceding element (see Table 2). In the learning phase, 48 sequences generated from the grammar were presented once each, in random order. In the test phase, 40 new sequences were presented: 20 sequences generated from the artificial grammar and 20 sequences that were pseudo-random (i.e., the occurrence of each element in the sequence was random except that no element could

Table 1. Overview of study design.

<table>
<thead>
<tr>
<th>Day 1 Pre-Training</th>
<th>Days 2–5 Sequence Training</th>
<th>Day 6 Post-Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speech Recognition In Noise</td>
<td>Group 1 Adaptive, Structural Regularities</td>
<td>Speech Recognition In Noise</td>
</tr>
<tr>
<td>Statistical-Sequential Learning</td>
<td>Group 2 Adaptive, No Regularities</td>
<td>Statistical-Sequential Learning</td>
</tr>
<tr>
<td></td>
<td>Group 3 Non-adaptive, No Regularities</td>
<td></td>
</tr>
</tbody>
</table>

doi:10.1371/journal.pone.0127148.t001

Table 2. Artificial grammars used to generate the order of stimuli.

<table>
<thead>
<tr>
<th>Colors/locations (n)</th>
<th>Constrained Grammar (n+1)</th>
<th>Unconstrained Grammar (n+1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>0.0</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>0.0</td>
</tr>
<tr>
<td>4</td>
<td>1.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

do:10.1371/journal.pone.0127148.t002
follow itself). The participants were not told that this was a test phase or that there were different types of sequences used in the experiment. From the perspective of the participant, the test phase was just the same sequence reproduction task they had been doing as before.

**Scoring.** In the test phase, a sequence was scored as correct if a participant correctly reproduced it. A score was given for each correctly reproduced sequence based on its length (i.e., a correctly reproduced sequence of length 5 was given a score of 5). As in previous studies [5], [18], [34] a learning score was then obtained by subtracting the total score for the ungrammatical sequences in the test phase from the grammatical sequences in the test phase. A higher learning score indicates better performance on novel statistically-structured sequences compared to random ones, suggesting that successful statistical-sequential learning has occurred.

**Measure of language.** The measure of language was a speech recognition in noise task that required participants to listen to 50 spectrally degraded sentences and then to write down the last word that they heard in each sentence, see [5] for full details. The sentences varied in terms of the final word’s predictability: high-predictability sentences (N = 25) had a final word that was highly predictable given the sentence context (e.g., “Greet the heroes with loud cheers”); whereas anomalous sentences (N = 25) had a final word that was not predictable given the sentence context (e.g., “The burglar was parked by an ox”). Sentences were presented in random order using a self-paced format.

**Scoring.** Responses were scored based on the number of correct final words for each of the two sentence types (high-predictability and anomalous). As in Conway et al. [5], a difference score was computed as the number of final words identified in high-predictability sentences minus the number of final words in anomalous sentences. This difference score reflects how well a participant is able to use sentence context to help perceive the final word in the sentence, a form of top-down language processing that has been argued to depend on how well one is able to track statistics in language [5]. For this reason, we expected that any improvements to SSP might carry over to improvements in how well participants are able to use sentence context to perceive words under poor listening conditions.

**Sequence training task.** The training task began in a separate session (on a different day) after the completion of the pre-training assessments. The sequence training task consisted of several blocks of sequence-reproduction trials that either adaptively increased in length as participants’ performance improved (Groups 1 and 2) or were non-adaptive (Group 3). On each trial, participants saw a series of green circles light up on the touchscreen monitor and were asked to reproduce the sequence they had just seen (see Fig 2). Sixteen circles were arranged on a 4x4 grid, inspired by the type of computerized training programs used by Klingberg et al. [7], [8]. Individual circles on the 4x4 grid were illuminated for 250ms and were off for 250ms between elements in the sequence. The participants’ task was to reproduce each sequence immediately following presentation by touching the green circles displayed on the touch-sensitive monitor in the correct order. As participants made their responses, each circle they pressed stayed illuminated for 250ms. At the end of the presentation of a sequence if the participant did not make a response within 2 seconds a new sequence was presented. Each session of the training task consisted of 3 blocks of 50 trials.

The order that the circles lit up either was dependent upon embedded structural regularities (Group 1) or was pseudorandom and did not follow structural regularities (Groups 2 and 3). The sequences with underlying structural regularities were generated so that each element in the sequence could be followed by 3 others in the set with equal likelihood. The sequences without underlying structural regularities were generated so that each element in the sequence could be followed by any other in the set with equal likelihood (that is, any of the 15 other elements). The underlying sequences themselves were the same for all participants (within each group). However, the actual mapping between each sequence element and each circle on the
screen was randomly determined for each participant. Thus, while the underlying sequences were the same for each participant (within the same group), the spatial representation was different between participants. Moreover, mapping was re-randomized for each participant at the onset of each new daily training session in order to encourage generalizability.

Participants were randomly assigned to 1 of 3 groups. Group 1 received adaptive training using sequences with underlying structural regularities. Group 2 received adaptive training on sequences without underlying structural regularities. Group 3 received non-adaptive training on sequences without underlying structural regularities. For Groups 1 and 2, sequence lengths
in the adaptive conditions were based on a 2 up 2 down staircase procedure. For example, if a participant started at sequence length 4 and correctly reproduced all items in that sequence then their next trial would be a sequence of length 4. If the participant correctly reproduced all elements in the second sequence of length 4 then they would move up to a sequence of length 5 in the next trial. If they incorrectly reproduced this sequence of length 5 then their next trial would be of a sequence of length 5. If they responded incorrectly to this sequence as well, then their next sequence would be moved down to length 4.

Whereas both Groups 1 and 2 incorporated the 2-up 2-down adaptive training staircase procedure, only Group 1 received sequences with structural regularities. Group 2 instead received adaptive training on sequences without any underlying structural regularities. In other words, this condition used the same 2 up 2 down staircase procedure as previously described; however, the sequences themselves were pseudo-randomly determined on each trial and were, therefore, without underlying structural regularities.

Finally, participants in Group 3 received training that did not adapt to their performance level. At each trial, the sequence lengths were determined randomly (varying in length from 4 to 16 elements). Like Group 2, the sequences in Group 3 were pseudo-randomly determined on each trial and, therefore, did not contain any underlying structural regularities.

**Post-training measures.** The post-training measures were identical to the pre-training measures. The post-training measures were administered in a separate session on the final day of the study, Day 6.

**Statistical Analysis**

**Comparison of Group Means**

A 3x2 mixed-design MANOVA with group (1, 2, 3) as the between-subjects factor and time of testing (pre, post) as the within-subjects factor was used to assess whether the training condition affected mean performance on the non-trained measure of SSP and the non-trained measure of language processing (both DVs described above). For the MANOVA, a given participant’s data was excluded if it was missing for either the pre or the post measure. This process resulted in data used in the analysis of both SSP and language processing for a total of N = 60. The MANOVA was performed using SPSS (IBM SPSS Statistics 21, Release Version 21.0.0.0).

**Mediation**

In addition to the MANOVA, we used a mediational model analysis to estimate the relative direct and indirect effects of cognitive training. The IV was training type (Group), defined as the SSP training received by Group 1 (described above) and the WM training received by Group 2 (described above), both relative to the control, or reference, group (Group 3, described above). The DV was language processing (Language), defined as the correct number of degraded spoken target words for high-predictability sentences (H) minus the correct number of target words for anomalous sentences (A) at post-measure. The mediator (M) was structured sequence processing (SSP) defined as the span score for the grammatical sequences minus the span score for the ungrammatical sequences in the sequence learning task test phase at post-measure.

The process of dummy coding was used in order to enter the multicategorical, group-membership based IV (Group) into the model. Two dummy coded variables labeled $D_1$ and $D_2$ were created from observations in Group 1 and Group 2, respectively. The reference group was Group 3. No transformations were done on the continuous variables SSP and Language prior to entering them into the model. Variables were uncentered, and the data contained no outliers beyond +/- 3 standard deviations. Six subjects were excluded from the analysis due to missing
Calculations were based on an ordinary least squares regression approach [see [32] for a description] and was determined by a test of significance of the indirect effect of the IV on the DV through M, as this approach is preferred in contemporary mediation analyses [35], [36]. Because it is particularly appropriate for small sample sizes, we used the bootstrapping technique suggested by Preacher and Hayes [37], [38], [39] in which a point estimate of the indirect effect was obtained from the mean of 10,000 estimates of path $a \times b$ and 95% percentile-based confidence intervals were computed using the cut-offs for the 2.5% highest and lowest scores of the empirical sampling distribution, and adjusted for bias in the bootstrap distribution. The indirect effect was considered statistically significant if this bias-corrected confidence interval did not include 0.

All analyses of the mediation model were performed using SPSS (IBM SPSS Statistics 21, Release Version 21.0.0.0) with the Hayes and Preacher [33] macro MEDIATE that can be used for bootstrapped mediation models with a multicategorical variable.

**Results**

**Comparison of Group Means**

A 3x2 mixed-design MANOVA contrasting group (1, 2, 3) and time of testing (pre-post revealed a significant multivariate main effect on the linear composite of the DVs SSP and Language for time of testing (pre-post) [Wilks’ $\lambda = .357$, $F(2, 56) = 50.534$, $p < .001$, partial eta squared = .643] and no interaction with group [Wilks’ $\lambda = .963$, $F(4, 112) = .539$, $p = .707$, partial eta squared = .019].

Univariate follow-up analyses indicated there was no significant main effect for time of testing (pre-post) on SSP [$F(1, 57) = .066$, $p = .799$, partial eta squared = .001] and no interaction with group [$F(2, 57) = 1.06$, $p = .353$, partial eta squared = .036]. Looking at **Table 3** at the mean values for the measure of SSP, only Group 1’s scores were higher from pre to post test. Both Group 2 and 3’s scores on the measure of SSP were worse from pre to post test. However, the univariate tests on the measure of SSP by itself indicated none of these changes were significant.

There was a significant main effect for time of testing (pre-post) on Language, [$F(1, 57) = 102.155$, $p < .001$, partial eta squared = .642] and no interaction with group [$F(2, 57) = .031$, $p = .969$, partial eta squared = .001]. The univariate follow-up tests on Language by itself indicated all 3 groups showed significantly lower scores at the post-test on the measure of language, a finding that is further illustrated by the mean values in **Table 3**.

In summary, the MANOVA findings suggest overall lower language scores at post-training, but no effects or interactions that would suggest that the SSP training had significant effects on SSP or language. Therefore, Hypothesis 1 predicting that adaptive sequence training with

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th></th>
<th>Group 2</th>
<th></th>
<th>Group 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>S.D.</td>
<td>M</td>
<td>S.D.</td>
<td>M</td>
<td>S.D.</td>
</tr>
<tr>
<td><strong>SSP (Pre)</strong></td>
<td>19.71</td>
<td>16.18</td>
<td>20.74</td>
<td>16.75</td>
<td>16.00</td>
<td>19.75</td>
</tr>
<tr>
<td><strong>SSP (Post)</strong></td>
<td>26.81</td>
<td>21.54</td>
<td>18.47</td>
<td>17.42</td>
<td>13.55</td>
<td>21.19</td>
</tr>
<tr>
<td><strong>Language (Pre)</strong></td>
<td>3.52</td>
<td>2.04</td>
<td>4.68</td>
<td>2.63</td>
<td>4.20</td>
<td>2.19</td>
</tr>
<tr>
<td><strong>Language (Post)</strong></td>
<td>-0.86</td>
<td>2.24</td>
<td>0.32</td>
<td>2.50</td>
<td>0.05</td>
<td>2.21</td>
</tr>
</tbody>
</table>

doi:10.1371/journal.pone.0127148.t003
structural regularities would result in improvements to both a non-trained SSP task and a language processing task, as compared to the other experimental group and the control group, was not supported.

Mediation

Although the group means did not demonstrate an effect of training, there is still utility in using the mediation analysis to determine whether there are underlying relationships among the constructs of interest. The final mediation model is presented in Fig 3. The results presented first pertain to the relative indirect effect of SSP training (Group 1) on Language, via SSP, compared to the control group and represented by path $a_1 \times b$ of $D_1$. From a mediation analysis conducted using bootstrapping, SSP training indirectly improved language processing through its enhancement of SSP. A 95% bias-corrected bootstrap confidence interval for the indirect effect ($a_1 \times b = 0.42, SE = 0.29$) based on 10,000 bootstrap samples did not include zero (0.03 to 1.25). What this shows is that participants in Group 1 who received adaptive sequence training with structural regularities were on average 13.26 units higher on SSP following training than participants in the control group, who received non-adaptive training on randomly-presented sequences ($p = .04$; see Table 4, path $a_1$). Furthermore, holding type of training constant, those participants who were higher on SSP were also higher on Language ($p = .03$, path $b$). Given the relative indirect effect is $a_1 \times b$, participants in Group 1 who received adaptive sequence training with structural regularities performed 0.40 units better on Language as a result.
of the increase in SSP performance. In contrast, adaptive sequence training without structural regularities (Group 2) had no indirect effect on language processing. A 95% bias-corrected bootstrap confidence interval for the indirect effect ($a_2 \times b = 0.15, SE = 0.21$) based on 10,000 bootstrap samples did include zero (-0.17 to 0.71).

The results presented next pertain to the relative direct effect of SSP training (Group 1) on Language, compared with the control group and represented by path $c'_1$ (see Fig 3). The results of the analysis revealed that SSP training directly lowered language processing. Specifically, when considering the direct path in isolation, participants who received adaptive sequence training with structural regularities were on average 1.32 units worse on Language than participants who received non-adaptive, randomly-presented sequences ($p = .07$; see Table 4, path $c'_1$). Thus, Hypothesis #3, predicting that adaptive sequence training with structural regularities would have a positive effect on language processing, was not supported. Furthermore, the direct effect of WM training (Group 2) on Language, compared with the control group, was not significant ($c'_2 = .11, p = .88$; see Table 4).

According to the approach implemented by Zhao, Lynch, and Chen [36], since the product of $a_1 \times b \times c'_1$ is negative (-0.53), this indicates that the model corresponding to SSP training (Group 1) is one of competitive mediation. These authors point out that if the direct effect $c$ is substantially larger than the indirect effect $a \times b$, then the total effect $c$ would also be negative [given the formula for the total effect is $c = (a \times b) + c'$] [36]. Potential implications of this unpredicted finding will be addressed in the Discussion.

### Discussion

The results of the comparison of group means (using MANOVA) did not support our first hypothesis. That is, adaptive sequence training with structural regularities did not lead to a significant improvement to SSP or language processing. There are a number of reasons why a non-significant result might have been obtained. For instance, it is possible that the training regimen was not strong or consistent enough to lead to significant improvements overall, even if the training itself has the potential to have a causal effect on SSP and language. Thus, even though the MANOVA resulted in non-significant effects of SSP training, using the mediation model allows us to better understand the potential underlying relationships among the variables of interest.

Along these lines, the results of the mediation model did show that there was a significant relative indirect effect of adaptive sequence training with structural regularities on language via SSP, compared with the control condition, supporting Hypothesis #2. This relative indirect path shows that SSP training has an underlying impact on language—specifically, the ability to
use knowledge of word order statistics to improve speech recognition in noise—through the mediator SSP. Previous research using an individual differences approach has established an empirical association between SSP and language ability [21], [5], [20]. Furthermore, there is evidence that language impairments are associated with impairments to SSP, e.g., [17]. However, the present findings are the first results that we know of that demonstrate a more direct connection between SSP and an aspect of language processing as revealed through experimental manipulation of SSP training itself. Likewise, these are also the first findings demonstrating that cognitive training techniques can potentially modify SSP.

The mediation model demonstrates that adaptive sequence training with structural regularities has the potential to generalize to improvements on a non-trained statistical-sequential learning task, as shown in path \(a_1\). This finding itself has remarkable implications about the plasticity of SSP and statistical learning processes and the potential for using such sequence training tasks to improve fundamental learning (and language) abilities. Thus, even though an examination of the group means revealed no significant effects of SSP training, the mediation model suggests that underlying relationships among these variables exist, providing the basis to further develop such training techniques to improve SSP and language.

In terms of Hypothesis #3, the significant indirect effect of \(a_1 \times b\) was accompanied by a significant—and opposite, or competing—direct effect (path \(c'_1\)). Thus, Hypothesis #3 was not supported. According Zhao, Lynch, and Chen [36], our model is one of competitive mediation, in which the total effect \(c_1\) is negative (-0.91, \(p = .22\), see Table 4), \([\text{given the formula for the total effect is } c = (a \times b) + c']\) [36]. It is possible that there is an unexplained mediator(s) in the direct path, thereby contributing to a negative relationship between SSP training and language. Although this is a valid possibility, it is also possible that SSP training directly negatively impacts language (through some as yet unexplained mechanism), and is thereby responsible for the negative total effect \(c_1\). This second possibility would not require an additional mediator, only an additional explanatory construct to explain how the variables already in the model behave on each of the different paths.

Why does SSP training have a positive underlying relationship with language performance via the indirect effect through the mediator SSP, but overall a negative underlying relationship with language performance via the direct effect? One intriguing possibility is that training on visual structural regularities—apart from any effect it has on SSP—might actually interfere with one’s knowledge or use of the structural regularities in spoken language. Recall that the measure of language was derived from a difference score: performance with high-predictability sentences (containing language regularities) minus performance with anomalous sentences (containing fewer regularities). An examination of the means on the high-predictability and anomalous sentences suggests that only in Group 1 does performance on the highly-predictable sentences get substantially worse from pre- to post-training. Performance on the anomalous sentences on the other hand does not worsen for any of the three groups. Thus, knowledge (or expression of) language regularities as measured by the highly-predictable sentences appears to be attenuated following sequence training with structural regularities. A similar type of interference was recently observed when participants engaged in a non-linguistic visual-motor SSP task concurrent with a sentence comprehension task [39]. This interference between the processing of visual structural regularities (contained in the sequence training task) and processing spoken language regularities (contained in the highly-predictable sentences) could be the mechanism driving the negative direct effect of path \(c'_1\). With these two competing pathways—an indirect benefit to language processing by strengthening SSP, but a simultaneous direct negative effect on language due to interference—the final effect in our case is an overall negative total effect or decrease in language processing. Theoretically, this is quite enlightening, and furthermore underscores the complex relationship between SSP and the processing of language.
regularities and sheds light upon why in some cases a near transfer effect but not a far transfer effect might be observed. In this case, the near transfer effect (improvement to SSP) would normally result in a far transfer effect (improvement to language), but because the training regimen itself has a negative direct effect on language, it cancels out the potential beneficial improvement to language.

As the above discussion helps illustrate, these findings accentuate the importance of pursuing designs that allow one to better understand the mechanisms underlying training-related changes to outcome measures. Some recent literature has been more critical of computerized WM training studies and has brought into question the generalizability of the findings e.g., [31]. The advantage of our design is that it helps inform the process of change, rather than simply comparing means of the changes to the outcomes themselves; we believe this may help address the concerns pertaining to the effectiveness of cognitive training techniques and possibly provide answers as to why near and far transfer effects are observed. In turn, this can serve to maximize the potential of these interventions. With a growing number of reports claiming the promise of cognitive training techniques, as well as other more recent studies that are more critical of their validity, our findings might offer clarity into the mechanisms of change themselves. For instance, given the present results suggesting the existence of two independent pathways for how sequence training might affect language, it is possible that previous training studies have used protocols that inadvertently emphasize one or the other pathway, leading to very different and inconsistent results across studies. In fact, a given experimental manipulation, such as changing the sensory modality or duration of the training task, may have different effects on the strength of each pathway. Discovering what the key manipulations are and how each affects different mechanisms of change is an important next step. With such knowledge, it may be possible to design a training regimen that better capitalizes on the indirect path in order to yield the greatest chance of demonstrating far transfer, in this case, enhancement to language performance. Importantly, the existence of these two competing paths would not have been known had one relied solely on the MANOVA analyses comparing the group means.

Likewise, it is possible that there may be ways to modify the training task to alleviate the negative, direct path between training and language performance. For instance, having a longer training regimen could provide an opportunity for participants to adapt to the novel structural regularities that they are exposed to, reducing the interference between the training task and language processing. If this is true, then with additional training trials, the direct (negative) effect of adaptive training with structural regularities on language might decrease, resulting in even stronger enhancements to language. Another possibility might be to modify the type of structural regularities that are present in the training sequences. For example, rather than having only adjacent sequential dependencies as was the case here, incorporating long-distance, non-adjacent dependencies into the training task might prove beneficial for improving the mechanisms that are recruited when processing long-distance dependencies in natural language [40],[41].

Although the positive underlying relationship between SSP and language (illustrated in path b shown in Fig 3), may seem relatively small (b = .03), it is still encouraging. It is true that the overall indirect path a1 x b may at first suggest that it takes a substantial improvement to SSP to see a small improvement to language processing; however, a few considerations are important to mention. First, the present design incorporated only 4 training sessions, a small number. It seems highly possible that with more training sessions, or by modifying the training task in some other way, even greater enhancement to SSP might be obtained, which could in turn boost the language score even more. Second, considering the long-term applied goal of how these types of cognitive training regimens might be used to improve language in typical and
atypical development, even a small gain could have a major impact, especially if such an inter-
vention was targeted early in development.

Conclusions

In conclusion, using a mediation model analysis, we have demonstrated that adaptive sequence
training with structural regularities has an underlying impact on language through the media-
tor SSP. More concretely, adaptive sequence training with structural regularities has a very
large impact on SSP while changes to SSP, in turn, have a more modest impact on language
processing. In competition with this indirect effect, our sequence training regimen appeared to
have a negative direct effect on language performance as well, resulting in overall a more damp-
ened effect on language ability and no overall improvements to language as assessed by MAN-
OVA. Additional work is currently underway to understand this negative direct effect, with the
aim of reducing its impact to improve the efficacy of such sequence training programs.

These findings have two implications. At a practical level, these findings show how funda-
mental learning abilities and language processing skills might be improved in typical and atypi-
cal development. At a theoretical level, these findings not only highlight the plasticity of
statistical-sequential learning and SSP but they also show an underlying link between SSP and
language, which in turn lends additional weight to the view that language acquisition is based
in large part on domain-general learning mechanisms rather than language-specific modules
or neural structures that solely mediate language alone.

Acknowledgments

Data for this project was initially collected as part of A. Bauernschmidt’s undergraduate hon-
or’s thesis while at Indiana University. We would like to thank Lee Branum-Martin, Hisako
Matsuo, and Jerome Daltrozzo for their help with earlier versions of this manuscript. We
would also like to thank Andrew Hayes for his consultation and tutorial on mediation with a
multicategorical IV (Hayes & Preacher, 2014). Data collection and manuscript preparation was
supported by the following grants from the National Institute on Deafness and Other Commu-
nication Disorders: T32DC000012, R01DC000111, and R01DC012037.

Author Contributions

Conceived and designed the experiments: CMC AB DBP. Performed the experiments: AB. An-
alyzed the data: GNLS AB. Wrote the paper: GNLS CMC.

References

2. Kelly MHM S.. Domain-general abilities applied to domain-specific tasks: Sensitivity to probabilities
4. Conway CM, Christiansen MH. Sequential learning in non-human primates. Trends in cognitive sci-
5. Conway CM, Bauernschmidt A, Huang SS, Pisoni DB. Implicit statistical learning in language processing:
   PMID: 19922909; PubMed Central PMCID: PMCPMC2823831.
6. Uddén J, Bahmann J. A rostro-caudal gradient of structured sequence processing in the left inferior
   frontal gyrus. Philosophical transactions of the Royal Society of London Series B, Biological sciences.
   Central PMCID: PMCPMC3367683.


Appendix B
Exploring the Neural Mechanisms Supporting Structured Sequence Processing and Language Using Event-Related Potentials: Some Preliminary Findings

Gretchen N.L. Smith (gsmith50@student.gsu.edu)
Department of Psychology, Georgia State University, P.O. Box 5010
Atlanta, GA 30320-5010 USA

Gerardo E. Valdez (gvaldez2@student.gsu.edu),
Department of Psychology, Georgia State University, P.O. Box 5010
Atlanta, GA 30320-5010 USA

Anne M. Walk (ameclur3@illinois.edu)
Department of Kinesiology and Community Health, University of Illinois, 405 North Mathews Avenue
Urbana, Illinois 61801 USA

John D. Purdy (jdprdy@gmail.com)
Department of Psychology, Saint Louis University, 3700 Lindell Blvd.
St. Louis, MO 63108

Christopher M. Conway (cconway@gsu.edu)
Department of Psychology, Georgia State University, P.O. Box 5010
Atlanta, GA 30320-5010 USA

Abstract
Structured sequence processing (SSP) refers to the neurocognitive mechanisms used to learn sequential patterns in the environment. SSP ability seems to be important for language (Conway, Bauernschmidt, Huang, & Pisoni, 2010); however, there are few neural studies showing an empirical connection between SSP and language. The purpose of this study was to investigate the association between SSP and language processing by comparing the underlying neural components elicited during each type of task. Healthy adult subjects completed a visual, non-linguistic SSP task incorporating an artificial grammar and a visual morphosyntactic language task. Both tasks were designed to cause violations in expectations of items occurring in a series. Event-related potentials (ERPs) were used to examine the underlying neural mechanisms associated with these expectancy violations. The results indicated the P3a component elicited by the SSP task and the P600 component elicited by the language task shared similarities in their topographic distribution. These preliminary analyses suggest that the P3a and P600 may reflect processes involving detection of sequential violations in non-language and language domains, which is consistent with the idea that language processing relies on general-purpose SSP mechanisms.

Keywords: Structured Sequence Processing; Sequence Learning; Statistical Learning; Artificial Grammar Learning; Language Processing; Syntax; Event Related Potentials; P3a; P600

Introduction
Structured sequence processing (SSP), also termed sequential learning or statistical learning, is a core cognitive mechanism used to learn patterns of information from the environment over time. SSP emerges early in development (Aslin, Saffran, & Newport, 1998) and is largely automatic and implicit (Cleeremans, Destrebecqz, & Boyer, 1998), though explicit processes likely occur in parallel (Sun, Slusarz, & Terry, 2005). SSP involves learning complex embedded patterns in which each item that occurs next is determined probabilistically based on what item occurred previously (see Conway & Christiansen, 2001 for a more detailed discussion on different types of sequential learning).

A key facet of SSP is that it serves as a tool for making predictions about which elements will occur next in a sequence (Christiansen, Conway, & Onnis, 2012). When sequential patterns are learned, this information can be used not only to generate expectancies about upcoming stimuli in the sequence, but also to detect when stimuli deviate from expectation (Ferdinand, Mecklinger, & Kray, 2008). Bar (2007) suggests that a “circular mechanism” occurs in which the brain limits processing of stimuli that are predictable, while allotting cognitive resources to stimuli that are novel and/or unexpected. These “predictive processing” operations are generally beneficial to many aspects of cognition, including perception, movement, decision-making (Bubic, von Cramon, & Schubotz, 2010) and language (Federmeyer, 2007).

SSP appears to be especially important in the domain of language (Conway, Bauernschmidt, Huang, & Pisoni, 2010). In particular, SSP may support knowledge and use of grammatical language, such as word order (Conway et al., 2010), phonology (Saffran, 2003), morphology and syntax.
(Ullman, 2004). However, the association between SSP and language has largely been assumed. Only recently have behavioral studies demonstrated empirical links between SSP and natural language processing (e.g., Conway et al., 2010). Additionally, even fewer studies have empirically compared these two mechanisms at a neural level (e.g., Patel, Gibson, Ratner, Besson, & Holcomb, 1998). In a neural-based investigation using a within-subject design, Christiansen et al. (2012) examined the electrophysiological responses elicited during a visual SSP task and a visual syntactic natural language processing task. The findings indicated both the SSP task and the natural language task elicited a late positive-going deflection in voltage potential—a P600 component—that has been linked with the processing of syntactic violations (Lelekov, Dominey, & Garcia-Larrea, 2000). Furthermore, topographic maps of the P600 effects showed similar distribution between conditions (Christiansen et al., 2012). Overall, these results provided some of the earliest direct, within-subject empirical evidence that the same neural mechanisms may be used for SSP and syntactic natural language processing (Christiansen et al., 2012).

However, more direct neural evidence of a link between SSP and natural language processing is needed, using different types of SSP and language tasks. Therefore, the purpose of this study was to investigate the relation between SSP and natural language processing by comparing the electrophysiological profiles elicited during each type of task, using a within-subject design. The SSP task was designed to resemble an artificial grammar learning (AGL) paradigm (Reber, 1967), in which complex statistical regularities are embedded in the sequences. One key aspect of the SSP task used in this study is that it is more purely non-linguistic in nature than previous SSP tasks using language-like stimuli (e.g., Christiansen et al., 2012) or stimuli that are readily verbalizable and easily mapped onto vocalizations (e.g., Patel et al., 1998). Evidence showing that similar neural responses are elicited during a more fundamentally non-linguistic SSP task and a natural language task would provide additional—and possibly more compelling—support that language processing is based in part on mechanisms utilized to extract and encode structured sequential information in a general-purpose manner.

It is possible our visual non-linguistic SSP task and our morpho-syntactic visual natural language processing task would both elicit a P600, similar to the Christiansen et al., (2012) findings. The authors of that study hypothesized that the P600 might reflect processing broadly involved with making predictions about upcoming items in a series, which is not confined solely to language (Christiansen et al., 2012). It is also possible our SSP task might elicit ERP components that have been associated with extraction and encoding of non-linguistic structured sequential patterns. Previous studies have suggested that the N200 (negative-going deflection, occurring approximately 200 milliseconds (ms) after stimulus onset) and P3b (positive-going deflection occurring approximately 300 ms after stimulus onset) components are elicited in sequential learning paradigms and may reflect the processing of expectancy violations (e.g., Carrion & Bly, 2007). Additionally, the P3a (positive-going deflection occurring approximately 250 ms after stimulus onset) has been evoked from “novel” stimulus paradigms (Courchesne, Hillyard, & Galambos, 1975), has been linked with the recognition of grammatical violations in a second language (Jakoby, Goldstein, & Faust, 2011), and has been associated with focused attention (Comerchero & Polich, 1999).

Given the present study was exploratory, we expected to observe any of the ERP components mentioned above. Consequently, the central hypothesis was simply that violations in a non-linguistic SSP task and violations in a morpho-syntactic natural language task would elicit similar electrophysiological response profiles.

**Method**

**Subjects**

Forty-three subjects (ages 18-22; 25 female) participated. All subjects were recruited from Saint Louis University, were native speakers of English, with normal to corrected-to-normal vision and who, at time of testing, reported no history of hearing loss, difficulty with speech, or history of cognitive, perceptual, or motor disorder.

**Experimental Paradigm**

Measures of SSP and language were administered separately in a single test session. All subjects performed the measure of SSP first and the measure of language second.

**Measure of SSP**

The measure of SSP was similar to the “Simon” visual-spatial SSP task used in previously published work (see Conway et al., 2010 for details). In this measure, subjects viewed sequences of 4 black squares appearing one at a time on a white background in 1 of 4 possible quadrants (upper left, upper right, lower left, lower right) (See Figure 1 below). The task was to reproduce each sequence immediately following presentation by touching the squares in the correct order on a touchscreen. Unknown to subjects, the measure of SSP consisted of two parts: a learning phase and a test phase, which differed in the types of sequences presented.

![Figure 1: SSP Task (on left) with rule structure (on right).](image-url)
In the learning phase, sequence elements were generated according to an underlying artificial grammar that specified the probability of a particular element in a sequence occurring given the preceding element (see Figure 1 above). For each sequence, the starting element (1-4) was randomly determined, and then the grammar was used to determine each subsequent element, until the full sequence length was reached. For example, given the starting element 3, the element 2 had a zero probability of occurring next, while the 1 and 4 elements had an equal (50%) chance of occurring. No element could follow itself in the sequence. The mapping of the rules to the locations was randomly determined for each subject; however, for each subject, the mapping remained consistent across all trials. All sequences were 5 elements long.

The learning phase consisted of 40 grammatical sequences. The phase began with a blank screen that appeared for 1 second. In the first part of the learning phase (20 sequences), each element in the sequence was displayed for 600 ms, followed by a 200 ms pause in which nothing was displayed on the screen. The final element in the sequence was followed by a 200 ms pause before the whole 2x2 grid of squares was displayed with a “Done” button in the middle. Using the touch screen, the subject then reproduced the sequence just presented, followed by pressing the word “Done”. Immediate feedback was given as to the correctness of each response. The second part of the learning phase (20 sequences) was the same as the first part, except each element in the sequence was displayed for 400 ms, followed by a 200 ms pause.

The test phase consisted of 64 sequences. One fourth of the sequences were “grammatical-trained” (i.e., the sequences were identical to grammatical sequences presented in the learning phase), one fourth were “grammatical-untrained” (i.e., new sequences sharing the same underlying structure as the other grammatical sequences), and one half were “ungrammatical” (i.e., the sequences violated the grammar). For the ungrammatical sequences, the starting element (1-4) was randomly determined, then any element could occur next in the sequence except repeating elements were not allowed. The timing of the test phase was identical to the timing used in the second half of the learning phase. The subjects were not told that this was a test phase or that there were different types of sequences (grammatical-trained, grammatical-untrained, and ungrammatical). From the perspective of the subject, the test phase was the same reproduction task they had been doing all along.

Scoring for the Measure of SSP For the test phase, a sequence was scored as correct if a subject correctly reproduced it. A score of 5 was given for each correctly reproduced sequence and was based on the length of each sequence. As in previous studies (e.g., Conway et al., 2010) a learning score was then obtained by subtracting the total score for the ungrammatical sequences in the test phase from the grammatical sequences in the test phase. A higher learning score indicates better performance on structured sequences compared to ones that violate the structure, suggesting that successful SSP occurred.

Measure of Language Sixty-four sentences were presented in the measure of language. These sentences varied according to whether or not they contained grammar violations. Thirty-two sentences were grammatically correct, and 32 sentences contained morpho-syntactic violations pertaining to verb agreement with the subject. For example, “The famous singer walks onto the stage.” was a grammatically correct sentence used in the task and “The famous singer walk onto the stage.” was a sentence with a violation. Each sentence began with a white fixation point (+) and was presented 1 word at a time in white text on a black screen. Each element (word or fixation point) appeared for 400 ms and was followed by a blank screen for 400 ms. Thirty-two 7-word sentences and 32 8-word sentences were presented. The 32 8-word sentences each contained an auxiliary verb. The target words (grammatical or violation) always occurred at the 4th word in the 7-word sentences and at the 5th work in the 8-word sentences. Target words were always verbs. The ratio of grammatically correct sentences to sentences with morpho-syntactic violations was 1:1, for each sentence length.

The phrase “Was that a good or a bad sentence? Press 1 for good, press 2 for bad.” appeared on the screen immediately following presentation of the final word in the sentence. The task was to make a keypad response on button 1 if the sentence was “good” and to respond on button 2 if the sentence was “bad.” Subjects were not given explicit instruction as to what “good” or “bad” meant (i.e., that grammatical sentences were “good” and sentences with violations were “bad”), nor were they told that some sentences were grammatical and some had violations. No feedback was given. A 1-second pause was given between a response and the presentation of the next sentence.

Scoring for the Measure of Language A sentence was scored correct if the subject made the correct grammaticality judgment for that sentence (i.e., a button press on “1”/“good” for grammatical sentences; a button press on “2”/“bad” for sentences with morpho-syntactic violations).

Expectancy Violations for Both the Measure of SSP and the Measure of Language Both measures were designed to cause violations in expectations of items occurring in a series (i.e., a violation of the learned sequence in the SL task and a violation of grammar in the language task). Event-related potentials (ERPs)—portions of ongoing electroencephalogram (EEG) time-locked to cognitive events of interest—were used to associated with these expectancy violations.
**EEG/ERP Data Acquisition and Preprocessing**

EEG was recorded during the test phase of the measure of SSP and throughout the measure of language using a 128-channel high-density sensor net with vertex recording reference (Electrical Geodesics, Eugene OR). Standard sensor net application techniques were followed. Recordings were made using NetStation acquisition software (Electrical Geodesics, Inc.), with a 0.1–100Hz bandpass filter and digitized at 250 Hz. Electrode impedances were kept below 50 kiloohms. Rest breaks were given as needed.

ERP for the measure of SSP was time-locked to the presentation of a stimulus that violated the artificial grammar and was compared to a stimulus in a similar position in a sequence that was grammatical. ERP for the measure of language was time-locked to the presentation of a word in the sentence that violated the morpho-syntactic grammar and was compared to a word in a similar position in a sentence that was grammatical.

Data was preprocessed using Netstation (Electrical Geodesics, Inc.). The continuous raw EEG recording was filtered through a 0.1 Hz high pass filter and a 30 Hz low pass filter. Channels were marked bad for a given trial if blinks or eye movements were detected, if amplitudes >150 µV, if the channel was flat (had zero variance), or if manual inspection suggested noise specific to that channel. Channels marked bad were interpolated in the raw EEG from data measured at nearby electrodes. After exclusion of artifacts, the continuous EEG was segmented into epochs in the interval -200 msec to +1000 msec with respect to the onset of the target stimulus (i.e., violation of grammar, for both the measure of SSP and the measure of language). Data were not re-referenced from the vertex channel.

Data from 3 subjects was excluded from analysis due to bad EEG channels that were either too high in number or too clustered together. Data from 8 subjects was excluded due to poor data quality or missing data. Therefore, data from a total of 32 subjects was analyzed.

**Regions of Interest**

Nine regions of interest (ROI) were defined for data analysis, with each containing 9 channels: frontal (FRz), central (CNz), posterior (POz), left anterior (LAn), left central (LCn), left posterior (LPo), right anterior (RAn), right central (RCn), and right posterior (RPo) (see Figure 2 below).

**Results**

**Behavioral Average Task Performance for the Measure of SSP and the Measure of Language**

Average accuracy given in percentage correct for reproduction of the three sequence types presented in the measure of SSP was as follows: 73% (grammatical-trained), 71% (grammatical-untrained), and 70% (ungrammatical). These three scores were not significantly different from one another (p=.999). Average accuracy given in percentage correct for the grammaticality judgment of the sentences presented in the measure of language was 93%.

**Electrophysiological Response Elicited by the Measure of SSP**

Visual inspection indicated a P3a component for ungrammatical sequences relative to both types of grammatical sequences in several ROI. Paired samples t-tests were conducted on the grand-averaged mean amplitude waveforms associated with the P3a component 270-330ms after the sequence violations, with significant effects in the central (CNz) [t(31)=3.968, p<.001], frontal (Frz) [t(31)=3.321, p=.002], and right anterior (RAn) [t(31)=2.303, p=.028] regions [See Figure 3 below for an example of the P3a effect in the frontal (Frz) region].

Correlations were computed between the grand-averaged mean amplitude waveforms associated with the significant P3a effects for ungrammatical sequences relative to both types of grammatical sequences and the averaged learning score on the measure of SSP (grammatical-ungrammatical). Results showed that learning score was significantly negatively correlated with the P3a effect in the frontal (Frz) region [r(31)= -.300, p=.05].

**Electrophysiological Response Elicited by the Measure of Language**

Visual inspection indicated a P600 component for ungrammatical sentences relative to grammatical sentence in several ROI. Paired samples t-tests were conducted on the mean amplitude waveforms associated with the P600.
the processing of syntactic violations. The task is consistent with findings from linguistic SSP tasks, the P3a to violations of a grammar (e.g., Opitz, Ferdinand, & Mecklinger, 2011). The presence of the P3a could be due to violations of the artificial grammar drawing attentional resources, corresponding with Bar’s (2007) “circular mechanism” of predictive processing previously described. The negative correlation between the SSP learning score—an indication of better performance on grammatical sequences—and the P3a effect for ungrammatical sequences relative to grammatical sequences supports this notion.

Although averaged behavior performance on the measure of SSP showed no learning effect as a group, the correlation between the SSP learning score and the ERP effect for the ungrammatical sequences suggests that even though an overall group learning effect was not observed, there is a distribution of learning scores that seem meaningful, with some individuals showing learning and others not showing learning. Future work will investigate whether individual differences in cognitive processes such as attention and working modulate learning of structured sequences.

One interpretation of the topomaps findings is that the P3a and P600 are distinct components, yet both reflect processes involving the detection of sequential violations in artificial and natural grammar processing tasks, respectively. It has been previously suggested that P300 and P600 components may both reflect the processing of incongruent information in different types of tasks (e.g., Christiansen et al., 2012). A similar role for both types of components, therefore, suggests some degree of overlap between SSP and language processing mechanisms.

The early phase of the P600 showed a distribution similar to the full P3a elicited in the SSP task, suggesting that they may have a common neural origin. Although the distribution of the full P3a is more confined than the full P600, this could be due to the relative unfamiliarity and limited exposure to the SSP task, whereas the wider scalp distribution of the P600 might be the result of the extensive and prolonged exposure humans have had with language. With more exposure to non-linguistic SSP tasks, the P3a elicited to violations in the artificial grammar might show similarities in the topographic profile for the two components; specifically, the early phase of the P600 (525-580ms) resembles the full P3a component. A correlation was computed between the difference waves (ungrammatical-grammatical) between the early phase of the P600 and the full P3a component. The results showed a positive correlation in the right anterior (RAn) region between the P3a (270-330ms) and the early P600 (525-580ms) that approached significance [t(32)=.291, p=.106].

**Discussion**

The present study provided some initial analyses comparing the electrophysiological responses elicited in a visual, non-linguistic SSP task and a visual morpho-syntactic natural language processing task. Following exposure to sequences that followed an embedded artificial grammar, subjects showed a P3a to violations of the grammar, while showing a P600 to morpho-syntactic violations in a visual natural language processing task. The P600 elicited in the language task is consistent with findings from paradigms that involve the processing of syntactic violations. The P3a elicited in

**Comparison Between the Electrophysiological Responses Underlying SSP and Language**

Topographical maps were created from ungrammatical minus grammatical difference waves associated with the P3a and P600 described above, to compare the scalp distribution of electrical activity for both components in the two tasks (See Figure 4 below). Visual inspection showed some similarities in the topographic profile for the two components; specifically, the early phase of the P600 (525-580ms) resembles the full P3a component. A correlation was computed between the difference waves (ungrammatical-grammatical) between the early phase of the P600 and the full P3a component. The results showed a positive correlation in the right anterior (RAn) region between the P3a (270-330ms) and the early P600 (525-580ms) that approached significance [t(32)=.291, p=.106].

**Figure 3:** P3a component in the frontal region and P600 component in the central region.

**Figure 4:** Topographic maps showing distribution of the P3a and P600 components, measured at the scalp.
robustness similar to the P600 elicited to violations in natural language grammar. On the other hand, the differences in the ERP correlates observed for the two tasks could instead be due to differences in the types of violations inherent to each (something akin to word order violations in the AGL task but subject-verb agreement violations in the natural language task).

Coulson, King, and Kutas (1998) noted similarities between the P600 and P3b elicited by manipulations to probability and saliency in an oddball paradigm. They concluded the P600 might be a part of the P300 family of components (Coulson et al., 1998). Still, similarity in distribution may not reflect similarity in neural generators [see Osterhout & Hagoort, 1999 (response to Coulson et al., 1998) for a more detailed discussion on cautions of attempting to determine similarity of neural mechanisms from EEG recorded at the scalp]. To help address this limitation, we are using source localization analyses to examine whether the components elicited in our two tasks share a common neural origin. Although preliminary, these findings suggest the possibility that the neurocognitive mechanisms involved in detecting sequential violations in a non-linguistic AGL task are similar to those involved in detecting morpho-syntactic violations in natural language, with the P3a possibly being an earlier version of the P600 or a reduced variant of it.

Acknowledgements


References


How the Brain Processes Linguistic and Nonlinguistic Structure:

The Anterior Superior Temporal Gyrus as a General-Purpose Pattern Processor

Gretchen N.L. Smith\textsuperscript{a} & Christopher M. Conway\textsuperscript{a}

\textsuperscript{a}Georgia State University
Department of Psychology
Atlanta, Georgia 30302-5010
United States
Abstract

Structured sequence processing (SSP) refers to the ability to acquire and process patterns of information from the environment over time. SSP appears to support knowledge and use of grammatical language. However, few studies have empirically associated these two processes directly at a neural level. The goal of this study was to examine the putative neural link between non-linguistic SSP and natural grammatical language processing. Healthy adult subjects (N=43) completed a visual-spatial (non-linguistic) SSP task and a grammatical language processing (reading comprehension) task. Source localization of event-related potentials showed that the electrophysiological responses elicited by the SSP and grammatical language processing tasks were associated with increased activation in left anterior superior temporal gyrus (STG). The striking overlap of neural activity elicited during the SSP and grammatical language processing tasks suggests that the anterior STG is part of a general-purpose “sequence processing network” that supports both non-linguistic SSP and natural language processing.

Keywords: Structured Sequence Processing; Sequence Learning; Grammatical Language Processing; Syntax; Event-Related Potentials; Source Localization
Introduction

Structured sequence processing (SSP), related to the constructs sequential learning and statistical learning, is a fundamental, general-purpose, neurocognitive mechanism used to learn patterns of information in the environment over time. SSP emerges early in development (Aslin, Saffran, & Newport, 1998; Kirkham, Slemmer, & Johnson, 2002; Saffran, Johnson, Aslin, & Newport, 1999) and is utilized throughout the lifespan for numerous aspects of cognition including perception, decision making, communication, motor skills, action planning, and musical experience (Bubic, von Cramon, & Schubotz, 2010; Clegg, DiGirolamo, & Keele, 1998; Herholz, Boh, & Pantev, 2011). SSP is largely automatic and implicit (Cleeremans, Destrebecqz, & Boyer, 1998), although there is evidence that explicit processing can occur in parallel with SSP (Batterink, Reber, Neville, & Paller, 2015; Sun, Slusarz, & Terry, 2005). SSP involves learning relatively complex patterns wherein each item that occurs next is determined probabilistically based on what item or items occurred previously, versus learning a simpler pattern such as a fixed, repeating sequence or a sequence generated deterministically (Conway & Christiansen, 2001). SSP is engaged across multiple modalities, including vision, audition, and even touch (Conway & Christiansen, 2005).

SSP has been operationalized extensively using variations of the artificial grammar learning (AGL) paradigm (Reber, 1967). In the AGL paradigm, strings (or sequences) of stimuli (e.g., letters, shapes, tones) are generated by a finite state grammar which transitions from one node to the next to produce full strings of elements, or exemplars. Learning can be assessed both through behavioral and neural measures, with facilitation observed for exemplars consistent with the grammar compared to items containing violations. SSP has also been instantiated by connectionist models of back-propagation networks (e.g., McClelland, Rummelhart, & the PDP
Research Group, 1986; Rumelhart, McClelland, & the PDP Research Group, 1986) and simple recurrent networks (e.g., Cleeremans, 1993; Elman, 1990) that reliably learn to predict the next element in a sequence based on information about the current element and the element that preceded it (Clegg et al., 1998).

A key aspect of SSP is that it serves as a tool for making predictions about which elements will occur next in a sequence (Christiansen, Conway, & Onnis, 2012). When sequential patterns are learned, this information can be used not only to generate expectancies about upcoming events, but also to detect when events deviate from expectation (Ferdinand, Mecklinger, & Kray, 2008). Bar (2007) describes this type of expectancy-driven cognition as a “circular mechanism” whereby top-down knowledge is recruited to limit cognitive resources for predictable stimuli, while bottom-up, sensory-level processing is engaged toward processing novel and/or unexpected stimuli. The brain’s tendency to predict what will occur next promotes processing efficiency that is generally beneficial to behavior (Bar, 2007).

SSP and predictive processing appear essential in the domain of language. In particular, SSP may support knowledge and use of grammatical language, such as word order (Conway, Bauernschmidt, Huang, & Pisoni, 2010), phonology (Saffran, 2003), and morphology/syntax (Ullman, 2004). Despite its intuitively ubiquitous presence in many facets of cognition, SSP is just beginning to gain traction in empirical investigations of how this core mechanism may support and modulate higher-order cognitive processes such as language. For example, only recently have behavioral studies demonstrated empirical links between SSP and natural language processing either by examining individual differences in SSP in typically-developing language users (e.g., Arciuli & Simpson, 2012; Conway et al., 2010; Conway, Karpicke, & Pisoni, 2007; Kidd, 2012; Misyak, Christiansen & Tomblin, 2010; Spencer, Kaschak, Jones, & Lonigan, 2014).
or by showing atypicalities to SSP in certain language and communication disorders (e.g., Conway, Pisoni, Anaya, Karpicke, & Henning, 2011; Evans, Saffran, & Robe-Torres, 2009; Grunow, Spaulding, Gómez, & Plante, 2006; Howard, Howard, Japiske, & Eden, 2006; Plante, Gómez, & Gerken, 2002).

1.1 Neural Mechanisms of SSP and Language Processing

A dearth of studies has experimentally compared these two mechanisms at a neural level, with most of the earlier investigations measuring SSP and language processing between different groups of subjects (e.g., Friederici, Steinhauer, & Pfeifer, 2002; Lelekov, Dominey, & Garcia-Larrea, 2000; Patel, Gibson, Ratner, Besson, & Holcomb, 1998). In the first of very few direct, within-subject neural studies in this area, Christiansen et al. (2012) used event-related potentials (ERPs)—portions of the ongoing electroencephalogram (EEG) time-locked to a cognitive event of interest—to examine the electrical responses elicited during a visual SSP task and a visual syntactic natural language processing task. The findings suggested both the SSP task and the syntactic language task elicited a P600 component, a late positive-going deflection in voltage potential that has been linked with the processing of syntactic violations (Osterhout & Holcomb, 1992). Furthermore, topographic maps of the P600 effects recorded at the scalp showed similar distribution between the SSP and syntactic language conditions. Christiansen et al. (2012) surmised that the P600 might reflect cognition broadly involved with making predictions about upcoming items in a series, processing that is not confined solely to language. Overall, these results provided some of the earliest direct, within-subject empirical evidence that the same neural mechanisms may be used for SSP and syntactic natural language processing (for similar findings, see also Daltrozzo et al., 2017; Tabullo, Sevilla, Segura, Zanutto, & Wainselboim, 2013).
In addition to the P600, other studies have suggested that the P3b component (a positive-going deflection occurring approximately 300 ms after stimulus onset) may reflect expectancy violations of non-linguistic SSP (Carrión & Bly, 2007; Jost, Conway, Purdy, Walk, & Hendricks, 2015; Schlaghecken, Stürmer, & Eimer, 2000), as well as expectancy violations of an artificial language grammar (e.g., Opitz, Ferdinand, & Mecklinger, 2011). A related component, the P3a (a positive-going deflection occurring approximately 250 ms after stimulus onset), has been evoked from “novel” stimulus paradigms (Courchesne, Hillyard, & Galambos, 1975), has been linked with the recognition of grammatical violations in a second language (Jakoby, Goldstein, & Faust, 2011), and has been associated with focused attention (Comerchero & Polich, 1999).

It is possible that the P300 and P600 components that have been elicited in SSP tasks reflect very similar underlying neural processes. Coulson, King, and Kutas (1998) examined the “oddball” response to infrequently occurring, unpredicted events and found similarities in the amplitudes and distribution of the P600 and the P300 components elicited by manipulating probability and saliency of syntactic violations presented in the experiment. Their primary conclusion was that the P600 is part of the broader family of P300 components. In contrast, it has been noted that similarity between components based on amplitude and topographical distribution may not reflect similarity in their underlying neural generators [see Osterhout & Hagoort, 1999 (response to Coulson et al., 1998) for a more detailed discussion on the cautions of attempting to determine similarity of neural mechanisms from EEG recorded at the scalp]. Still, it is worth considering that the P300 and P600 might not be completely distinct and that either component (or both) could be electrical correlates of SSP.

Evidence from behavioral lesion studies and from imaging studies using the AGL paradigm suggest that activity in inferior frontal cortex (IFC) [Brodmann areas (BA) 44/45, or
Broca’s area, which has largely been linked with language-specific functions, may be associated with performance on general-purpose SSP tasks (e.g., Abla & Okanoya, 2008; Bahlmann, Schubotz, & Friederici, 2008; Forkstam, Hagoort, & Fernández, 2006; Friederici, Bahlmann, Heim, Schubotz, & Anwander, 2006; Karuza et al., 2013; Opitz & Friederici, 2003; Petersson, Folia, & Hagoort, 2012). Furthermore, in an investigation of a putative causal relation between activity in Broca’s area and SSP, Uddén et al. (2008) found that offline repetitive transcranial magnetic stimulation (rTMS) to left BA 44/45 enhanced grammaticality classification in an AGL-based SSP task. According to Ullman (2001; 2008), the neurocognitive mechanisms supporting the acquisition of a range of sequentially or hierarchically organized rule-based cognitive and motor skills involve basal ganglia thalamocortical circuitry projecting to and looping back from posterior/dorsal regions of frontal cortex in Broca’s area corresponding to BA 44/45. In the macaque, basal ganglia project via the thalamus to pre-motor regions, including the supplementary motor area and F5 (Middleton & Strick, 2000; Ullman 2004), with F5 a possible homologue of BA 44 in Broca’s area (Rizzolatti, Fadiga, Gallese, & Fogassi, 1996).

Collectively, there is a growing body of empirical support indicating Broca’s area may be associated with global nonlinguistic SSP, rather than specialized language functions.

1.2 Current Study

Although the initial empirical investigations of a link between SSP and natural language processing are promising, additional neural evidence is needed using different types of tasks and analysis techniques. Specifically, a neural mechanistic approach toward clarifying the putative association between SSP and grammatical language processing would have value toward a richer understanding of the role of a general-purpose pattern processor in what has been traditionally been viewed as a domain-specific language network (Friederici, 2011).
The purpose of this study was to investigate the relation between SSP and grammatical language processing by comparing neural responses elicited in both types of tasks, using a within-subject design. The first analysis uses ERPs to compare the neural markers elicited in each type of task; the second uses source localization of the electrical responses to pinpoint the particular regions in the brain associated with each. One key aspect of the measure of SSP used in this study is that it is more purely non-linguistic than previous neural-based measures of SSP that used language-like stimuli (Christiansen et al., 2012) or stimuli that are readily verbalizable and/or easily mapped onto vocalizations (Patel et al., 1998). Evidence demonstrating that similar neural responses are elicited during a more non-linguistic measure of SSP and a measure of grammatical language would provide additional—and possibly more compelling—support that grammatical language processing is based on mechanisms used to extract and encode structured sequential information in a general-purpose manner. Furthermore, our two-pronged analysis approach was aimed to help elucidate the role of the P300 and P600 in SSP and language processing, while also specifying the underlying neural generators recruited for both by modeling the source of electrical activity involved with each of these constructs. This technique is useful for estimating the neural generators of SSP and grammatical language processing based on electrical activity, versus solely displaying their topographic distribution at the scalp.  

We predicted that we would observe a P600 elicited by our measure of grammatical language processing, in line with the generally shared view that this component reflects syntactic violations or grammar that is difficult to parse (Osterhout & Holcomb, 1992). As did Christiansen et al., (2012) it was possible we would also observe a P600 elicited by our measure

---

1 Modeling neural mechanisms in the brain based on electrical observations recorded at the scalp is known as “the inverse problem” leading to analytic constraints that can be addressed with certain data collection protocol and analysis approaches, but that cannot be fully solved. The “inverse problem” of source localization and our steps to reduce it will be discussed in greater detail in other sections below.
of SSP. On the other hand, given the similarity of our non-linguistic measure of SSP to other SSP tasks eliciting a P3b, it seemed just as likely we would observe a P300 component instead. As described earlier, it is possible that the P300 and P600 are not as distinct as might be believed, and merely differ mainly in terms of the timing of the associated cognitive process. Unlike other previous within-subject ERP comparisons of SSP and language (Christiansen et al., 2012; Daltrozzo et al., 2017; Tabullo et al., 2013), our analysis was not solely focused on latency, amplitude, and scalp distribution of the electrical responses to our measures. Rather, we also localized the source of electrical responses elicited by our measures of SSP and grammatical language processing, which we predicted would indicate the same neural generator. Specifically, given the evidence indicating Broca’s area may be associated with global rule-based SSP as well as the language network (Friederici, 2011), our hypothesis was that we would observe the same neural generators of electrical activity for SSP and grammatical language processing in Broca’s area and/or in neighboring regions of the putative language network having direct connections with Broca’s area, such as the superior temporal gyrus (STG).

Method

2.1 Subjects

Forty-three subjects (ages 18-22; 25 female) participated. All subjects were recruited from Saint Louis University, spoke English as the first language, had normal to corrected-to-normal vision, and reported no history of hearing loss, difficulty with speech, or history of cognitive, perceptual, or motor disorders. Subjects were either compensated monetarily or assigned credit as part of the Department of Psychology participant pool. Informed consent was obtained from each subject prior to experimentation.
2.2 Experimental Paradigm

Measures of SSP and grammatical language processing were administered separately in a single test session. All subjects performed the measure of SSP first and the measure of language second.

2.2.1 Measure of SSP. The measure of SSP was a version of the “Simon” visual-spatial SSP task used in previously published work (e.g., Conway et al., 2010). In this measure, subjects viewed sequences of black squares appearing one at a time on a white background in 1 of 4 possible quadrants (upper left, upper right, lower left, lower right) on a touchscreen (Figure 1 below). The task was to reproduce each sequence immediately following presentation by touching the squares in the correct order directly on the touchscreen. Unknown to subjects, the measure of SSP consisted of two parts: a learning phase and a test phase, which differed only in the types of sequences presented.

![Diagram of SSP task and rule structure](image)

*Figure 1. SSP Task (on left) with the rule structure (on right).*

In the learning phase, sequence elements were generated in accordance with an underlying artificial grammar that specified the probability of a particular element occurring given the preceding element (see Figure 1 above). This grammar (similar to ones used by Conway et al., 2010 and Jamieson & Mewhort, 2005) has an advantage over many other artificial
grammars commonly used in that there are no positional constraints. Each element of the grammar can occur at any position, with equal frequency. This means that position information, such as which elements or pairs of elements occur at the beginning versus the ending of sequences, cannot influence learning and, thus, is not a confound. This grammar is also considered to be relatively complex as measured, for instance, by Wilson et al.’s (2013) complexity metric.

For each sequence generated from this grammar, the starting element (1-4) was randomly determined, and then the grammar was used to determine each subsequent element, until the full sequence length was reached. For example, given the random starting element 3, the element 2 had a zero probability of occurring next, while the 1 and 4 elements had an equal (50%) chance of occurring. No element could follow itself in the sequence. The mapping of the rules to the locations was randomly determined for each subject; however, for each subject, the mapping remained consistent across all trials. All sequences were 5 elements long.

The learning phase consisted of 40 grammatical sequences (8 different grammatical sequences each presented 5 times). The phase began with a blank screen that appeared for 1 second. In the first part of the learning phase (20 sequences), each element in the sequence was displayed for 600 ms, followed by a 200 ms pause in which nothing was displayed on the screen. The final element in the sequence was followed by a 200 ms pause before the whole 2x2 grid of squares was displayed with a “Done” button in the middle. Using the touch screen, the subject then reproduced the sequence just presented, followed by pressing the word “Done”. Immediate feedback was given as to the correctness of each response. The second part of the learning phase (20 sequences) was the same as the first part, except each element in the sequence was displayed for 400ms, followed by a 200 ms pause.
The test phase consisted of 64 sequences (32 different sequences each presented 2 times). One fourth of the sequences were “grammatical-trained” (i.e., the sequences were identical to grammatical sequences presented in the learning phase), one fourth were “grammatical-untrained” (i.e., new sequences sharing the same underlying structure as the other grammatical sequences), and one half were “ungrammatical” (i.e., the sequences violated the grammar). Each element in an ungrammatical sequence was determined just like the elements in the grammatical sequences described above, except that the fourth element in the sequence always violated the grammar; the remaining items in the sequence followed the rules of the artificial grammar. The timing of the test phase was identical to the timing used in the second half of the learning phase. The subjects were not told that this was a test phase or that there were different types of sequences (grammatical-trained, grammatical-untrained, and ungrammatical). From the perspective of the subject, the test phase was the same reproduction task they had been doing all along.

2.2.2 Scoring for the Measure of SSP. A score of 1 was given for each correctly reproduced sequence (i.e., if all 5 elements were correctly reproduced, the sequence was scored a 1). A score of 0 was given for each incorrectly reproduced sequence (i.e., if all 5 elements were not correctly reproduced, the sequence was scored a 0). No partial credit was given for correctly reproducing only some of the sequence elements. Similar with previous studies (e.g., Conway et al., 2010), a learning score was then obtained by subtracting the total score for the ungrammatical sequences in the test phase from the grammatical sequences in the test phase. A higher learning score indicates better recall for structured sequences compared to ones that violate the structure.
2.2.3 Measure of Grammatical Language Processing. Sixty-four sentences were presented, 32 sentences that were grammatically correct, and 32 sentences containing morpho-syntactic violations pertaining to verb agreement with the subject. For example, “The famous singer walks onto the stage” would be a grammatically correct sentence and “The famous singer walk onto the stage” would be a sentence with a violation. Each sentence began with a white fixation point (+) and was presented 1 word at a time in white text on a black screen. Each element (word or fixation point) appeared for 400 ms and was followed by a blank screen for 400 ms. Thirty-two 7-word sentences and 32 8-word sentences were presented. The 32 8-word sentences each contained an auxiliary verb. The target words (grammatical or violation) always occurred at the 4th word in the 7-word sentences and at the 5th work in the 8-word sentences. Target words were always verbs. The ratio of grammatically correct sentences to sentences with morpho-syntactic violations was 1:1, for each sentence length.

The phrase “Was that a good or a bad sentence? Press 1 for good, press 2 for bad” appeared on the screen immediately following presentation of the final word in the sentence. The task was to make a keypad response on button 1 if the sentence was “good” and to respond on button 2 if the sentence was “bad.” Subjects were not given explicit instruction as to what “good” or “bad” meant (i.e., that grammatical sentences were “good” and sentences with violations were “bad), nor were they told that some sentences were grammatical and some had violations. No feedback was given. A 1-second pause was given between a response and the presentation of the next sentence. The same list of 64 sentences was presented to each subject. Sentences were presented in random order.

2.2.4 Scoring for the Measure of Grammatical Language Processing. A sentence was scored correct if the subject made the correct grammaticality judgment for that sentence (i.e., a
button press on “1”/“good” for grammatical sentences; a button press on “2”/“bad” for sentences with morpho-syntactic violations).

2.3 EEG/ERP Data Acquisition and Preprocessing

Both measures were designed to cause violations in expectations of items occurring in a series (i.e., a violation of the artificial grammar in the measure of SSP and a violation of natural grammar in the measure of grammatical language processing). ERPs were used to examine the electrical responses associated with these expectancy violations. EEG was recorded during the test phase of the measure of SSP and throughout the measure of grammatical language processing using a 128-channel high-density sensor net with vertex recording reference (Electrical Geodesics, Inc., Eugene OR). Standard sensor net application techniques were followed. Recordings were made using NetStation acquisition software (Electrical Geodesics, Inc.), with a 0.1–100Hz bandpass filter and digitized at 250 Hz. All electrode impedances were kept below 50 kΩ, with the majority of channels maintaining impedance levels below 20 kΩ throughout the experiment. Rest breaks were given as needed.

ERP for the measure of SSP was time-locked to the presentation of the element in the sequence that violated the artificial grammar and was compared to the same element in a sequence that was grammatical (for both sequence types this element was always element 4). ERP for the measure of language was time-locked to the presentation of a word in the sentence that violated the morpho-syntactic grammar and was compared to a word in a similar position in a sentence that was grammatical (this word was always element 4 for 7-word sentences and element 5 for 8-word sentences).

Data was preprocessed using Netstation (Electrical Geodesics, Inc.). The continuous raw EEG recording was filtered through a 0.1 Hz high pass filter and a 30 Hz low pass filter.
Channels were marked bad for a given trial if blinks or eye movements were detected, if amplitudes were >150 µV, if the channel was flat (had zero variance), or if manual inspection suggested noise specific to that channel. Channels marked bad were interpolated in the raw EEG from data measured at nearby electrodes. After exclusion of artifacts, the continuous EEG was segmented into epochs in the interval -200 msec to +1000 msec with respect to the onset of the target stimulus (i.e., violation of grammar, for both the measure of SSP and the measure of language). The categories that were segmented for both the measure of SSP and the measure of grammatical language processing pertained to the “grammatical” sequences or sentences and to the “ungrammatical” sequences or sentences. Data were not re-referenced from the vertex channel.

Data from 3 subjects were excluded from analysis due to bad EEG channels that were either too high in number or too clustered together. Data from 8 subjects were excluded due to poor data quality or missing data. Therefore, data from a total of 32 subjects were analyzed. Individual pre-processed ERP data files for the 32 subjects included in analysis were grand-averaged for both the measure of SSP and the measure of grammatical language processing.

2.4 Regions of Interest

Nine regions of interest (ROI) were defined prior to and for the ERP data analysis, with each containing 9 channels: frontal (FRz), central (CNz), posterior (POz), left anterior (LAn), left central (LCn), left posterior (LPo), right anterior (RAn), right central (RCn), and right posterior (RPo) (Figure 2 below).

2.5 Source Localization

Source localization takes measurements of the voltage potential recorded at the scalp to give a best fit estimate of the current generators inside the brain, thereby using extracranial EEG
observations and working backward to fit an intracranial model of neural activity represented by current dipoles (i.e., the inverse problem). A number software packages have been developed to estimate source localization that vary in their technical specifications and in the types of data that best suit their parameters, the scope of which is beyond the topic of this paper (for a review of various source localization approaches for solving the inverse problem see Grech et al., 2008). The accuracy of source localization is improved by reducing head-modeling/coordinate placement errors, maximizing the EEG signal-to-noise ratio (e.g., reducing channel impedance, extraneous electrical noise, and head and body movements of the subject), increasing the number of channels measuring voltage potential to >100 (Yamazaki, Tucker, Terrill, Fujimoto, & Yamamoto, 2013) and achieving spatial accuracy of the source localization ≤5 mm (Baillet & Garnero, 1997). Therefore, we ensured these conditions were met. We used the sLORETA approach to EEG source localization, which calculates the standardized current source density at certain voxels of an MNI-atlas brain based on a linear weighted sum of electrical voltage.

Figure 2. 2-D layout of the 128-channel sensor net (top represents the front of the net, the portion nearer to the nose when 3-D positioned). For data analysis, the channels were grouped into 9 regions of interest (outlined and labeled in black above), each consisting of 9 channels.
recorded at the scalp, then estimates their neural generators based on the assumption that the neighboring voxels have similar electrical activity (Nguyen, Matsumoto, Tran, Ono, & Nishijo, 2014). The sLORETA method of source localization has been validated for its precision up to zero localization error (Pascual-Marqui, 2002).

**Results**

**3.1 Behavioral Results**

Average correct reproduction percentage of the three SSP sequence types were as follows: 73% (grammatical-trained), 71% (grammatical-untrained), and 70% (ungrammatical). Although performance on the grammatical sequences was numerically higher than the ungrammatical sequences as expected if learning occurred, these three scores were not significantly different from one another ($p=.999$). Average percentage correct for the grammaticality judgment task was 93%. The scores indicated that subjects could, on average, perform both tasks at a level above chance, although for the measure of SSP they did not behaviorally distinguish among sequence types.

**3.2 Electrical Responses of SSP**

Visual inspection indicated a P3a component for ungrammatical sequences relative to both types of grammatical sequences in multiple ROI. Paired samples t-tests were conducted on the grand-averaged mean amplitude waveforms associated with the P3a component 270-330ms after the sequence violations, with significant effects in the CNz [$t(31)=3.968$, $p<.001$], FRz [$t(31)=3.321$, $p=.002$], and RAn [$t(31)=2.303$, $p=.028$] regions (See Figure 3 below for the P3a effect in the frontal region where this component is commonly observed).

Correlations were computed between the grand-averaged mean amplitude waveforms associated with the significant P3a effects for ungrammatical sequences minus both types of
grammatical sequences collapsed and the averaged learning score on the measure of SSP (grammatical minus ungrammatical). Results showed that the learning score was significantly negatively correlated with the P3a effect (ungrammatical minus grammatical) in the FRz region \( r(31) = -.300, p = .05 \).

**Figure 3.** In color. (Left top) P3a component recorded from sensors located in the frontal region and (left bottom) P600 component recorded from sensors located in the central/parietal region. (Right) Topographic distribution of electrical activity detected across the scalp for the P3a associated with the measure of SSP and the P600 associated with the measure of grammatical language processing.

### 3.3 Electrical Responses of Grammatical Language Processing

Visual inspection indicated a P600 component for ungrammatical sentences relative to grammatical sentence in multiple ROI. Paired samples t-tests were conducted on the mean amplitude waveforms associated with the P600 component 511-925ms after the syntactic violation, with significant effects in the CNz \( t(31) = 6.616, p < .001 \), RPo \( t(31) = 2.880, p = .007 \), LPo \( t(31) = 5.360, p < .001 \), RAn \( t(31) = 7.610, p < .001 \), LAn \( t(31) = 2.902, p = .007 \), LCh \( t(31) = 3.433, p = .002 \) regions (See Figure 3 above for the P600 effect in the central/parietal region where this component is commonly observed).
Taken together, the ERP results suggest our measures of SSP and grammatical language processing elicited P3a and P600 responses, respectively.

3.4 Topographic Distribution of Electrical Responses

Difference waves for both the measure of SSP and the measure of grammatical language processing were calculated by subtracting the grammatical waveforms from the ungrammatical waveforms associated with the measure of SSP and the measure of grammatical language processing. Topographical maps were created from the difference waves associated with the P3a and P600, to compare the scalp distribution of electrical activity for both components in the two tasks (Figure 3 above). For the measure of SSP the grammatical-trained and grammatical-untrained waveforms were first collapsed and then entered into the ungrammatical minus grammatical difference wave. Although the P600 shows a much more widespread distribution of electrical activity, especially in the later phases of the component, Figure 3 also suggests similarities in the topographic profiles between the two components. Specifically, the earliest phases of the P600 (511ms-539ms) resembled the full P3a. This qualitative exploration suggests similar topographic distributions for the two components.

3.5 Source Localization of Electrical Responses

The measurements of voltage potential for the ungrammatical minus grammatical difference waves associated with the P3a in the latency period 270-330 ms post-sequence violation and with the P600 in the latency period 511-925ms post-syntactic violation were analyzed using sLORETA to estimate the source location of electrical activity elicited by each task. The minimum norm estimates (MNEs; estimates of current density) of the dipoles activated by the measure of SSP and measure of grammatical language processing were extracted and analyzed to determine if they were correlated.
For the measure of SSP, source localization with sLORETA at 300ms revealed the highest levels of activation in the anterior region of the left superior temporal gyrus (STG) for sequences that contained a violation relative to non-violation sequences (Figure 4 below; highest levels of activation = yellow). For the natural language task, source localization with sLORETA at 600ms revealed bilateral activation in the anterior region of the STG for sentences that contained a syntactic violation relative to non-violation sentences (Figure 4 below; highest levels of activation = yellow). The minimum norm estimates (MNEs) of the current density of dipoles activated by the measure of SSP and the measure of grammatical language processing were significantly positively correlated ($r(56)=.426$, $p=.001$).
Figure 4. In color. (Top) sLORETA source localization (SSP ungrammatical > SSP grammatical) at 300ms; (Bottom) sLORETA source localization (syntax ungrammatical > syntax grammatical) at 600ms. (Top & Bottom) Highest levels of activation (colored yellow) show overlap in left anterior STG.

Discussion

We examined the electrical activity in the brain while subjects engaged in a non-linguistic SSP task and a grammatical language processing task. Similar with previous research (e.g., Christiansen et al., 2012; Tabullo et al., 2013), we expected to observe overlap in the neural mechanisms recruited for both types of tasks. However, unlike previous research, our primary aim was to compare the sources of electrical activity generated in the brain versus solely analyzing the ERP waveforms and topographic distribution across the scalp. Although we took a number of steps to promote accuracy with our source localization analysis, lending as much support of overlap between the mechanisms supporting SSP and grammatical language processing as we believe is afforded by this technique, we acknowledge it is not possible to completely solve the inverse problem to estimate neural generators inside the brain. Future investigations using imaging techniques such as functional magnetic resonance imaging (fMRI) and diffusion tensor imaging to further examine the underlying neural mechanisms recruited for general-purpose SSP and grammatical language processing are necessary to provide converging evidence toward our present findings.

4.1 ERP Responses to the Measures of SSP and Grammatical Language Processing

Following exposure to visual sequences that followed an artificial grammar, subjects showed a P3a to violations of the grammar, consistent with previous AGL ERP studies showing a P300 component in response to violations (e.g., Opitz, Ferdinand, & Mecklinger, 2011). The same subjects also showed a P600 to morphosyntactic violations in a visual natural language
processing task, consistent with findings from paradigms that involve the processing of syntactic violations (Osterhout & Holcomb, 1992). Previous research indicates that the P3a component is associated with attentional focus (Comerchero et al. 1999), as would be expected if learning is taking place. That is, the presence of the P3a could be due to violations of the artificial grammar drawing attentional resources, corresponding with Bar’s (2007) “circular mechanism” of predictive processing whereby the brain reduces cognitive resources for stimuli that are predictable, while allotting additional resources to stimuli that are novel and/or unpredicted.

Following this line of reasoning, the negative correlation between the SSP behavioral learning score and the P3a ERP effect could indicate that a greater allocation of attention to the ungrammatical sequences improves recall for the ungrammatical sequences. With better performance on the ungrammatical sequences, the learning difference score would become smaller, thus explaining the negative correlation. This is a somewhat counter-intuitive result and it suggests that while the behavior and the neural measures are related, in that they both reflect learning, they are tapping into slightly different aspects of the process. Overall, it appears that subjects had learned to predict and expect grammatical sequences but when presented with a violation of a grammatical sequence, their attention was focused on the unexpected input. This, in turn, suggests that although we operationalized learning through the behavioral difference score of grammatical minus ungrammatical, there may also be a second consequence of learning, which is better recall for the ungrammatical sequences due to a greater devotion of attention to the sequences that violate the grammar. This perspective could also explain why behavioral accuracy scores on the SSP task showed no difference between ungrammatical and grammatical sequence types. In sum, there would seem to be two conflicting effects of learning the sequential regularities in the SSP task. On the one hand, recall improves for grammatically-consistent
sequences as has been shown in previous AGL studies (e.g., Conway et al., 2010), but on the other hand, learning of the grammar can lead to better recall on the ungrammatical sequences as well, due to a focusing of attention. One way or another, there appears to be a distribution of behavioral learning scores that appear meaningful and that result in different levels of electrical activity for the P3a effect.

In terms of the topographic distributions of the two components, the close similarity that was observed between the P3a and P600 elicited in the SSP and language tasks could suggest that these two components both reflect processes involving the detection of sequential violations (e.g., Christiansen et al., 2012). The early phase of the P600 showed a distribution similar with the full P3a elicited in the SSP task, qualitatively suggesting that they may have a common neural origin. Although the distribution of the full P3a is more confined than the full P600, this could be due to the relative unfamiliarity and limited exposure to the SSP grammatical regularities, whereas the wider scalp distribution of the P600 might be the result of the extensive and prolonged exposure our subjects have had with natural language. It is possible that with more exposure to non-linguistic sequences generated from the artificial grammar, the P3a elicited for violations to the artificial grammar might begin to resemble the P600 elicited for violations of natural language grammar in terms of distribution. On the other hand, the differences in the ERP correlates observed for the two tasks could instead be due to differences in the types of violations inherent to each (something parallel to word order violations in the AGL task but subject-verb agreement violations in the natural language task).

4.2 Source Localization of Electrical Activity: The Role of the STG

As previously mentioned, Coulson et al., (1998) noted similarities between the P600 and the P3b elicited by manipulations to probability and saliency in an oddball paradigm and
concluded the P600 might be a part of the P300 family of components. However, as with the Christiansen et al. (2012) study and our own present study, there are challenges to making claims about the similarity of neural mechanisms in the brain from EEG measurements taken at the scalp. To help address this limitation, we used the sLORETA source localization method to examine whether the electrical activity elicited by our measures of SSP and grammatical language processing shared a common neural origin. The source localization activity during the two tasks revealed a striking overlap in the anterior STG, with the MNEs of dipole current density elicited in the two tasks significantly correlated with one another. These source localization findings using a non-linguistic measure of SSP provide a stronger level of support for shared neural mechanisms between non-linguistic SSP and natural language processing than has been previously demonstrated from AGL paradigms using linguistic stimuli (e.g., Friederici, Makuuchi, & Bahlmann, 2009).

What is the role of the anterior STG, which was activated in both tasks? It is known that the STG is an integral part of the language network (Friederici, 2011), connecting with Broca’s area encompassing BA 44/45 and the deep frontal operculum (FOP) via the ventral pathway (Anwander, Tittgemeyer, von Cramon, Friederici, & Knösche, 2007; Friederici, 2011; 2012), which is thought to play a critical role in human syntactic processing (Friederici, 2004). Using fMRI, Friederici, Rüschemeyer, Hahne, and Fiebach (2003) observed increased activation to syntactic violations in the left anterior STG, in the left posterior FOP, and in the putamen of the left basal ganglia, whereas they observed no activation in BA 44/45—the traditional Broca’s area in humans. Findings from more recent studies using functional and structural imaging analyses suggest computation of sequences with adjacent dependencies activate FOP and anterior STG, whereas computation of sequences with non-adjacent dependencies activate FOP and BA 44/45.
Friederici et al. (2006) reasoned that FOP may support the evaluation of the incoming element against the predicted element and, thus, responds in a general manner to any violations of sequential structure whenever they are encountered. The anterior STG together with FOP is recruited for an early phase of structure building when local, adjacent syntactic dependencies are processed (Friederici, Wang, Herrmann, Maess, & Oertel, 2000). Additional recruitment of BA 44/45 (Broca’s area) is needed only when the sequential structure involves non-adjacent dependencies/long-distance transitional probabilities, possibly modulated by the amount of demand on working memory (Friederici et al., 2006). These authors further postulated an evolutionary development of SSP—from the phylogenetically older FOP for processing transitional probabilities in general to the phylogenetically younger Broca’s area for processing hierarchical structure specifically—concluding that different brain regions may support general-purpose SSP computations, but still have domain specificity as part of the language network (Friederici et al., 2006).

Additionally, it has been suggested that left STG is recruited for fine-grained semantic-type interpretation pertaining to extraction of and encoding of literal or contextually relevant meaning, while right STG does essentially the same computation but in a much broader fashion in order to get the gist of the meaning (Jung-Beeman, 2005). Bilateral activation of the anterior STG is recruited specifically for semantic integration—linking input at the message level—in order to detect when the input deviates from the global context (Jung-Beeman, 2005). Our finding showing left-lateralized anterior STG activation only for the measure of SSP makes sense, given it would arguably be more difficult for healthy adults to process the global context
for patterns in a relatively new and unfamiliar non-linguistic SSP task than it would to process the global context for patterns in a natural language reading comprehension syntax task.

Consistently, much of the recent research on SSP has focused on Broca's area being a domain-general sequence processor as part of a domain-specific “language network” that includes STG. Our findings support the notion that SSP recruits anterior STG, a region known to have connections with FOP and BA 44/45 via the ventral pathway. We propose the neural circuitry including anterior STG, FOP, and BA 44/45 is not a “language network” with certain regions performing general-purpose computations, but rather this system is a “sequence processing network” that happens to be engaged by language, motor, and other cognitive domains that necessitate it. In a recent comparative fMRI investigation using an auditory SSP paradigm involving adjacent dependencies, violations to the artificial grammar activated ventral FOP in humans and its functional counterpart in rhesus macaques (Wilson et al., 2015). These findings provide some of the first empirical evidence that certain ventral frontal regions recruited for language in modern-day humans originally evolved in our ancestors to support general-purpose SSP (Wilson et al., 2015). The anterior STG in the macaque has also been identified as a pattern processor with projections to the ventral and orbital prefrontal cortex (Karnath, 2001), and macaque ventral temporal-frontal circuitry similar with such circuitry in humans projects to the macaque homologue of human Broca’s area (Petrides & Pandya, 2009). One intriguing possibility is that humans and certain non-human primates do not diverge in their acquisition of language because of differences in their respective sequence processing networks per se, but rather because of differences in executive functions such as attentional control or working memory capacity that may be necessary for processing the hierarchical, long-distance dependencies so abundant in modern human language (Diego-Balaguer, Martinez-Alvarez, &
Pons, 2016; Friederici, 2004; Rauschecker, 2012). It would be informative for comparative studies on this topic to include chimpanzees—a genus closer to humans—to further clarify the mechanisms supporting the development of hierarchical, recursive language.

**Summary/Conclusion**

We observed marked overlap in the left anterior STG as the source of electrical activity elicited by a measure of general-purpose, non-linguistic SSP and a measure of grammatical natural language processing. These findings, taken together with an emerging evolutionary framework, suggest previous conceptualizations that connections in FOP, anterior STG, and BA 44/45 are part of a “language network” should be reconsidered. We propose that these regions constitute a general-purpose “sequence processing network” that pre-dates language, and that the evolution of hierarchical language might pivot more on the capacities of other cognitive domains, such as attentional control and working memory.
Acknowledgements

A portion of this research was initially conducted as part G.N.L. Smith’s dissertation while at Georgia State University, Department of Psychology, Cognitive Sciences and while a GSU Language & Literacy Graduate Fellow.

We would like to thank Juan Galvis, Nick Buchholz, Jerome Daltrozzo, Gwen Frishkoff, Rocky Haynes, Elizabeth Hilvert, Sanjay Pardasani, Pooja Parupalli, J.D. Purdy, Ben Rickles, Grace Signiski, Sonia Singh, Ryan Town, Gerardo Valdez, Anne Walk, and Kate Winderman for their contributions, as well as 5 anonymous reviewers who commented on an earlier version of these data.

Funding: This work was supported by the National Institutes of Health, R01DC012037 awarded to Christopher M. Conway.
Appendix A
Learning and Test Sequences for the Measure of Structured Sequence Processing

<table>
<thead>
<tr>
<th>Learning Sequences</th>
<th>Test Sequences (Gram-T)</th>
<th>Test Sequences (Gram-UT)</th>
<th>Test Sequences (U-Gram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4-3-1-4</td>
<td>1-4-3-1-4</td>
<td>1-4-3-4-3</td>
<td>1-4-3-2-1</td>
</tr>
<tr>
<td>1-4-2-1-2</td>
<td>1-4-2-1-2</td>
<td>1-4-2-3-1</td>
<td>1-4-3-2-3</td>
</tr>
<tr>
<td>1-2-1-2-1</td>
<td>1-2-1-2-1</td>
<td>1-2-1-4-2</td>
<td>1-4-2-4-3</td>
</tr>
<tr>
<td>1-2-3-4-3</td>
<td>1-2-3-4-3</td>
<td>1-2-3-1-4</td>
<td>1-4-2-4-2</td>
</tr>
<tr>
<td>2-1-4-2-3</td>
<td>2-1-4-2-3</td>
<td>2-1-4-3-4</td>
<td>1-2-1-3-1</td>
</tr>
<tr>
<td>2-1-2-3-1</td>
<td>2-1-2-3-1</td>
<td>2-1-2-1-2</td>
<td>1-2-1-3-4</td>
</tr>
<tr>
<td>2-3-1-4-2</td>
<td>2-3-1-4-2</td>
<td>2-3-1-2-1</td>
<td>1-2-3-2-1</td>
</tr>
<tr>
<td>2-3-4-3-4</td>
<td>2-3-4-3-4</td>
<td>2-3-4-2-3</td>
<td>1-2-3-2-3</td>
</tr>
</tbody>
</table>

Note: Gram-T, Grammatical-Trained; Gram-UT, Grammatical-Untrained; U-Gram, Ungrammatical
## Appendix B

### Sentences Used for the Measure of Grammatical Language Processing

<table>
<thead>
<tr>
<th>Grammatical 7 Word Sentences</th>
<th>Ungrammatical 7 Word Sentences</th>
</tr>
</thead>
<tbody>
<tr>
<td>The tired boy sleeps in his bed.</td>
<td>The brave man catch the dumb thief.</td>
</tr>
<tr>
<td>The cute bunny eats a fresh carrot.</td>
<td>The famous singer walk onto the stage.</td>
</tr>
<tr>
<td>The funny clown spills the cold water.</td>
<td>The nice nurses helps the sad child.</td>
</tr>
<tr>
<td>The proud soldier carries a heavy backpack.</td>
<td>The wild ducks splashes in the pond.</td>
</tr>
<tr>
<td>The clever students find the lost cow.</td>
<td>The happy baby laugh at the puppy.</td>
</tr>
<tr>
<td>The slim turtles crawl under a rock.</td>
<td>The strong fireman carry a heavy hose.</td>
</tr>
<tr>
<td>The famous artist draws a funny cartoon.</td>
<td>The nice teacher speak to the class.</td>
</tr>
<tr>
<td>The shy boy talks to his friend.</td>
<td>The shy lizard hide under a rock.</td>
</tr>
<tr>
<td>The kind nurse asks me some questions.</td>
<td>The hungry mouse eat cheese and fruit.</td>
</tr>
<tr>
<td>The curious child looks in the window.</td>
<td>The slow snail crawl across the trail.</td>
</tr>
<tr>
<td>The tired soldiers walk to their tent.</td>
<td>The pretty ladies smiles at the children.</td>
</tr>
<tr>
<td>The furry kittens play with a string.</td>
<td>The brave pilots flies in bad weather.</td>
</tr>
<tr>
<td>The sleepy turtles rest on the beach.</td>
<td>The wild horses jumps over the fence.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grammatical 8 Word Sentences</th>
<th>Ungrammatical 8 Word Sentences</th>
</tr>
</thead>
<tbody>
<tr>
<td>The talented artist will paint a beautiful picture.</td>
<td>The tiny baby will drinking milk all day.</td>
</tr>
<tr>
<td>The white cat will lick its front paw.</td>
<td>The old dog will barking at the mailman.</td>
</tr>
<tr>
<td>The graceful dancer is smiling at the audience.</td>
<td>The busy farmer is drives a green tractor.</td>
</tr>
<tr>
<td>The helpful teacher is reading from a book.</td>
<td>The little pony is carries the young child.</td>
</tr>
<tr>
<td>The hungry girls will eat in the kitchen.</td>
<td>The friendly ladies will helping the new neighbor.</td>
</tr>
<tr>
<td>The big dogs will sleep in the doghouse.</td>
<td>The fast horses will running around the track.</td>
</tr>
<tr>
<td>The little babies are touching the shiny toy.</td>
<td>The friendly doctors are listen to my heart.</td>
</tr>
<tr>
<td>The sleepy lions are resting under a tree.</td>
<td>The silly monkeys are swing through the trees.</td>
</tr>
<tr>
<td>The kind babysitter will tell a funny story.</td>
<td>The good doctor will looking in my ear.</td>
</tr>
<tr>
<td>The proud lion will roar at the zebras.</td>
<td>The tall pilot will flying a fast airplane.</td>
</tr>
<tr>
<td>The nice lady is buying us a toy.</td>
<td>The calm dentist is speaks to the patient.</td>
</tr>
<tr>
<td>The clever boys will build a sand castle.</td>
<td>The tame horse is runs into the barn.</td>
</tr>
<tr>
<td>The sleepy pigs will sleep in the mud.</td>
<td>The large elephants will walking down the road.</td>
</tr>
<tr>
<td>The young girls are dancing on the stage.</td>
<td>The green frogs will jumping into the water.</td>
</tr>
<tr>
<td>The thirsty tigers are drinking from a river.</td>
<td>The kind ladies are sing the slow song.</td>
</tr>
<tr>
<td></td>
<td>The little puppies are play with the children.</td>
</tr>
</tbody>
</table>
References


doi:10.1371/journal.pbio.1000170


Appendix C
TRAINING AND PLASTICITY OF STRUCTURED SEQUENCE PROCESSING AND
NATURAL LANGUAGE GRAMMAR: A PROOF OF CONCEPT STUDY

Gretchen N.L. Smith & Christopher M. Conway
Department of Psychology, Georgia State University
Atlanta, United States
Introduction

Six- to eight-million children and adults in the United States have some form of difficulty with language processing (NIDCD, 2016), which can be either developmental (e.g., Autism Spectrum Disorder) or acquired (e.g. aphasia following stroke). Individuals who struggle with language face serious and cascading consequences to quality of life, including but not limited to areas such as school, work, and social interaction (NIDCD, 2017). Consequently, there is a great need to design effective language interventions that are cost-effective, accessible, easy to implement, and have the potential to start improving language outcomes relatively quickly. Traditional interventions generally focus on directly improving behavioral language and communication abilities through explicit instruction with vocabulary, phonology, and syntax. (Law, Garrett, & Nye, 2010). However, an alternative approach is to identify core neurocognitive mechanisms that are believed to be crucial to language processing and development, and then design interventions that target those mechanisms with the expectation that such improvements would generalize to language functions. Such approaches that target the neurocognitive mechanisms recruited for language processing could be a promising way to use the brain’s potential for plasticity (Kleim & Jones, 2008; van Praag, Kempermann, & Gage, 2000) functionally to reorganize disrupted circuitry to help language processing become more efficient.

One such core mechanism is structured sequence processing (SSP), closely related to the constructs implicit learning (Reber, 1989), statistical learning (Saffran, Aslin, & Newport, 1996), sequence learning (Bullmer et al., 1987), and procedural learning (Ullman 2004; 2008). SSP can be thought of as a fundamental, general-purpose, neurocognitive mechanism that is used to learn patterns of information in the environment over time in a largely automatic and implicit manner. SSP is likely utilized for making efficient and accurate predictions about what events will occur
next, which is generally beneficial to everyday functioning (Bar, 2007). Crucially, SSP is particularly important for the development and use of language, allowing for the discovery and learning of the structure inherent in grammatical and predictive-based language processing such as word order (Conway et al., 2010), phonology (Saffran, 2003) and morphology and syntax (Ullman, 2004). Furthermore, disturbances to SSP are found in several language and communication disorders, including Autism Spectrum Disorder (Klinger et al., 2007), dyslexia (Vicari et al., 2003), agrammatism (Christiansen et al., 2010), specific language impairment (Tomblin et al., 2007), and hearing loss (Conway et al., 2011).

In our recent work, we have shown that a computerized training regimen designed to target SSP abilities can potentially modulate both SSP and language processing in healthy adults (Smith, Conway, Bauernschmidt, & Pisoni, 2015). To further explore these training-related effects, the current study attempts to determine how such training impacts the neural responses underlying SSP and grammatical language processing. Before describing the study in detail, we first briefly review several computerized cognitive training studies that inspired our training program, and then discuss the possible neural effects that we might expect such training to impact.

**Computerized Cognitive Training**

Evidence suggests that it may be possible to use computerized training techniques to improve aspects of cognitive processing. One cognitive domain that has received a great deal of coverage in the cognitive training literature is working memory (WM). WM refers to the temporary storage and manipulation of information necessary for complex cognitive tasks (Baddeley, 1992). Whereas the WM training tasks and populations have varied, the general goal of the WM training studies was to determine if WM training regimens could improve WM
capacity and show transfer to non-trained WM tasks, attention, and other cognitive functions such as fluid intelligence or mathematic reasoning. In one of the seminal studies out of the CogMed WM training research group (CogMed; Stockholm, Sweden), Klingberg and colleagues (2002; 2005) designed a computerized WM training task that was originally used with children with ADHD (Klingberg, Forssberg, & Westerberg, 2002; Klingberg et al., 2005). Participants performed several visuospatial and/or verbal WM tasks over a period of 5 weeks. The visuospatial task involved remembering and repeating the position of objects on a 4 x 4 grid, and the verbal task required remembering and repeating phonemes, letters and digits (Klingberg et al., 2005). Difficulty level of the tasks was adapted to match each child’s performance. It was hypothesized that the adjustment of difficulty level continually to match the child’s performance was a critical manipulation, keeping the children engaged in the training without it being too easy or too difficult. A control group performed the same tasks, except the length of items to recall remained constant rather than adapting to performance level. At post-training sessions both 5 to 6 weeks and 3 months following the baseline measures, participants showed significant improvement compared to the control group for non-trained WM tasks and improvement for non-trained executive tasks including digit span, the Stroop task, and Raven’s matrices.

Overall, the results from numerous WM training studies suggest that WM can be enhanced through adaptive computerized training (e.g., Brehmer, Westerberg, & Backman, 2012; Holmes & Gathercole, 2013; Kronenberger, Pisoni, Henning, Colson, & Hazzard, 2011). In addition, WM training may also transfer from one domain to another, or generalize, to nontrained tasks of WM and other aspects of cognition such as inhibition (Klingberg, Forssberg, & Westerberg (2002); Klingberg et al., 2005; Olesen, Westerberg, & Klingberg, 2004), attention
(Westerberg et al., 2007), and verbal WM (Thorell, Lindqvist, Bergman Nutley, Bohlin, & Klingberg, 2009).

Although there has been critique about the effectiveness of WM training (e.g., Melby-Lervag & Hulme, 2013; Shipstead, Redick, & Engle, 2012), centered primarily on aspects of methodology and on the validity and replicability of the generalizable transfer of WM capacity to non-WM domains, the findings from the relatively large body of WM training literature still show some promise that WM and other aspects of cognition such as SSP can be modifiable by training and experience. Using these WM training studies as inspiration, we have recently demonstrated that it is possible to behaviorally improve SSP through cognitive training and that SSP may serve as a mediator between computerized training and language outcomes (for details see Smith et al., 2015). This study was a promising step toward understanding the behavioral process by which SSP and grammatical language processing interact with each other. Furthermore, using a type of training designed to impact statistical learning, Onnis, Lou-Magnuson, Yun, and Thiessen (2015) demonstrated that training could modulate a behavioral preference to process strings of phonemes according to forward or backward transition probabilities. SSP and implicit statistical learning are tightly coupled constructs; therefore, this early evidence showing that they both can be modified by training is encouraging. However, the neural mechanisms underlying the effects of such training have not been examined, and it is not completely clear if improvements to SSP would result in gains to language functions.

**Potential Neural Components Related to SSP and Grammatical Language Processing**

Event-related potentials (ERPs)—portions of the ongoing electroencephalogram (EEG) timelocked to a cognitive event of interest—is an approach for measuring task-related neural activity. The ERP components of interest that have been previously been shown to be elicited by
measures of SSP and grammatical language processing are the P3a/P3b and P600, respectively. These components are known to be broadly related to attention, sequencing, memory, and grammatical language processing (for more details on each component see Luck, 2005). Accordingly, we predicted that these ERP components would show modulations following SSP training.

**P3a/P3b components.** The P3b is a positive deflection in voltage potential typically with central/parietal maximum amplitude (Fjell, Walhovd, Fischl, & Reinvang, 2007) that appears approximately 300 ms after stimulus onset (Eimer, Goschke, Schlaghecken, & Stuermer, 1996; Ferdinand, Mecklinger, & Kray, 2008). The P3b reflects the evaluation of incoming information and the updating of contextual representations (Ferdinand et al., 2008) and WM (Kok, 2001). It has been associated with the allocation of attentional resources (Patel & Azzam, 2005; Rueda et al., 2005) and/or consciously-mediated or controlled processing mechanisms (Jost, Conway, Purdy, Walk, Hendricks, 2015).

A variant of the P3b is the P3a, a positive deflection in voltage potential with frontal/central maximum amplitude and peak latency approximately 250 ms after stimulus onset (Comerchero & Polich, 1999). The P3a has been evoked from “novel” stimulus paradigms (Courchesne, Hillyard, & Galambos, 1975), has been linked with the recognition of grammatical violations in a second language (Jakoby, Goldstein, & Faust, 2011), and has been associated with a stimulus context requiring a great deal of attentional focus (Comerchero & Polich, 1999).

**P3b/P3a in SSP-related paradigms.** The P3b component has been elicited in SSP-related paradigms, with evidence suggesting it may reflect expectancy violations of non-linguistic SSP (Carrión & Bly, 2007; Jost, Conway, Purdy, Walk, & Hendricks, 2015; Schlaghecken, Stürmer, & Eimer, 2000), and/or expectancy violations of an artificial language
grammar (e.g., Opitz, Ferdinand, & Mecklinger, 2011). The P3b has also been elicited by the “oddball” paradigm, in response to infrequently occurring, unpredicted events (e.g., Coulson, King, and Kutas, 1998). In addition, the P3a component has been elicited in a visuospatial SSP paradigms, possibly indicating that violations of the artificial grammar pulled attentional toward the stimuli that were novel/and or unexpected (Smith & Conway, 2017; see Bar (2007) for a description of how a “circular mechanism” of predictive processing whereby predictable stimuli are inhibited, while novel and/or unpredicted stimuli attract attentional focus). Given that both the P3b and the P3a have been observed in SSP-related paradigms involving artificial grammar violations and/or unexpected events into the sequences of stimuli, we predicted at least one of these P300-family variants would be elicited by the measure of SSP used in the present study.

**P600 component.** The P600 component is a positive deflection in voltage potential with central/parietal or frontal maximum amplitude and peak latency at approximately 600 ms after stimulus onset that has been linked with the processing of syntactic violations (Neville, Nicol, Barss, Forster, & Garrett, 1991; Osterhout & Holcomb, 1992; Smith & Conway, 2017). It has also been reasoned that the P600 reflects cognition broadly involved with making predictions about upcoming items in a series, processing that is important for language but not confined solely to language (Christiansen, Conway, & Onnis, 2012).

Initial evidence for the postulation the P600 may reflect processing related to SSP as well as language came from between-subject comparisons of performance on SSP-like artificial grammar learning (AGL; Reber, 1967) paradigms and performance on natural syntactic language paradigms (e.g., Friederici, Steinhauer, & Pfeifer, 2002; Lelekov, Dominey, & Garcia-Larrea, 2000; Patel, Gibson, Ratner, Besson, & Holcomb, 1998). In the first of very few direct, within-subject neural studies in this area, Christiansen et al. (2012) examined the electricalphysiological
responses elicited during a visual SSP task and a visual syntactic natural language processing task. The findings suggested both the SSP task and the syntactic language task elicited a P600 component to grammar violations (i.e., violations to the artificial grammar in the SSP task and violations to the natural grammar in the syntactic language task). Furthermore, topmaps of the P600 effects recorded at the scalp showed similar distribution between the SSP and syntactic language conditions (for similar findings, see also Daltrozzo et al., 2017; Tabullo, Sevilla, Segura, Zanutto, & Wainselboim, 2013). Given the evidence that the P600 elicited by grammar violations in both SSP and natural syntactic language paradigms, it seems possible that this component could reflect detection of sequential violations more generally (as suggested by Christiansen et al., 2012). In line with the more robust finding that the P600 is associated with syntactic violations of natural language grammar (e.g., Osterhout & Holcomb, 1992), we predicted the measure of grammatical language processing used in the present study would elicit a P600. Likewise, we also left open the possibility a P600 might be elicited by our measure of SSP as well.

Present Study

The aim of the present study was to demonstrate the feasibility of using computerized training techniques to modulate the neural mechanisms recruited for SSP and grammatical language processing with typically-developing adults. The training task was developed by our group (Smith et al., 2015) and specifically targets SSP by incorporating structured (non-linguistic) sequences into the training task. The general prediction was that this computerized training would result in modulation of the ERP components underlying non-trained measures of SSP (P3a/P3b) and grammatical language processing (P600). This study is a proof of concept to demonstrate that the neural underpinnings of SSP can be modulated by targeted SSP training and
that this modulation can, in turn, lead to modulation of the neural underpinnings of grammatical language processing. The long-term goal is that this approach could help lead to the formulation of a novel and innovative intervention that could provide immediate benefit to individuals with difficulty with aspects of language processing.

**Method**

**Subjects**

TD adults (N=34, aged 18-30, 19F) were recruited from Saint Louis University. All participants were native speakers of English, with normal to corrected-to-normal vision and who, at time of testing, reported no history of hearing loss, difficulty with speech, or history of cognitive, perceptual, or motor disorder. All participants were right-handed. Language history such as experience with a second language was also recorded, but not used as an exclusionary criterion unless the subject reported obtaining a level of fluency in the second language (e.g., a self-report of having a year or two of second language instruction in high school and remembering only a few phrases in that language did not exclude the subject from participating in the study). Participants were compensated monetarily for participation. Informed consent was obtained from each subject prior to experimentation. All study procedures were performed in a research lab setting.

Random assignment was used to assign participants to one of three conditions—an SSP training condition (Group 1, experimental group), an active control training condition (Group 2, active control group), and a control condition (Group 3, passive control group, test/retest only). All three groups completed ERP pre/post-training measures of SSP and grammatical language processing. Group 1 (n=12) received 10 days of behavioral visuospatial SSP training in between the pre/post measures, group 2 (n=11) received 10 days of behavioral visuospatial active control
training (loosely based on the WM training literature), while group 3 (n=11) did not come into the lab during the interim 10 days.

**Materials**

For the non-trained measure of SSP and for the computerized training tasks, stimuli were displayed on a touchscreen with subjects’ behavioral responses being made directly onto the touchscreen. For the non-trained measure of grammatical language processing, sentences were also displayed on a touchscreen but participants responded via a button-press on a separate keypad.

**Procedure**

Participants took part in the experimental paradigm for 12 days, with no more than 2 intervening days between study sessions. On Day 1 all participants were assessed on measures of SSP and grammatical language processing (abbreviated GLP in tables and figures that follow) incorporating both behavioral and ERP recordings. During the next 10 days participants received behavioral adaptive SSP training with structural regularities (Group 1, SSP training), behavioral non-adaptive sequence reproduction without structural regularities (Group 2, active control), or the control condition of pre/post training measures only (Group 3, passive control). On Day 12 all participants were re-assessed on the same behavioral and ERP measures as Day 1. An overview of the study design is given in Table 1 below.
Pre-training measures. All participants were assessed on the experimental non-trained measures of SSP and grammatical language processing. All participants performed the measure of SSP first and the measure of grammatical language processing second.

Measure of SSP. The measure of SSP was a version of the “Simon” visual-spatial SSP task used in previously published work, in which an artificial grammar is embedded into a WM span task (e.g., Conway, Bauernschmidt, Huang, & Pisoni, 2010; Conway, Karpicke, Pisoni, 2007; Karpicke & Pisoni, 2004).

In the measure of SSP, participants viewed sequences of black squares displayed on a touchscreen with sequence elements appearing one at a time on a white background in 1 of 4 possible quadrants (upper left, upper right, lower left, lower right; Figure 1 below). The task was to reproduce each sequence immediately following presentation by touching the squares in the correct order directly on the touchscreen. Unknown to subjects, the measure of SSP consisted of two parts: a learning phase and a test phase, which differed only in the types of sequences presented.
In the learning phase, sequence elements were generated according to an underlying artificial grammar that specified the probability of a particular element occurring given the preceding element (see Figure 1 above). This grammar (similar to ones used by Conway et al., 2010 and Jamieson & Mewhort, 2005) had no positional constraints. Each element of the grammar could occur in any position with equal frequency. This means that position information, such as which elements or pairs of elements occur at the beginning versus the ending of sequences, cannot influence learning and is not a confound. This grammar is also considered to be relatively complex as measured, for example, by Wilson et al.’s (2013) complexity metric.

For each sequence generated from this grammar, the starting element (1-4) was randomly determined, and then the grammar was used to determine each subsequent element, until the full sequence length was reached. For example, given the random starting element 3, the element 2 had a zero probability of occurring next, while the 1 and 4 elements had an equal (50%) chance of occurring. No element could follow itself in the sequence. The mapping of the rules to the locations was randomly determined for each subject; however, for each subject, the mapping remained consistent across all trials. All sequences were 5 elements long.
The learning phase consisted of 40 grammatical sequences (8 different grammatical sequences each presented 5 times). This phase began with a blank screen that appeared for 1 second. In the first part of the learning phase (20 sequences), each element in the sequence was displayed for 600 ms, followed by a 200 ms pause in which nothing was displayed on the screen. The final element in the sequence was followed by a 200 ms pause before the entire 2x2 grid of squares was displayed with a “Done” button in the middle. Using the touch screen, the subject then reproduced the sequence just presented, followed by pressing the word “Done”. Immediate feedback was given as to the correctness of each response. The second part of the learning phase (20 sequences) was the same as the first part, except each element in the sequence was displayed for 400 ms, followed by a 200 ms pause.

The test phase consisted of 64 sequences (32 different sequences each presented 2 times). One fourth of the sequences were “grammatical-trained” (i.e., the sequences were identical to grammatical sequences presented in the learning phase), one fourth were “grammatical-untrained” (i.e., new sequences sharing the same underlying structure as the other grammatical sequences), and one half were “ungrammatical” (i.e., the sequences violated the grammar). Each element in an ungrammatical sequence was determined just like the elements in the grammatical sequences described above, except that the fourth element in the sequence always violated the grammar. All other elements in the sequence followed the rules of the artificial grammar. The timing of the test phase was identical to the timing used in the second half of the learning phase. The participants were not told that this was a test phase or that there were different types of sequences (grammatical-trained, grammatical-untrained, and ungrammatical). From the perspective of the subject, the test phase was the same sequence reproduction task they had been doing all along.
Scoring for the measure of SSP. A score of 1 was given for each correctly reproduced sequence (i.e., if all 5 elements were correctly reproduced, the sequence was scored a 1). A score of 0 was given for each incorrectly reproduced sequence (i.e., if all 5 elements were not correctly reproduced, the sequence was scored a 0). No partial credit was given for correctly reproducing only some of the sequence elements.

Measure of grammatical language processing. Sixty-four English sentences were presented during the measure of grammatical language processing. Thirty-two sentences were grammatically correct and 32 sentences contained a morpho-syntactic violation pertaining to verb agreement with the subject. For example, “The famous singer walks onto the stage” would be a grammatically correct sentence and “The famous singer walk onto the stage” would be a sentence with a violation. Each sentence began with a white fixation point (+) and was presented 1 word at a time in white text on a black screen. Each element (word or fixation point) appeared for 400 ms and was followed by a blank screen for 400 ms. Thirty-two 7-word sentences and 32 8-word sentences were presented. The 32 8-word sentences each contained an auxiliary verb. The target words (grammatical or violation) always occurred at the 4th word in the 7-word sentences and at the 5th word in the 8-word sentences, resulting in 4 sentence types that were labeled “gram4”, “syn4”, “gram5”, & “syn5”. Target words were always verbs. The ratio of grammatically correct sentences to sentences with morpho-syntactic violations was 1:1, for each sentence length.

The phrase “Was that a good or a bad sentence? Press 1 for good, press 2 for bad” appeared on the screen immediately following presentation of the final word in the sentence. The task was to make a keypad response on button 1 if the sentence was “good” and to respond on button 2 if the sentence was “bad.” Participants were not given explicit instruction as to what
“good” or “bad” meant (e.g., that grammatical sentences were “good” and sentences with violations were “bad), nor were they told that some sentences were grammatical and some had violations. No feedback was given. A 1-second pause was given between a response and the presentation of the next sentence. The same list of 64 sentences was presented to each subject. Sentences were presented in random order.

Scoring for the Measure of Grammatical Language Processing. A sentence was scored correct if the subject made the correct grammaticality judgment for that sentence (i.e., a button press on 1/good” for grammatical sentences; a button press on 2/bad for sentences with morpho-syntactic violations).

EEG/ERP Data Acquisition for the Measures of SSP and Grammatical Language Processing. Both the measure of SSP and the measure of grammatical language processing were designed to cause violations in expectations of items occurring in a series (i.e., a violation of the artificial grammar in the measure of SSP and a violation of natural grammar in the measure of grammatical language processing). ERPs were used to examine the electrical responses associated with these expectancy violations. ERP for the measure of SSP was time-locked to the presentation of the element in the sequence that violated the artificial grammar and was compared to the same element in a sequence that was grammatical (for both sequence types this element was always element 4). ERP for the measure of grammatical language processing was time-locked to the presentation of a word in the sentence that violated the morpho-syntactic grammar and was compared to a word in a similar position in a sentence that was grammatical (this word was always element 4 for 7-word sentences and element 5 for 8-word sentences).

EEG was recorded during the test phase of the measure of SSP and throughout the measure of grammatical language processing using a 128-channel high-density sensor net with
vertex recording reference (Electrical Geodesics, Inc., Eugene OR). Standard sensor net
application techniques were followed. Recordings were made using NetStation acquisition
software (Electrical Geodesics, Inc.), with a 0.1–100Hz bandpass filter and digitized at 250 Hz.
All electrode impedances were kept below 50 kΩ. To reduce eye and movement artifacts,
instructions were given to try within comfort level to avoid or limit face and body movements
throughout the experiment except those required to complete the task. Each subject was then
shown their continuous raw EEG on the computer monitor and asked to blink, move their jaw,
and other face and body movements to demonstrate how readily this type of artifact can be
picked up by the electrodes and interfere with recording of the neural signal. This step was done
to help each subject try to reduce the introduction of this type of noise into the EEG data. Rest
breaks were given as needed throughout the experiment.

**SSP training task sessions.** The 10 SSP training task sessions began during a separate
appointment on the day following the pre-training measurements. Each training task session
occurred on a separate day, and all 10 sessions were completed within a 14 to 18-day period. The
SSP task (first used in Smith et al., 2015) consisted of several blocks of a sequence-reproduction
task. For each trial, participants observed a series of green circles illuminate on a touchscreen
monitor. Sixteen circles were arranged on a 4x4 grid (Figure 2 below), inspired by the type of
computerized WM training programs used by Klingberg et al., 2002; 2005 (CogMed). Individual
circles on the 4x4 grid were illuminated for 250 ms and were off for 250 ms between elements in
the sequence. The task was to reproduce each sequence immediately following presentation by
touching the green circles in the correct order directly on the touchscreen monitor. As
participants made their responses, each circle they pressed stayed illuminated for 250 ms. If the
subject did
not make a response within 2 seconds of the presentation of the final element in the sequence, then a new sequence was presented. Each session of the training task consisted of 3 blocks of 50 trials. Unknown to the subjects, each circle that illuminated next in a sequence was not determined randomly but, instead, conformed to underlying regularities. Specifically, any given circle that lit up had only 3 other circles that could legally follow it. In addition, the lengths of the sequences presented to each subject was adaptive based on their performance level. Sequence lengths were based on a 2 up, 2 down “staircase” performance paradigm. The underlying sequential patterns that governed which circles/locations could legally occur at a given time were re-randomized for each subject on each training day. This re-randomization of underlying sequential patterns was done to encourage generalization of learning. Feedback was given was given at the end of each block. Participants in the SSP training group performed 5 training sessions each week for approximately 2 consecutive weeks on a touchscreen computer in the lab setting. Each session lasted approximately 45 minutes.
**Active control sessions.** The 10 active control sessions began during a separate appointment on the day following the pre-training measurements. Each session occurred on a separate day, and all 10 sessions were completed within a 14 to 18-day period. The active control task consisted of several blocks of sequence-reproduction and was similar with SSP training task described above (e.g., same 4x4 grid of green circles, same presentation timing), except that it was designed to have a low impact on SSP. The specific manipulations that differed between the active control task and the SSP training task were that 1) each sequence element was presented at random 2) and the task was not adaptive to performance level (all sequence lengths were fixed at 3 elements). The active control task sessions did require the participants to reproduce sequences in the correct order on the same touchscreen used for the SSP training task. Feedback was given at the end of each block. Participants in the active control group performed 5 sessions a week for 2 consecutive weeks on a laptop computer in the lab setting. Each session lasted approximately 35-45 minutes (the shorter sequence lengths resulted in a generally shortened duration compared with the average duration of the adaptive SSP training task).

**Test/Retest Sessions.** Participants in the passive control group only participated in pre-training and post-training measures of SSP and grammatical language processing, administered 14-18 days apart. They did not come into the lab during the interim between the pre and post measures of SSP and grammatical language processing.

**Post-training measures.** The post-training measures were identical to the pre-training measures. The post-training measures were administered during a separate appointment on the day following the final day of the SSP training task and active control task sessions, for participants in Group 1 or Group 2.
EEG/ERP Data Preprocessing for the Measures of SSP and Grammatical Language Processing

Data were preprocessed using Netstation software (Electrical Geodesics, Inc; EGI.) and the EEGLAB toolbox (Delorme & Makeig, 2004) for MATLAB software (MATLAB and Statistics Toolbox Release 2017a, The MathWorks, Inc., Natick, Massachusetts).

**Netstation preprocessing.** Continuous data and data epochs of each individual file were first manually visually inspected by scrolling through channels vertically and horizontally to observe qualitatively that each data file contained the proper epochs and that all channels generally were free of excessive noise that would be unsuitable for standard EEG preprocessing and data cleaning procedures. Individual data files were then preprocessed using Netstation. The continuous raw EEG recordings were filtered through a 0.1 Hz high pass filter and a 30 Hz low pass filter. Channels were marked bad for a given trial if blinks or eye movements were detected, if amplitudes were >150 µV, if the channel was flat (had zero variance), or if manual visual inspection suggested noise specific to that channel. Channels marked bad were interpolated in the raw EEG from data measured at nearby electrodes. After exclusion of artifacts, the continuous EEG was segmented into epochs in the interval -200 msec to +1000 msec with respect to the onset of the target stimulus (i.e., violation of grammar, for both the measure of SSP and the measure of language). The 3 epochs that were segmented for the measure of SSP at pre and post-test corresponded with the grammatical-trained, grammatical-untrained, and ungrammatical sequence types. The 4 epochs that were segmented for the measure of grammatical language processing at pre- and post-test corresponded with the gram4, syn4, gram5, and syn5 sentence types. The mean signal over the -200 ms baseline interval prior to the presentation of the stimulus was computed and then subtracted from the signal at all time points.
in a baseline correction procedure. Data were not re-referenced from the vertex channel in Netstation.

Following preprocessing with Netstation, data from 1 subject in Group 1 was excluded from analysis due to bad EEG channels that were too high in number or too clustered together, along with poor quality data. Therefore, data from a total of 33 participants was analyzed (n=11 for all 3 Groups). The 33 individual ERP files preprocessed in Netstation were then converted into MATLAB format and imported into the EEGLAB toolbox for processing electrophysiological data in MATLAB.

**EEGLAB Preprocessing.** Individual channels for each data file imported into EEGLAB were mapped onto EGI Hydrocel Geodesic Sensor Net (GSN) with 128 channel locations corresponding to an EGI 3-D Cartesian file to visually inspect the data. Individual data files were further preprocessed through the EEGLAB analysis functions for average reference conversion and bad channel rejection based on abnormally distributed data, as measured by the amount of kurtosis in each recorded electrode set at a threshold of 5 standard deviations from mean kurtosis value (the default setting in EEGLAB for automatic channel rejection based on kurtosis). Channels marked bad by EEGLAB automatic bad channel detection were rejected and interpolated from data measured at nearby electrodes. Continuous data and data epochs of each individual file were manually visually inspected by scrolling through channels vertically and horizontally to observe qualitatively that each data file contained the proper epochs and did not appear artificially distorted following the preprocessing steps (e.g., channels that appeared observationally much flatter or peaked than they did prior to preprocessing).

Individual ERP data files were then grand mean averaged across the 3 different groups of participants and for each condition (i.e., for the measures of SSP and grammatical language
processing at pre and post). This processes resulted in the following 12 grand mean averaged
data files each containing n=11 individual data files: 1) Group 1 SSP Pre, 2) Group 1 SSP Post,
3) Group 2 SSP Pre, 4) Group 2 SSP Post, 5) Group 3 SSP Pre, 6) Group 3 SSP Post, 7) Group 1
GLP Pre, 8) Group 1 GLP Post, 9) Group 2 GLP Pre, 10) Group 2 GLP Post, 11) Group 3 GLP
Pre, 12) Group 3 GLP Post.

The two segmented epochs corresponding with the grammatical-trained and grammatical
untrained conditions in the measure of SSP were collapsed, and the two segmented epochs
corresponding with the gram4 and gram5 conditions and the syn4 and syn5 conditions in the
measure of grammatical language processing were collapsed. This function was done for the
purpose of power and because visual inspection indicated no clear difference between each type
of “grammatical” and “ungrammatical” sequences and sentences. This function produced two
segmented epochs corresponding with the grammatical and ungrammatical sequence types in the
measure of SSP and two segmented epochs corresponding with the grammatical and
ungrammatical sentence types in the measure of grammatical language processing.

All data plots were made in EEGLAB using the STUDY function.

**Region of Interest**

The grand mean averaged ERP waveforms were recorded from sensor locations in the
frontal/central region (FRz/CNz) consistent with the following 6 channel numbers of the of the
128-channel EGI Hydrocel GSN: 20, 12, 5, 118, 13, 6, 112 (highlighted in yellow in Figure 3
below). The general frontal/central region was selected *a priori* based on where effects were
observed in previous study of ours using the same measures of SSP and grammatical language
processing (Smith & Conway, 2017), but the actual sensors chosen for analysis was partially
based on visual inspection.
Figure 3. 2-D layout of the 128-channel sensor net (top represents the front of the net, the portion nearer to the nose when 3-D positioned). For data analysis, the region of interest included sensors in the frontal/central region (highlighted in yellow).

Results

ERP Results from the Measure of SSP

SSP at Pre-test. Figure 4 below shows the grand mean averaged ERP waveforms recorded in frontal/central sensors at pre-test during the measure of SSP, time-locked to a presentation of a violation of the artificial grammar compared with an element in the same position in the sequence that was grammatical. Visual inspection suggested a positivity consistent with the P3a component in the latency period 225-300 ms post-stimulus for both sequence types (grammatical & ungrammatical) in all 3 groups of subjects.

Paired-sample t-tests conducted on ungrammatical and grammatical trials associated with this 225-300 ms latency period revealed that the difference between the grammatical and
ungrammatical P3a waveforms was not significant for any of the 3 groups at pre-test [Statistics in numerical order by group (1, 2, 3) for ungrammatical vs. grammatical sentence types; t(6)=0.61, p=.56(ns); t(6)=−1.33, p=.23(ns); t(6)=2.29, p=.06(ns)].

**Figure 4.** ERP waveforms elicited by the measure of SSP at pre-test for all groups and recorded from sensors in the frontal/central region.

**SSP at Post Test.** Figure 5 below shows the grand mean averaged frontal/central ERP waveforms elicited at post-test by the measure of SSP, time-locked presentation of a violation to the artificial grammar compared with an element in the same position in a sequence that was grammatical. Visual inspection suggested the P3a-like positivity in the latency period 225-300 ms post-stimulus for both the grammatical and ungrammatical sequence types was still present at post-measure in Group 2 and Group 3. However, following SSP training Group 1 showed a P3a in the latency period 225-300 ms post-stimulus for only the ungrammatical sequence types.
Paired-sample t-tests conducted on ungrammatical and grammatical trials associated with this 225-300 ms latency period revealed this difference between the ungrammatical and grammatical waveforms observed in Group 1 at post-test was significant. [Statistics in numerical order by group (1, 2, 3) for ungrammatical vs. grammatical sentence types; t(6)=4.35, p=.01; t(6)=0.45, p=.67(ns); t(6)=2.17, p=.07(ns)].
In addition, Group 3 showed, on observation, a slight increased positivity in the latency period 600-750 ms post-stimulus for ungrammatical sequences relative to grammatical sequences that was not as robust in amplitude as the characteristic P600 component that has been widely observed in natural language and AGL paradigms containing syntactic violations, but was qualitatively observable enough to warrant testing it quantitatively. However, this observation was not statistically significant.

**Behavioral Results from the Measure of SSP**

Figure 6 below shows each group’s overall accuracy in percent correct for sequence reproduction at pre- and post-test on the measure of SSP. Pre-test performance for all 3 groups was between 70-74% percent accurate reproducing sequences of both sequence types (Group 1: 72%; Group 2: 70%; Group 3: 74%). Behavioral performance did not significantly improve from pre- to post-test for Group 2 and Group 3, with post-test accuracy at 74% and 79%, respectively. Only Group 1 showed significant improvement \([t(10)=4.87, p=.001]\) in sequence reproduction following SSP training, with overall accuracy for both sequence types (grammatical and ungrammatical) increasing to 91% at post-test.

![Figure 6](image)

*Figure 6.* Behavioral results of all three groups for the measure of SSP at pre-test and post-test, as measured by overall percentage accurate on sequence reproduction.
ERP Results from the Measure of Grammatical Language Processing

Grammatical Language Processing at Pre-test. Figure 7 below shows the grand mean averaged frontal/central ERP waveforms elicited at pre-test by the measure of grammatical language processing, time-locked to the presentation of a violation to natural morpho-syntactic grammar and compared with a word in the same position in a sentence that was grammatical.

Figure 7. ERP waveforms elicited by the measure of grammatical language processing at pre-test for all groups and recorded from sensors in the frontal/central region.

Visual inspection indicated a positivity consistent with the P600 component for ungrammatical sentences relative to grammatical sentences for all 3 groups of participants in the latency period 475-650 post-stimulus. Paired samples t-tests were conducted on the mean amplitude waveforms associated with this positivity observed after violations of morpho-syntactic structure compared with grammatical structure, revealing significant P600 effects to
grammatical violations in all 3 groups [Statistics in numerical order by group (1, 2, 3) for ungrammatical vs. grammatical sentence types; t(6)=2.77, p=.03; t(6)=7.12, p<.001; t(6)=8.94, p<.001].

**Grammatical Language Processing at Post Test.** Figure 8 below shows the grand mean averaged frontal/central ERP waveforms elicited at post-test by the measure of grammatical language processing, time-locked to the presentation of a violation to natural morpho-syntactic grammar and compared with a word in the same position in a sentence that was grammatical.

*Figure 8. ERP waveforms elicited by the measure of grammatical language processing at post-test for all groups and recorded from sensors in the frontal/central region.*

Visual inspection indicated the significant P600 component observed at pre-test for ungrammatical sentences relative to grammatical sentences in the latency period 475-600 post-stimulus was still present at post-test for all three groups [Statistics in numerical order by group (1, 2, 3) for ungrammatical vs. grammatical sentence types; t(6)=9.63, p<.001; t(6)=6.60, p=.001;
t(6)=5.77, p=.001]. However, only Group 1 (SSP training group) appeared to show two earlier increased positivities that were not observed in any group at pre-test.

The first early positivity in Group 1 at post-test was consistent with a P200-like component for grammatical sentences relative to ungrammatical sentences in the latency period 150-295ms post-stimulus. Paired-sampled t-tests for sentence types in the 150-295ms latency period post-stimulus revealed the positivity effect for the grammatical waveforms relative to the ungrammatical waveforms was significant \[t(6)=3.62, p=.01].

The second early positivity in Group 1 at post-test was consistent with a P3b component for ungrammatical sentences relative to grammatical sentences in the latency period 295-425ms post-stimulus. Paired-sampled t-tests for sentence types in the 295-425ms latency period post-stimulus revealed the P3b effect in the ungrammatical waveforms relative to the grammatical waveforms was significant. \[t(6)=3.97, p<.01].

**Behavioral Results from the Measure of Grammatical Language Processing**

Accuracy on the measure of grammatical language processing in overall percentage correct was at ceiling level for all three groups pre-and post-test (>95%).

**Discussion**

**Effects of Training on SSP**

**ERP.** At pre-test all three groups showed a P3a—a component reflecting focus of attention (Comerchero & Polich, 1999)—for both sequence types (grammatical, ungrammatical). That the P3a showed no significant difference between the grammatical and ungrammatical sequences would seem to indicate a lack of learning on the task. However, the lack of significant ERP effects may simply be a power issue. In a recent study using this identical SSP task but with a larger sample (n=32), Smith and Conway (2016) did obtain a significant P3a effect.
It is important that, whereas Groups 2 (Active Control) and 3 (Passive Control) showed no differences in the P3a waveforms from pre- to post-training, Group 1 (SSP Training) did show a modulation of the P3a. Specifically, Group 1 showed a significant difference in the P3a between the ungrammatical and grammatical sequence types at post-training. Thus, following SSP training, only the ERPs for Group 1 made a distinction among the sequence types.

One interpretation of these training-related ERP effects is that at post-training, Group 1 focused attention—as reflected by higher amplitude of the P3a component—specifically to ungrammatical sequences versus grammatical sequences, suggesting that the 10 days of computerized training improved the ability to distinguish the ungrammatical sequences from grammatical sequences. Conceivably, the ungrammatical sequences might have been attracting more attention because of a pop-out effect, in a similar way pop-out elements stand out among consistent or uniform background elements in visual search paradigms (Luck & Hillyard, 1994) or because they were more difficult to parse.

Overall, the neural-level distinction between sequence types observed only in Group 1 following SSP training suggests some degree of learning had occurred or was more likely to occur due to the training-related experience, despite the fact that the same participants failed to show learning prior to training.

**Behavior.** At pre-training, none of the three groups distinguished behaviorally among the 2 sequence types (grammatical, ungrammatical), with overall accuracy on all sequence types ranging from 70-74% among all three groups. This behavioral finding is consistent with the ERP results in that no learning appears to have taken place in any of the groups before training. On the other hand, using the same measure of SSP with a larger sample we found that an average learning score computed by subtracting the behavioral scores for grammatical sequences minus
the ungrammatical sequences was significantly negatively correlated with the P3a effect the frontal region similar, suggested some degree of learning during the SSP task itself (Smith & Conway, 2017). One reason why behavioral learning effects were not observed in the present study is that the distinction between grammatical and ungrammatical sequences was quite subtle. Only one item in the ungrammatical sequence made it ungrammatical, unlike previous studies where multiple items in the sequence violate the grammar, (Conway et al., 2010; 2011; Karpicke & Pisoni, 2004; & Smith et al., 2015). Need to check to see if what I’m saying here is true that these other grammars had multiple violations in the ungrammatical sequences. Our more recent method of creating an ungrammatical sequence makes them more similar with the ungrammatical sentences presented in the natural language task used in the present study. Thus, the non-linguistic artificial grammar used in the present study was arguably especially difficult to learn for our sample of TD adults who prior to the test phase had only been exposed to the 40 grammatical sequences presented in the learning phase. In contrast, task difficulty likely did not exist with the measure of grammatical language processing using sentences to which typically-developing, first-language English speakers would have been continuously exposed throughout their life. With exposure to more trials during the measure of SSP, the participants may have shown learning difference between ungrammatical and grammatical sequence types in the single pre-training session.

At post-training, Group 2 (Active Control) and Group 3 (Passive Control) showed no behavioral change in overall accuracy for either grammatical or ungrammatical sequences compared to pre-training. Group 1 was the only group to show a change in behavioral results from pre-to post-training in the form of a substantial and significant improvement in overall accuracy from 72% to 91% for both sequence types. Following only 10 days of SSP training,
Group 1 showed significant improvement in accuracy for the measure of SSP that the other 2 groups did not show. There are two possible interpretations. The simplest is that the computerized training improved participants’ ability to attend to, remember, and reproduce sequences, regardless of if they obeyed the rules of the grammar. This would indicate that, like some previous WM training studies (e.g., Klingberg et al., 2002; 2005, Olesen et al., 2004, Thorell et al, 2009, & Westerberg et al., 2007), the SSP training task improved working memory capacity and generalized to a non-trained WM task. The second possibility is that the SSP training resulted in participants being more sensitive to the regularities of the artificial grammar, but this had two seemingly competing effects: for some participants, the training gave them a benefit to recalling sequences consistent with the grammar; for other participants, the training made them more sensitive to violations of the grammar, shifting their attention and improving their recall of ungrammatical sequences. The net result is an improvement at the group level for both sequence types (see Smith & Conway, 2017 for further discussion on this effect).

However, regardless of the interpretation, the behavioral improvement is noteworthy and in conjunction with the training-related ERP effects observed in Group 1 described above, demonstrates that the SSP training had generalizable effects to attention, memory and/or learning of nonlinguistic sequences.

**Effects of Training on Grammatical Language Processing**

**ERP.** At pre-training, all three groups showed a P600—a component known to be linked with processing syntactic violations (Osterhout & Holcomb, 1992)—for ungrammatical sentences compared with grammatical sentences. The P600 effect has been well-replicated in TD samples such as the one represented in the present study and is not surprising. At post-training the P600 component observed for ungrammatical sentences relative to grammatical sentences
was unchanged and still present in all three groups; therefore, the P600 does not appear to have been modulated by SSP training.

It is interesting that at post-training following SSP training, Group 1 shows 2 earlier increased positive deflections that were not observed in any group at pre-training or in any other group at post-training. The first positivity is a P200-like component for grammatical sentences relative to ungrammatical sentences, and the second is a P3b component for ungrammatical sentences relative to grammatical sentences.

The P200 is a positive deflection in voltage potential with frontal maximum amplitude peaking around 200-250 ms after stimulus onset. The P200 has been associated with perceptual and attentional processing related to visual search (Luck & Hillyard, 1994). It is also enhanced for repeated relative to novel visual stimuli as well as for “highly-predictive sentence contexts” that are stored into memory (Curran & Dien, 2003; Evans & Federmeier, 2007; Federmeier, Mai, & Kutas, 2005; Misra & Holcombe, 2003). It would seem to make sense that the P200 has a stronger response to grammatical relative to ungrammatical sentences, as the grammatical sentences are “repeated” and “highly-predictive” in the sense of being more frequently encountered, relative to ungrammatical sentences. In addition, because the P200 is related to attentional processes, it is possible that the P200 reflects participants’ allocation of attention to the grammatically correct sentences that were presented. Although the emergence of this component at post-training following SSP training was not predicted, its occurrence suggests that SSP training can modulate neurocognitive mechanisms tied to the processing of natural language grammar.

In addition to the P200 for grammatical relative to ungrammatical sentences, a P3b also emerged for ungrammatical relative to grammatical sentences at post-training only for Group 1.
The P3b has been associated with context updating, (Ferdinand et al., 2008), WM (Kok, 2001), the allocation of attention (Patel & Azzam, 2005; Rueda et al., 2005) and controlled processing (Jost et al., 2015). The occurrence of the P3b to the ungrammatical sentences suggests that participants directed controlled attention toward holding in WM the ungrammatical sentences to make sense of them, which may have required more controlled reparsing of the verb to its grammatical form to understand the context of the sentence. Whatever processing technique the participants in Group 1 were employing at post-training to figure out the ungrammatical sentences, they were directing controlled cognitive resources toward trying to understand the ungrammatical sentences in a way they had not shown at pre-training and that the 2 control groups never showed at all. The ungrammatical sentences may have been processed by the Group 1 participants as a new structure to make sense of and learn, rather than a clear grammatical violation that might otherwise be readily inhibited and corrected by a sample of TD adults with English as a first language.

**Behavior.** None of the three groups showed any change in their behavioral performance on the language task. However, this is likely due to performance already being at ceiling. It isn’t surprising that TD adults who are all efficient language users didn’t improve their language processing with training. What is somewhat surprising and intriguing is that we nonetheless did see neural changes for these adults, supporting the possibility that a younger and/or developmentally delayed group of participants might benefit from such training.

In sum, the combined occurrence of the P200 and P3b in the SSP training group participants only at post-training, suggests that the computerized training resulted in a generalized heightened level of sensitivity or attention to structure in a broad sense. The fact that healthy adults with highly functional levels of grammatical language abilities showed evidence
of a neural change in grammatical language following SSP training is highly encouraging in terms of what benefit such training might be gained in individuals who have difficulty with grammatical language processing and, thereby, more room to improve in these functions.

**Limitations**

Because this study did not include a group who engaged in an adaptive training task without an underlying structure or a group who engaged in a structured training task without the continual adaptation to performance level, it is unknown if either the structure on its own or the adaptive nature of the task on its own is the critical manipulation. One way to test this directly in future work would be to include a group who engaged in an adaptive training task without an underlying structure (as was done in Smith et al., 2015) and a group who engaged in a structured training task without the adaptation of sequence length matched to participants’ ongoing performance level.

Another limitation is that post-training measures were only administered on the day following training. It is unknown if the training effects observed in this study would persist over time. Future studies that address the longevity of the training effects and if there are benefits of “booster training” and at what intervals are needed (for similar WM training longevity assessment at 3 or 6 month follow-up see e.g., Bigorra, Garolera, Guijarro, & Hervás, 2016; Conklin, Ashford, Clark, & Zhang, 2016; Fuentes & Kerr, 2017; Holmes, Gathercole, & Dunning, 2009; Klingberg et al., 2005).

**Conclusion**

In conclusion, this proof of concept study demonstrated that computerized training targeting nonlinguistic SSP abilities in healthy adults resulted not only in modulation of neural mechanisms recruited during a non-trained SSP task, but also to behavioral improvement on
memory for non-trained sequences as well as modulation of neural mechanisms recruited during grammatical language processing. It is likely that most or all of these effects were mediated by changes to attention and/or working memory. These outcomes support the notion that the neural mechanisms recruited for SSP and for grammatical language processing are modifiable across the lifespan, which is in line with evidence that the human brain has the quality of plasticity (Kleim & Jones, 2008; van Praag, Kempermann, & Gage, 2000). These results also suggest a causal relationship between SSP and language outcomes. An important next step is to show feasibility that SSP training can not only enhance the neural mechanisms recruited for SSP and grammatical language processing, but that those neural enhancements will coincide with behavioral improvements to measures of SSP and grammatical language processing with clinical samples of participants who have difficulty with SSP and/or language, such as children with autism, deaf children with cochlear implants, and adults with agrammatism.
References


*Psychophysiology, 38,* 557–577.


