

DISSERTATION

**PLASTICITY IN EEG OSCILLATIONS ASSOCIATED WITH
AUDITORY VERBAL LEARNING**

Submitted by

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In partial fulfillment of the requirements

for the Degree of Doctor of Philosophy

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ABSTRACT OF DISSERTATION

PLASTICITY IN EEG OSCILLATIONS ASSOCIATED WITH AUDITORY VERBAL LEARNING

On a frequent basis, humans need to vocally learn and remember a list of unrelated items.

Advances in cognitive neuroscience have begun to identify the brain regions involved. However, the mechanisms by which those regions interact during learning remain elusive. There is growing support for the proposition that the oscillations within and among these regions provide a substrate for their interaction. This proposition is investigated in the present study by evaluating changes in brain oscillations during verbal learning. Previous research in this domain has provided only limited clues about the influence of ecologically significant factors such as repetition and mnemonics on learning performance and brain dynamics. The present study evaluates independent components analysis, power spectral analysis, and coherence of 32-channel electroencephalogram recorded while subjects learned a list of unrelated nouns. The learning task included repetition and either conventional spoken learning or learning with a musical mnemonic. The results show that as subjects make the transition from repetition to learning, their alpha₁ frequency band activity undergoes a state transition from synchronized to desynchronized oscillations over right posterior cortex. A similar state transition is observed when learning includes a musical mnemonic, but its topographic distribution in the right hemisphere is reversed and relative desynchrony occurs over right prefrontal cortex. The results suggest that verbal learning, even in the context of repetition, is associated with modulation of brain oscillations and that an anatomically distinct network is recruited when learning includes a musical mnemonic. The study has implications for the basic cognitive neuroscience of learning, clinical rehabilitative applications using learning mnemonics, and the architectures of biologically-plausible machine learning algorithms.

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TABLE OF CONTENTS

1	Introduction	1
1.1	Verbal Learning	2
1.2	Brain Activity Associated with Verbal Learning	2
1.3	Study Scope and Objective	4
1.4	Organization of Remainder of Document	5
2	Background	7
2.1	Brain Activity Associated with Verbal Learning.....	7
2.2	EEG Measures of Verbal Learning	9
2.3	Musical Mnemonics	16
2.4	Critique of Most Closely Related Literature	18
2.5	Objective	25
3	Methods	27
3.1	Experimental Design	27
3.2	Data Acquisition	34
3.3	Data Analysis	39
4	Results	42
4.1	Verbal Learning – Behavior	42
4.2	Physiology of Spoken Verbal Learning	43
4.3	Physiology of Musical Verbal Learning	50
4.4	Comparing Spoken and Musical Verbal Learning	55
4.5	Controlling for Time-on-Task	60
4.5	Results Summary	61

5	Discussion	64
5.1	Verbal Learning – Behavior	64
5.2	Verbal Learning Involves Desynchronized Cortical Oscillations	67
5.3	Verbal Learning Involves Modified Interregional Oscillatory Coupling ...	73
5.4	A Musical Mnemonic Involves Less Desynchronization in Oscillations	75
5.5	The Spatial Organization of Oscillatory Desynchronizations Differs between Spoken and Musical Verbal Learning.....	76
6	Conclusions	80
6.1	Key Results and Contributions	80
6.2	Significance	83
6.3	Implications for Biological and Machine Learning.....	86
6.4	Limitations and Future Work	90
A	Subject Forms	97
B	Subject Preparation and Electrode Cap Application	100
	References	102

Chapter 1. Introduction

Learning is a pervasive aspect of human behavior. It occurs with and without conscious involvement. It is required for developing motor skills we take for granted and for grasping complex abstract concepts. Although learning is clearly a life long endeavor, we often view formal education as the canonical environment for learning. Children and adolescents spend the majority of their time in formal education. Many adults forego paid employment to extend their education well beyond their teenage years. Developed societies clearly place a high value on education. Yet we do not understand how the human brain facilitates learning. In 1997 John Bruer posed the challenge to the neuroscience and education communities to bridge the gap between the two fields (Bruer, 1997). He suggested that, although cognitive science has long had a positive influence on educational practice, our understanding of the brain was still too limited to be helpful. A variety of initiatives have begun to address this discrepancy. In a recent report describing brain science as a "mutual opportunity for the physical and mathematical sciences, computer science, and engineering", an NSF steering group noted that (National Science Foundation, 2006, p.7):

"A more fundamental understanding of brain mechanisms of plasticity and learning, coupled with corresponding advances in cognitive science, could form the basis of a richer and more biologically based approach to teaching and learning."

Thus the report suggests that our understanding of learning and how to optimize it could benefit from research at the intersection of plasticity in neuroscience and learning in cognitive science. The present study was designed to take an important step in precisely that direction. In the remainder of this chapter, I introduce verbal learning and the role of repetition and mnemonics in verbal learning, approaches for studying the associated brain activity, and specific scope, objective, and research questions of this study.

1.1 Verbal Learning

Humans have for many centuries used verbal communication as the dominant medium by which to share information. Only in relatively recent history have written and electronic means of communicating come to the fore. Nevertheless, spoken communication remains an important part of every day life. It is still the centerpiece of interpersonal communication and the primary modality used for teaching.

Verbal learning refers to the process of learning verbal material for subsequent use. Thus a common metric for the success of verbal learning is the extent to which the individual can later reproduce the material from memory. There are many strategies for enhancing verbal learning. As with other forms of learning, practice helps. Generally, the probability of remembering verbal information is increased if one is repeatedly exposed to it. Another strategy is the use of mnemonics. A "mnemonic" refers to the mental manipulation of the material to be learned. Examples include visual mnemonics (using the knuckles to remember the number of days in each month), acronym mnemonics (colors of the rainbow "Roy G. Biv"), and musical mnemonics. Mathematician and musical satirist Tom Lehrer's 1959 song *The Elements* recites all of the 102 elements known at the time, inspired by Ira Gershwin's song "Tchaikovsky and other Russians". Although repetition and musical mnemonics are known to have strong influences on learning, they have received little attention in studies of the brain activity associated with verbal learning. Thus the influence of repetition and musical mnemonics figure prominently in the design of the present study.

1.2 Brain Activity Associated with Verbal Learning

Until the past few decades most information about the brain's role in verbal function came from neuropsychological assessment of brain-damaged individuals. If verbal functions were impaired and the patient had known damage to specific brain regions, those regions were deemed

necessary for those functions. However, such cases were limited in number, varied substantially from one patient to the next, and could not identify brain regions that were sufficient for verbal function. With the advent of functional neuroimaging in the latter half of the twentieth century, one could measure metabolic changes in the healthy human brain non-invasively. Thus for the first time we could identify the collection of brain areas involved in verbal function with greater numbers of individuals and without the confound of pathologic conditions. The result is that a distributed network of several brain areas has been identified to play a role in verbal function, and in verbal learning in particular. What remains unclear, however, are the mechanisms by which these areas interact during verbal learning.

Although functional neuroimaging methods measure metabolic activity with good spatial resolution, they lack the ability and time resolution to measure the brain's electrical activity. Yet emerging evidence and theoretical studies suggest that rhythmic oscillations in the electrical activity in the brain's distributed networks may play a prominent role in a wide array of cognitive functions, including verbal learning.

The scalp-recorded electroencephalogram (EEG), despite poor spatial resolution, can measure the brain's macroscopic electrical activity with millisecond resolution. In laboratory tests of verbal learning, subjects are given list of words one at a time and then subsequently tested on their memory for the words. A growing body of evidence has demonstrated that the strength of oscillations recorded with the EEG during learning can distinguish between words that are subsequently remembered versus ones that are not. However, this previous research has not incorporated factors such as repetition and musical mnemonics. EEG studies of repetition and learning are usually conducted in isolation, making it difficult to disentangle their contributions to learning that involves repetition. In verbal learning, words to be remembered are usually presented only once and tested only once. In repetition studies, words are repeated but there is no explicit instruction to learn the words for subsequent recall. The bulk of verbal learning research with EEG uses words presented in the visual modality. Yet Weiss and Rappelsberger (1998)

illustrate that the changes in EEG oscillations associated with verbal learning differ between auditory and visual modalities. The research in the present study was designed to address these shortcomings.

1.3 Study Scope and Objective

This study used a task that involved repetition, the auditory modality, and an adaptation to incorporate a musical mnemonic. To investigate the role of brain oscillations in verbal learning, the study included several oscillatory EEG metrics typically used individually in previous research. The objective of this study was to determine the oscillatory neural plasticity associated with verbal learning. The study involved two conditions: conventional spoken verbal learning and verbal learning with a musical mnemonic. The study's research questions are:

1. What is the neural plasticity associated with verbal learning?
2. Does a musical mnemonic improve learning performance over conventional spoken verbal learning?
3. How does a musical mnemonic influence the neural plasticity associated with verbal learning?

The term “plasticity” is widely used in neuroscience and some clarification as to its definition for the present study is in order. Early in the development of neuroscience, plasticity was defined as “activation without completely yielding” (James, 1890; Konorski, 1948). More simply, it is commonly defined as the capacity to change. It refers to many forms of brain changes, including pre- and postnatal development, endogenous responses to neurological insult as from injury or stroke, and exogenous influences to modify behavior in healthy individuals or rehabilitate function in neurologically impaired patients. Plasticity also refers to persistent changes at different levels of the nervous system, from the molecular machinery of intracellular signaling, to electrophysiology of single synapses and multineuronal ensembles, to gross observable changes in behavior. For purposes of the present study, plasticity is operationally defined as changes in

the EEG measures of brain oscillations. For example, when a subject makes the transition from not learning a word to learning the word, the associated changes in brain oscillations are viewed as the plasticity related to learning.

As elaborated in the final chapter, approaches like those taken in this study have potentially significant implications for both basic science and clinical applications. Determining the brain oscillations associated with learning, and how they are influenced by repetition and mnemonics, provides important clues into the neurobiological basis of verbal learning. The same results may also prove helpful for rehabilitative strategies in clinical settings. If verbal learning with musical mnemonics relies on a different form of neural plasticity than conventional spoken verbal learning, it is compelling physiological evidence that such mnemonics may prove useful for circumventing dysfunctional systems in the brains of neurologically impaired individuals.

The results of this study, detailed later in the document, will show that verbal learning is associated with changes in brain oscillations that are dissociable from repetition. The results also show that a musical mnemonic modulates the learning-related oscillatory dynamics and are consistent with the proposition that music recruits a different network of brain regions during verbal learning.

1.4 Organization of Remainder of Document

Chapter 2 provides more detailed background for the study, highlighting neurobiological approaches to studying verbal learning. It describes why and how electrophysiological oscillations are implicated in verbal learning, with an emphasis on studies using scalp recorded EEG. It also provides background on the specific measures of EEG oscillations used in the present study. Chapter 3 gives the detailed methods used in the study, including experimental design, equipment, and procedures. It also provides details on how the data were collected and analyzed. The study's results are presented in Chapter 4. After illustrating that subjects exhibit successful verbal learning with and without a musical mnemonic, the chapter includes details on

the various changes in EEG oscillations that accompany verbal learning and how they are influenced by use of a musical mnemonic. Chapter 5 includes discussion of the results both in terms of how they may be interpreted and how they relate to previous research in verbal learning. The chapter also includes a brief discussion of implications of the results for machine learning and the biological basis of plasticity in the brain. Chapter 6 summarizes the study's key results and contributions as well as its significance for the basic science of learning, the applied science of learning and memory rehabilitation deficits in clinical populations, and the continued development of biologically-inspired machine learning systems. The chapter concludes with a discussion of the study's limitations and directions for future research.

Chapter 2. Background

Section 2.1 is a brief outline of the evolution of neuroscientific studies that have given rise to the idea that changes in brain activity associated with verbal learning can be indirectly measured with oscillations in the EEG. Three such methods for measuring EEG oscillations are described in Section 2.2. Section 2.3 describes the motivation for considering the role of musical mnemonics in verbal learning and the associated neural plasticity. The most relevant related literature is critiqued and summarized in section 2.4. Section 2.5 describes how past results summarized in this chapter motivate the objective and methods of this study.

2.1 Brain Activity Associated with Verbal Learning

Neuropsychological exams

Verbal learning played a prominent role in experimental psychology of the early 20th century (Leahy, 1992). However, the brain activity associated with verbal learning is poorly understood. Patient studies in the mid-19th century demonstrated that lesions in Wernicke's or Broca's areas of the brain produce deficits in language comprehension and production, respectively (Wernicke, 1910; Berker, Berker, & Smith, 1986). Wernicke's area refers to a left cortical area at the temporoparietal junction, and Broca's area refers to the posterior part of the left inferior frontal cortex (see Figure 2.1). Subsequent research in brain lesion patients expanded our understanding of the number of brain regions involved in verbal function to include bilateral prefrontal, temporoparietal, and medial temporal cortical areas (Wagner, Koutstaal, & Schacter, 1999; Staresina & Davachi, 2006). Although patient studies demonstrate that specific brain regions are *necessary* for a given verbal function, such studies do not allow us to determine the brain regions *sufficient* for verbal function.

Functional neuroimaging

Over the past 30 years, advances in functional neuroimaging like functional magnetic resonance imaging (fMRI) have allowed researchers to non-invasively monitor brain activity in the healthy human brain and identify the brain regions that are implicated in normal verbal function. Learning and memory rely on the interaction of many brain regions over complex cortical networks. In the case of verbal learning, the primary constituents are prefrontal cortex and medial temporal lobe (Fletcher, Frith, & Rugg, 1997; Fernandez et al., 1998; Strange, Otten, Josephs, Rugg, & Dolan, 2002; Brassen, Weber-Fahr, Sommer, Lehmbeck, & Braus, 2006). The medial temporal lobe includes the parahippocampal cortex, also depicted in Figure 2.1. Although neuroimaging techniques offer great spatial resolution, their temporal resolution is generally on the order of seconds and therefore their ability to measure the physiological mechanisms by which these brain regions interact during verbal function is limited, as described in the next section.

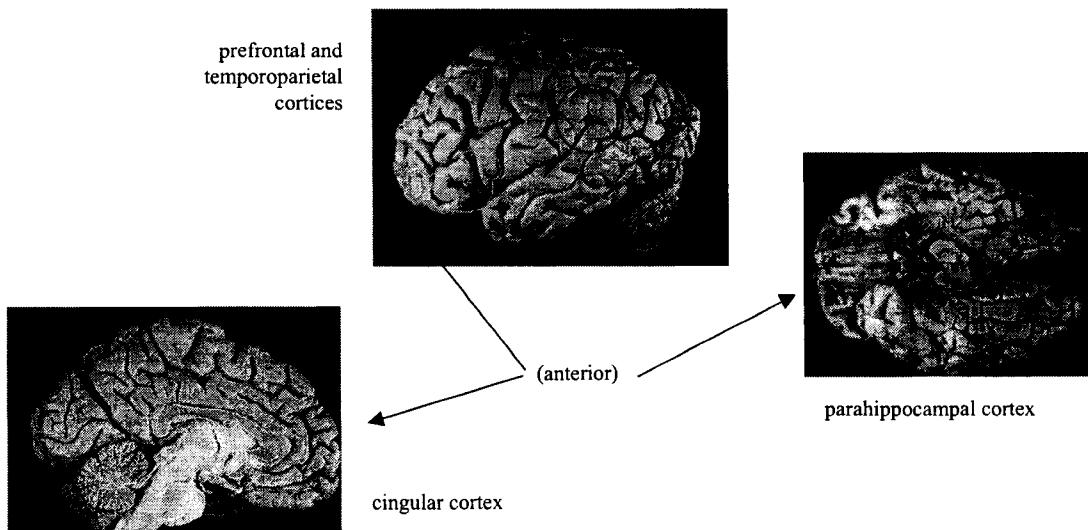


Figure 2.1 Gross cortical regions associated with verbal learning. Left image: mid-sagittal view, upper image: left lateral view, right image: inferior view. (Images from the Temple University Neuroanatomy Lab's Gross Brain Atlas.)

Oscillatory circuit views

Humans can process verbal information at rates over one word per second. Thus the multiple processes that underlie verbal function (sensory, perceptual, memory, decision making, motor planning and production), which are generally believed to occur in a mostly sequential fashion, must involve neuronal activity in periods well under a second. Furthermore, there is a long history of evidence from neuroanatomy, electrophysiology, and modeling that a wide array of brain functions rely on oscillatory activity in recurrent networks within and between brain regions (Freeman, 2000; Buzsâaki, 2006), including verbal memory (Jensen & Lisman, 1998). This oscillatory activity is generally in the range of 1-100 Hz. By Nyquist's law, one needs to sample such activity at a rate of at least 200 Hz in order to veridically represent it. Non-invasive electrophysiological methods, such as the EEG and its magnetic field counterpart the magnetoencephalogram (MEG), measure brain activity with temporal resolution on the order of a millisecond (Lopes da Silva & Rotterdam, 1999). Thus, EEG and MEG are better suited than functional neuroimaging methods for the study of brain oscillations.

Learning involves changes in stored knowledge, and must involve a corresponding change in the state or activity of related brain networks. Verbal learning is associated with cortical plasticity (Tallal, 2000; Burgess & Hitch, 2006) and it is believed that plasticity in cortex may be related to changes in recurrent networks in cortex. Changes in oscillations of these networks can be measured indirectly with the EEG.

2.2 EEG Measures of Verbal Learning

The EEG has been used to study how brain activity during encoding affects storage into memory and subsequent retrieval (Rugg, 1995; Wagner et al., 1999; Rugg & Allan, 2000). By comparing words that are subsequently correctly recalled to words that are not, one can characterize the differential brain activity associated with successful encoding, thereby measuring the neural plasticity associated with learning.

Various metrics derived from the EEG have been used to study human cognition, including verbal learning and memory. Three categories of metrics are discussed below: per-electrode spectral power, inter-electrode coherence, and independent component analysis (ICA). The first two provide different measures of the oscillations in the brain, and ICA is used as a preprocessing step in support of subsequent power spectral analysis.

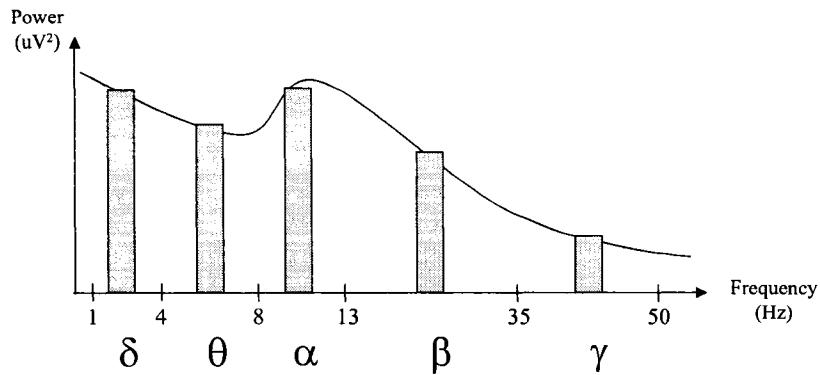


Figure 2.2 Frequency band definitions commonly used for measuring per-electrode spectral power in the EEG. Line depicts continuous spectral power, shaded bars depict spectral power amplitudes averaged over the discrete frequency bands.

Per-electrode spectral power

The oscillatory activity of cortical networks can be indirectly measured by the spectral power in various frequency bands (see Figure 2.2) of the EEG (Gevins, Smith, McEvoy, & Yu, 1997; Klimesch, 1997; Dujardin, Derambure, Bourriez, & Guieu, 1999). Historically, EEG oscillations were often associated with various levels of arousal and sleep stages. Posterior-dominant alpha oscillations are visually evident in the time-domain EEG signal when a subject is awake with eyes closed. Since Berger's original descriptions of the EEG, however, the associations between various EEG frequency bands and various behavioral and cognitive functions have exploded (Swartz & Goldensohn, 1998). Oscillations have long been theorized to underlie short-term memory (Gerard, 1949; Hebb, 1949; Dudai, 1989). The basic premise has been that oscillatory reverberations in brain circuits provide a continuously updated "activation" of a representation. Learning also induces changes in the EEG spectra, both in motor learning

(Jantzen, Fuchs, Mayville, Deecke, & Kelso, 2001) and cognitive learning associated with practice effects in working memory (McEvoy, Smith, & Gevins, 1998). Thus changes in brain oscillations measured by the EEG can serve as a marker of neural plasticity associated with verbal learning.

In verbal memory studies, differences in EEG spectra during word encoding associated with later memory-based performance are commonly known as the subsequent memory effect (SME) (Friedman, Ritter, & Snodgrass, 1996; Rypma & D'Esposito, 2003). Brain activity is recorded during stimulus presentation (i.e., when the subject may be encoding the stimulus). Individual stimuli are divided into two groups: those that are subsequently recalled and those that are not. The differences in brain activity during encoding between these two groups of stimuli are referred to as the SME. The SME has been demonstrated with intracranial and extracranial electrophysiology (Paller & Wagner, 2002) and with oscillations in those electrophysiological measures (Klimesch, Doppelmayr, Russegger, & Pachinger, 1996; Weiss & Rappelsberger, 2000; Sederberg, Madsen, Seelig, Donner, & Kahana, 2002; Gruber & Muller, 2006). In particular, verbal memory has been associated with enhanced oscillatory activity in 1-4 Hz delta (Weiss & Rappelsberger, 2000), 4-8 Hz theta (Klimesch et al., 1996; Gevins et al., 1997; Sederberg et al., 2002), and 35-50 Hz gamma frequency bands (Sederberg et al., 2002; Schack & Weiss, 2005) and with either enhanced or reduced oscillatory activity in 8-13 Hz alpha subbands, depending on the subbands and their definition (Gevins et al., 1997; Klimesch, 1997; Karrasch et al., 2006). Collectively, per-electrode spectral measures are the most commonly used metric of the EEG used to study oscillatory brain activity.

Inter-electrode coherence

Probably the second most common feature of the EEG used for studying oscillatory brain dynamics is coherence. EEG coherence (mathematically defined in Chapter 3) refers to the correlation between two separate EEG electrodes' oscillatory activity. Increased spectral power

in individual electrodes is often referred to as increased oscillatory “synchronization”, even though it is a single signal that is being measured. It is sometimes referred to as “synchronization” because, in order to be measurable at the scalp level, it relies on the synchronized activity of a large mass of neural tissue in underlying cortex. However it is a different measure than coherence (see Figure 2.3). Because coherence explicitly incorporates a measure of spatial coordination, coherence addresses the question of how topographically remote brain regions interact. Coherence provides a more explicit reflection of synchronous widely-distributed network activity than per-electrode spectral power. Thus coherence may be a logical metric of brain activity to consider, because verbal learning involves many widely distributed brain regions and their collective network activity.

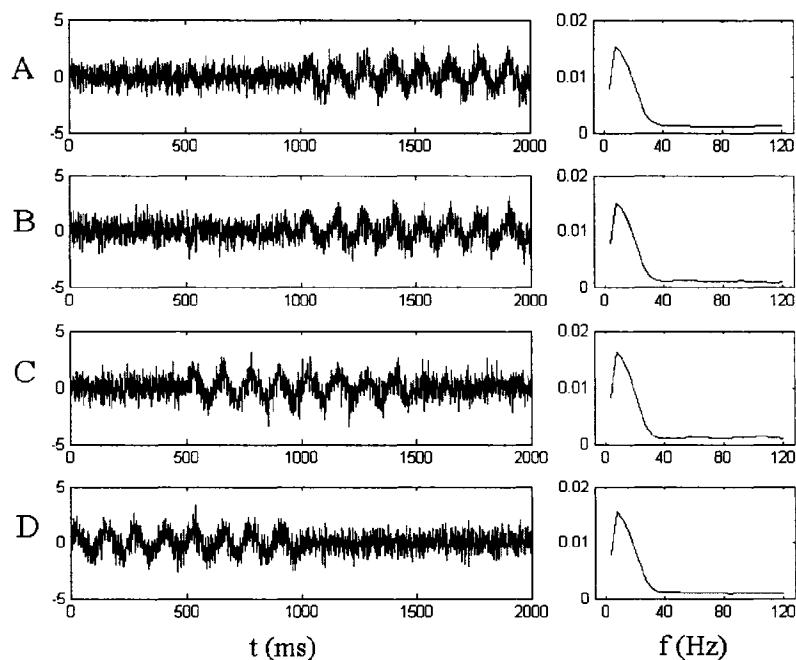


Figure 2.3 Synthetic illustration of coherence. Left: two-second, 1000 Hz sampled time series consisting of $N(0,1)$ noise and a one-second segment of 8 Hz sinusoid. Right: power spectra showing consistent 8 Hz peak for each corresponding signal on the left. Coherence values: between A and B: 0.97, between A and C: 0.17, between A and D: 0.004.

Changes in coherence have been found in several higher brain functions that probably subserve verbal learning. Coherent oscillations are thought to play a role in perceptual processes (Engel, Fries, & Singer, 2001), providing a top-down influence probably originating in prefrontal and parietal cortical areas (Frith & Dolan, 1997). Auditory word processing is associated with decreased frontal alpha coherence (Weiss & Rappelsberger, 1996). Gamma coherence is higher during associative learning (Miltner, Braun, Arnold, Witte, & Taub, 1999). Relatively few inter-electrode coherence studies have been done in explicit verbal learning and memory. An exception is a study by Weiss and Rappelsberger (Weiss & Rappelsberger, 2000). They found increased theta coherence associated with successful verbal encoding. Although related, per-electrode spectral power and inter-electrode coherence are not necessarily correlated. In some studies, researchers have found a learning-related change in EEG coherence but *not* spectral power (Weiss & Rappelsberger, 2000; Fell et al., 2003). In other words, those studies suggest learning may involve changes in the way oscillations are temporally coordinated between different brain regions without corresponding changes in the regions' individual power spectra. This concept is illustrated in Figure 2.3.

Independent components analysis (ICA)

Given a set of observations, blind source separation (BSS) methods such as independent component analysis (ICA) (Hyvarinen, Karhunen, & Oja, 2001) attempt to find a linear transformation of the observations that results in a set of independent observations. The result is illustrated with a synthetic example in Figure 2.4. The example shows how the linear mixing of the sinusoidal and triangle-wave sources produces the projections. ICA is given only the projections; the sources and the weights used in their linear mixing are unknown. The result is a pair of estimated sources qualitatively very similar to the original sources, although generally in a different order and with amplitude scaling. Unlike principal components analysis (PCA), ICA produces bases that do not need to be orthogonal and the transformations take into account higher

order statistics, not just the 2nd order statistic of variance. When applied to EEG, the “observations” are the multi-electrode time series. ICA decomposes multi-electrode EEG signals into spatially fixed, temporally independent sources. Assumptions about how independent brain sources are mixed and map to the recorded scalp electrodes, and the corresponding relevance for BSS methods, are discussed extensively in (Jung, Makeig, Westerfield et al., 2001). In brief, it is reasonable to assume that multiple independent “sources” of brain activity are linearly summed to compose scalp-recorded EEG. Thus, because activity in different brain regions is combined at individual scalp locations, ICA can be used to separate independent brain activity that would otherwise remain mixed in the original EEG signals. In principle, ICA’s ability to unmix sources could lead to EEG features that more accurately reflect the true underlying brain activity and therefore provide stronger dissociations between various learning situations than would otherwise be possible.

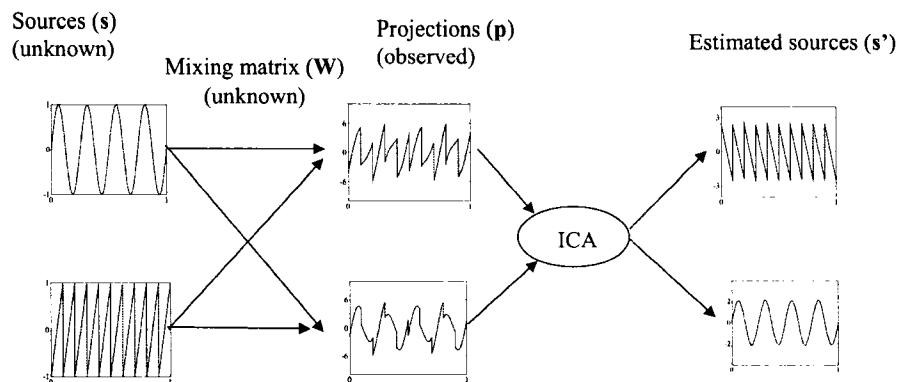


Figure 2.4 Synthetic illustration of ICA. Observed signals (**p**) are assumed to consist of an unknown but linear mixture (**W**) of unknown source signals (**S**). ICA is used to estimate (**s'**) the original source signals.

ICA has been used extensively in analyses of human brain activity, including EEG (Makeig et al., 1999; Jung, Makeig, McKeown et al., 2001), MEG (Vigario, Sarela, Jousmaki, Hamalainen, & Oja, 2000; Tang & Pearlmuter, 2002), and fMRI (Jung, Makeig, McKeown et al., 2001). Some have suggested that ICA is particularly good for studying complex cognitive functions with lower signal-to-noise ratios than, say, perceptual experiments (Tang &

Pearlmutter, 2002). Oscillations in ICA components dissociate conditions in spatial selective attention (Makeig et al., 1999). However, the theoretical argument for using ICA with EEG in cognitive studies has, thus far, only limited empirical support.

In previous work, we have shown that spectral power analysis used in conjunction with ICA provides a stronger dissociation than spectra of the original time series for all eight out of eight subjects in a visual imagery task (Peterson, Knight, Kirby, Anderson, & Thaut, 2005). In that study, 32-electrode EEG was recorded while subjects underwent a mental imagery task. Upon seeing the word “yes” or “no” momentarily displayed on a computer monitor, they were instructed to visualize the word for the subsequent three seconds. The task was designed to be a proxy for a brain-computer interface in which subjects could simply visualize a response to a simple yes/no question. The subjects’ EEG data was evaluated with spectral analyses preceded by BSS.

Peterson et al. compared two approaches to BSS: Infomax ICA (Bell & Sejnowski, 1995) and minimum noise fraction (MNF) (Hundley, Kirby, & Anderle, 2002; Anderson & Kirby, 2003). We also compared the ability of a support vector machine (SVM) classifier (Vapnik, 1998; Schölkopf, Burges, & Smola, 1999) to distinguish between different mental images based on broadband power spectra from the original EEG signals and the ICA and MNF transformations of those signals. Figure 2.5 shows for each of eight subjects how the classification accuracies compare for spectra of the original signals and the two BSS transformations. For every subject, at least one of the BSS transformations leads to better classification accuracy than the original signals. Spectra of Infomax and MNF transformations performed statistically significantly better than the spectra of the original signals for every subject except subject 1 and MNF for subject 5 (Wilcoxon rank-sum test, alpha = 0.05). The question remains, however, whether ICA would help dissociate brain oscillation dynamics associated with verbal learning.

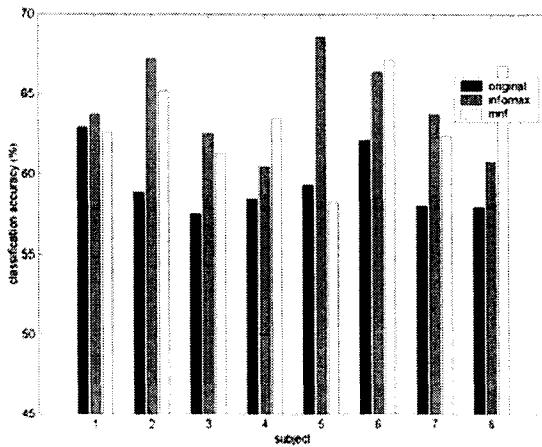


Figure 2.5. BSS transformations improve the dissociating strength (classification accuracy) of subsequent spectral representations (Peterson et al., 2005).

2.3 Musical Mnemonics

A mnemonic is defined as "a system that enables people to organize, store and retrieve information more efficiently" (Wilson & Clare, 2002). Through its regular temporal and melodic structure, music provides a system for organizing information. If information is embedded into the structure of music, then music could, in principle, provide a mnemonic that facilitates storage and retrieval of that information. Before delving into the potential for music to serve as a mnemonic for verbal learning, some background on music's influence on a broader scope of cognitive function is in order.

Music has a strong influence on the organization of brain activity (Sacks, 2006). It can enhance a diverse array of cognitive functions, such as spatiotemporal reasoning (Sarnthein et al., 1997; Shaw & Bodner, 1999), attention (Large & Jones, 1999; Drake, Jones, & Baruch, 2000), and memory (Deutsch, 1982; Cook, 1999; Glassman, 1999; Kilgour, Jakobson, & Cuddy, 2000; Ho, Cheung, & Chan, 2003; Thaut, Peterson, & McIntosh, 2005). Memory benefits from relational processing that strengthens inter-item associations, and the regular temporal structure of music can be used to increase inter-item associations. Text is remembered better when accompanied by music (Yalch, 1991; Wallace, 1994). Music provides a helpful mnemonic for

verbal function throughout life, most notably during early development and in educational settings (Calvert & Billingsley, 1998). Music also provides learning disabled and developmentally disabled students a helpful rehearsal mechanism for learning nonmusical material (Gfeller, 1983; Wolfe & Hom, 1993; Claussen & Thaut, 1997). Despite the converging behavioral evidence that music can influence cognitive function including verbal learning, there remains a dearth of evidence for how music might change brain activity during verbal learning.

How might music influence the mechanisms by which verbal learning is implemented in the brain? There are at least three possible mechanisms: 1. music has an inherent temporal structure, 2. music has a close relationship to language, and 3. music processing involves a different (and perhaps broader) network of brain systems than conventional spoken language. Each of these is discussed in the following paragraphs.

Music can play a role in brain plasticity through its temporal structure (Merzenich, Schreiner, Jenkins, & Wang, 1993; Pantev, Wollbrink, Roberts, Engelien, & Lutkenhoner, 1999; Thaut, Kenyon, Schauer, & McIntosh, 1999; Thaut, 2005). The temporal structure of music provides a good mnemonic (Gfeller, 1983) and influences the brain activity associated with short-term memory for auditory patterns (Peterson & Thaut, 2002). The structure and redundancy in a musical mnemonic chunks the material into more manageable units (Deutsch, 1982). "Temporal structured learning" research has demonstrated the significance for memory of how information is temporally grouped (Hitch, Burgess, Towse, & Culpin, 1996). Temporal structure during encoding can enhance short-term memory (Hitch et al., 1996). In summary, there is growing evidence that music influences learning-related brain activity by providing a temporally structured mnemonic for learning.

There is a tight coupling between music and language. Neuroimaging evidence and cognitive theory argue for overlap between (rather than entirely separate systems for) language and music processing at the syntactic level (Patel, 2003). Universal properties of music can be predicted from the statistical structure of human speech (Schwartz, Howe, & Purves, 2003).

Broca's area, necessary for language production, may be involved in processing musical syntax (Maess, Koelsch, Gunter, & Friederici, 2001). Thus music and language share common brain systems and thus music may influence activity in the brain's non-musical language systems.

In addition, there is accumulating evidence that music processing involves a broad, distributed network of brain regions that only partially overlaps with regions involved in verbal function. Lesion (Halpern, 2001; Peretz, 2002), functional imaging (Zatorre, Halpern, Perry, Meyer, & Evans, 1996; Platel et al., 1997; Parsons, Hodges, & Fox, 1998), EEG (Peterson & Thaut, 2002) and MEG (Tecchio, Salustri, Thaut, Pasqualetti, & Rossini, 2000; Maess et al., 2001) studies have suggested that music-related processing in the brain involves cortical and subcortical networks that are more widely distributed than non-musical verbal function. Melody and text are encoded in different areas of the brain (Samson & Zatorre, 1991). Different aspects of music can be ascribed to the brain hemispheres (Baeck, 2002). The left hemisphere is active in rhythm discrimination, pitch familiarity, interval structure, and temporal and sequential aspects of music. The right encodes tone pitch, melody, timbre and harmony. Thus music may help facilitate verbal learning not only as a mnemonic device that strengthens associations in normal verbal memory pathways, but also by recruiting complementary brain networks for encoding and retrieving words from memory.

2.4 Critique of Most Closely Related Literature

This section summarizes and critiques other research in three areas: 1) EEG studies of verbal memory, 2) EEG studies of the effects of repetition, and 3) the effects of musical mnemonics on verbal learning and memory. The section concludes with a summary of the limitations in the related research that motivated many of the specific research questions in the present research.

EEG studies of verbal memory

There are thousands of studies of memory using the EEG. This section summarizes and critiques several that are most closely related to the auditory verbal learning and oscillatory EEG approach employed in the scope of the present research.

In (Summerfield & Mangels, 2005), subjects viewed 45 words during a study phase, and then viewed 90 probe words during the test phase. During the test phase subjects had to indicate whether the words were “old” or “new”. The 64-electrode EEG was recorded during encoding. Spectral power and coherence were only calculated for the theta (4-8 Hz) frequency band. Per-electrode spectral power was computed for all electrodes. Coherence was limited to a subset of only 190 electrode pairs. ICA was applied to the corresponding spectral and coherence maps. Values were considered statistically significant if they fell above the 95th percentile of the corresponding randomly shuffled distribution (i.e., trials shuffled among conditions).

Encoding was associated with enhanced theta power in left anterior regions and with enhanced anterior-posterior coherence in the left hemisphere. ICA of the theta power increase showed that independent components accounting for the greatest variance of theta power had strong frontal projections. The authors attribute the left hemispheric dominance of the effects to encoding processes sufficient for recognition, and posit that recall may recruit a similar effect bilaterally.

The study did not include repetition; the words were shown only once. The study did not include an auditory modality. The experiment tested only recognition, not recall. In their EEG analysis, Summerfield and Mangels considered only the theta band. Also, they examined independent components of the spectral signals rather than spectra of the independent components. These operations are not symmetric so this unconventional application of ICA to EEG makes it impossible to compare results between theirs and other studies using the more common convention of evaluating spectra of the independent components.

Van Strien et al. (2005) gave subjects a continuous recognition memory task. Over 330 trials, subjects viewed 30 words ten times each, and an additional set of 30 filler words, in pseudo-random order. On each trial, subjects had to indicate whether the word was new or old. EEG was recorded at 30 electrodes and was low-pass filtered at 30 Hz. EEG spectral power during encoding was calculated for delta (2-4 Hz), theta (4-8 Hz), and alpha (8-12 Hz) frequency bands.

Repetitions evoked more delta power than new words, and this effect decreased with repetitions 2-9. Repetitions also evoked more theta power than new words. Both of these effects were most prominent in left anterior electrodes. Repetitions also evoked increased low-alpha power in central electrodes.

The experiment did not consider auditory word presentation; only visual presentation was used. The experimental design involved a continuous recognition procedure such that retrieval and response activities overlap with encoding. As a result, there is temporal overlap between explicit retrieval processes and encoding so the corresponding EEG includes brain activity associated with both rather than primarily encoding. The study used only recognition and did not include any free recall. In their EEG analysis, the investigators did not consider coherence between electrodes. Also, their low-pass filtering precluded analysis of activity in higher (e.g., beta and gamma) frequency bands.

In (Smith, McEvoy, & Gevins, 1999), subjects were given a continuous performance verbal working memory task, in which they were required to indicate whether a given letter displayed on the monitor is equivalent to the letter seen 3-letters back. Subjects participated in three sessions over several days lasting a total of 6-8 hours. The EEG was simultaneously recorded over 27 electrodes and the spectral power calculated in theta and alpha frequency bands.

Frontal midline theta power increased with task practice. The authors suggest this effect is associated with increased concentration over the course of the task. Both a centrally distributed low alpha power and a more posterior high alpha power increased with task practice. Citing the

traditional belief that alpha oscillations are associated with an “idling” brain state, the authors interpreted the alpha increases as evidence that cortical regions not necessary for the task become less active with practice.

The verbal information in the experiment was single letters presented visually. Because subjects need only compare the current letter stimulus to a previously seen letter, the task implicitly involves recognition and does not require free recall. Also, the continuous performance nature of the task means that retrieval and response activities overlap with encoding (as in the case of Van Strien et al. above). In their EEG analysis, Smith et al. did not include any analysis of inter-electrode coherence.

In (Weiss & Rappelsberger, 1998), subjects were given lists of words, presented one at a time, in alternating blocks of either auditory or visual presentation. Subjects were instructed to memorize the words, and were asked to recall as many as possible after each block. The EEG was simultaneously recorded from 19 electrodes. The per-electrode spectral power was calculated in delta (1-4 Hz), theta (5-7 Hz), alpha-1 (8-10 Hz), alpha-2 (11-12 Hz), beta-1 (13-18 Hz), and beta-2 (19-31 Hz) frequency bands. Inter-electrode coherence was also calculated in the same frequency bands for 30 intrahemispheric pairs and 8 interhemispheric pairs of electrodes. Resting EEG (between blocks) was used as the baseline EEG period. Modality-specific effects were only examined in the alpha-1 band.

Word encoding during auditory presentation was associated with decreased alpha-1 power in bilateral temporal electrodes and increased alpha-1 power everywhere else. Visual presentation was associated with decreased alpha-1 power across the scalp. Intrahemispheric coherence between frontal and temporal regions increased during auditory presentation but decreased during visual presentation. Interhemispheric coherence increased for both modalities, but was primarily frontal for auditory and posterior for visual presentation.

Individual words were presented only once in the study. The investigators used resting EEG as their baseline rather than the tighter controls of per-trial or per-word baseline periods.

Despite measuring the EEG in all but the gamma frequency bands, inter-modality differences were analyzed in only one EEG frequency band (alpha-1).

EEG studies on the effect of repetition

Many studies that evaluate the effect of repetition on verbal function use lexical decision tasks. In these tasks, subjects are presented a list of stimuli, one at a time, and simply asked to indicate whether or not the stimulus is a word. If a stimulus is repeated it is usually recognized faster and more accurately. This is the notion of “repetition priming” (Schacter, 1992). It occurs even when the subject is exposed to other intervening stimuli between repeated presentations of the stimulus. Thus the task involves incidental memory. Although the subject is not explicitly instructed to remember the stimuli, their behavior on any given trial is influenced by earlier parts of the experiment.

While this behavioral effect has been widely studied, the associated effect on oscillations in the EEG has not. Investigation of repetition’s effect on oscillatory EEG is even rarer in the domain of verbal function. One notable exception is work by Fiebach et al. They have found that the effect of word repetition on EEG oscillations depends on whether or not the stimuli are familiar (Fiebach, Gruber, & Supp, 2005). When familiar words were used they found “repetition suppression”, i.e., that the amplitude of EEG oscillations decreases with repetition. When (unfamiliar) pseudowords were repeated, EEG oscillations were strengthened.

In (Tachibana et al., 1999), implicit and explicit word memory tasks were given to 21 patients with subcortical strokes and 14 controls. The implicit task involved sequential auditory presentation of 360 words and 130 pronounceable non-words in pseudo random order. Sixty words were repeated after each of zero, 5, or between 11-77 intervening words. Subjects were instructed to respond with a button press whenever they heard a non-word. The explicit memory task, Rey’s Auditory Verbal Learning Test (AVLT – discussed at length in the Chapter 3), was administered separately in person.

In the implicit memory task and for both the patient and control groups, word repetition attenuated the amplitude of the N400. The N400 is a negative-directed peak in the time-domain amplitude of the across-trial averaged EEG (the event-related potential, or ERP). It peaks around 400 ms post-stimulus onset and is normally associated with word recognition. The result is consistent with earlier studies and is believed to reflect the brain's identification of a repeated stimulus occurrence while attention is not focused on that particular stimulus. Unfortunately, the investigators only measured the EEG during the implicit memory task. The EEG was not recorded during the explicit learning and memory task (the AVLT). Also, the EEG analysis considered only time-domain amplitude of the EEG and no spectral analysis of oscillations in the EEG. What has not yet been studied are the EEG oscillations associated with the interaction of repetition and explicit verbal learning.

Studies on the effect of musical mnemonics in verbal learning

As mentioned earlier, a number of studies demonstrate the interaction between music and cognitive functions. However to date only two studies were found that specifically involve music and verbal learning. In the first study (Yalch, 1991), subjects were given a list of 20 advertising slogans and asked to write the name of the corresponding sponsoring brand for each slogan. Half of the slogans were from ads using a “jingle” format, and the other half from those not using jingles. Brand names were significantly more likely to be recalled in the case of a jingle. The results suggest that a musical mnemonic enhances memory for the brand name. However, because brand recall is cued by the slogan (“jingle”), this is more of an “associative” memory task and thus is more like recognition than free recall. Also, brain activity was not recorded.

In the second study (Wallace, 1994), subjects heard three verses of a ballad containing approximately 80 words in either a spoken or sung condition. The ballad was repeated 5 times, and subjects were asked to recall the words in writing after the 1st, 2nd, and 5th trials. In both conditions subjects demonstrated learning as evidenced by recall rates of approximately 20, 45,

and 75% on the recall trials. Subjects in the “sung” condition performed significantly better than those in the “spoken” condition, recalling on average 15% more words on any given trial. This effect was preserved beyond the initial learning trials to include a recall trial approximately 20 minutes after the last learning trial. Although the study suggests a musical mnemonic enhances verbal learning, the investigators did not record brain activity during the experiment. Also, word lists came from ballads rather than a list of unrelated words, which is more common in verbal learning research.

Summary of related research

There has been substantial progress toward understanding the neural basis of verbal learning. However, previous research suffers from shortcomings in both the experimental design and their EEG analysis. Previous EEG research in verbal learning and memory has not incorporated ecologically-salient factors such as repetition, musical mnemonics, and delayed free recall. Instead, words to be remembered are usually presented only once and tested only once. Yet it is commonplace to use repetition and rehearsal when trying to learn. Although the effect of a musical mnemonic on memory has been studied, there have been virtually no studies of that effect that incorporate simultaneous measures of brain activity. Also, the test phase of verbal memory studies often involves recognition rather than recall, despite a large body of cognitive psychological research that highlights the differences between the two forms of retrieval (Eichenbaum, 2002; Squire & Schacter, 2002) and recent evidence suggesting that repeated recall facilitates learning better than repeated study (Carpenter & DeLosh, 2005). Of course, recall is important in many ecologically-relevant settings in which one needs to produce the item to be remembered, not just recognize it from a set of alternatives. Some tests of verbal memory that examine simultaneous EEG do not isolate encoding and retrieval phases, because they use continuous performance methods that require subjects to engage in retrieval processes that overlap with the time course of encoding a new word on the list. Thus those studies cannot

separate the brain activity associated with encoding from the brain activity associated with retrieval.

The bulk of verbal memory research with EEG uses words presented in the visual modality. Yet Weiss and Rappelsberger (1998) illustrate that the changes in EEG oscillations associated with verbal learning differ between auditory and visual modalities. Furthermore, they only looked at one subband of alpha frequencies in that comparison. Thus the neural basis of verbal learning appears to differ depending on the modality (visual or auditory) and the modality sensitivity may extend to oscillatory dynamics in other frequency bands.

In terms of EEG analysis, the verbal learning field has not yet considered ICA as a preprocessing step prior to spectral analysis even though ICA has been helpful in dissociating conditions in other cognitive tasks. Also, even some of the most recent work (e.g., Summerfield and Mangels 2005 and Van Strien et al. 2005) evaluates only a subset of the EEG frequency bands known to reflect differential cognitive processing. Finally, investigators have typically evaluated either per-electrode spectra or coherence features of the EEG, not both.

The research described herein addresses all of these shortcomings. Unlike most experimental paradigms recording EEG while studying verbal memory, the experiments involve a task that includes repeated study/test learning and free recall. The task uses the auditory modality and was adapted to incorporate a musical mnemonic. The present research also evaluates, in one single study, several of the oscillatory EEG metrics typically investigated individually in separate studies.

2.5 Objective

The objective of this study is to determine the oscillatory neural plasticity associated with ecologically salient verbal learning. The study involved two conditions: conventional spoken verbal learning and verbal learning with a musical mnemonic. The study's research questions and hypotheses are the following:

1. What is the neural plasticity associated with verbal learning? For each condition:

Hypothesis 1: Verbal learning is associated with increased frequency-domain amplitude (spectral power) in the EEG.

Hypothesis 2: Verbal learning is associated with increased frequency-domain amplitude (spectral power) in the ICA-transformed EEG.

Hypothesis 3: Verbal learning is associated with increased inter-electrode coherence in the EEG.

2. Does a musical mnemonic improve learning performance over conventional spoken verbal learning?

Hypothesis 4: A musical mnemonic improves verbal learning performance compared to conventional spoken verbal learning.

3. How does a musical mnemonic influence the neural plasticity associated with verbal learning? In other words, for each type of EEG feature (as in 1. above), how do the features differ for the two conditions (i.e., spoken vs. musical learning)?

Hypothesis 5: Verbal learning with a musical mnemonic induces neural plasticity that involves a different spatial distribution than the plasticity associated with spoken verbal learning.

Chapter 3. Methods

Section 3.1 includes information on the study’s experimental design, including the subjects, task, and stimuli. The section also includes details on the specific equipment and procedures used in the study. The methods for collecting the behavioral and physiological data are described in Section 3.2. The section also describes how the EEG data is preprocessed to derive measures of brain oscillations. Section 3.3 completes the chapter by describing how the data is statistically analyzed.

3.1 Experimental Design

Subjects

Colorado State University’s institutional review board (IRB), the Human Subjects committee of the Regulatory Compliance office, approved the study under the title “The Cognitive Neuroscience of Auditory Rhythms”, protocol number 99-299H. Students in the undergraduate Introductory Psychology (PY100) course at Colorado State University were recruited to participate in the study. By participating in the study, students were given partial credit toward the research requirements of the course. To be eligible for participation, students had to:

- be at least 18 years old,
- be right-handed,
- be a non-musician,
- be a non-smoker,
- have normal or corrected vision,
- have normal or corrected hearing,
- not have a past history of significant brain injury,

- not have a past history of neurological or psychiatric conditions (e.g., epilepsy, depression), and
- not be allergic to latex.

After students signed up for the experiment, they were called to 1) confirm they meet inclusion criteria, 2) describe the pre-experiment preparation requirements, and 3) schedule the experimental session. The preparation requirements include dry hair with no use of conditioners, gel, or hairspray. Subjects were also told that, if they normally wear contacts, the experiment would likely be more comfortable if they wear glasses instead. Contacts tend to increase blinking, which causes undesirable artifacts in the EEG.

All subjects provided written, informed consent approved by Colorado State's Institutional Review Board. They were randomly assigned to one of two experimental conditions in a between-subjects design: with and without a musical mnemonic, hereafter referred to as the "musical" and "spoken" conditions. The study included 10 subjects in each condition. As described in section 3.2, one subject from each group was excluded from further analysis due to excessive artifact in the EEG. For the remaining subjects, age ranges were 18-26 yrs (mean = 19.8, SD = 2.8) for the "spoken" condition and 18-21 yrs (mean = 19.0, SD = 1.0) for the "musical" condition. Each condition included seven females.

Verbal learning task

Verbal learning was tested with a modified version of the classic neuropsychological assessment test, Rey's Auditory Verbal Learning Test (AVLT – see Figures 3.1 and 3.2) (Lezak, 1995). Subjects hear a standard ("A") list of 15 words repeated in five trials, and the subjects are asked to recall as many words as possible after each list presentation. Subjects then hear and were asked to free recall a new distractor ("B") list. This distractor list serves to test whether an increase in performance was merely a general time-dependent effect. If subjects' performance in

recalling the single presentation of the B list is not similar to their performance on the first repetition of the A list, it would suggest that changes in performance during the five learning (A-list) trials were perhaps due to some general time-dependent factor. Subjects were then given a 20-minute distractor task in which they were instructed to visualize briefly displayed images of the words “yes” and “no”. On the memory trials before (“m1”) and after (“m2”) the distractor task, subjects were asked to free recall the original list. The 15 words in each list are semantically unrelated. Thus, because the span of words that can typically be retained in memory is 7 +/- 2 (Miller, 1956), the AVLT is considered a supraspan verbal learning and memory task. The words are presented at a rate of one per second and the presentation order is the same on every trial. On each trial, subjects are instructed to listen carefully as they will subsequently be asked to recall as many words as possible, and that order is not important. Subjects were not given feedback on any trials. The number of words correctly recalled on each of the five learning trials serves as the behavioral evidence of verbal learning. Recall of the list was tested without further presentation of the original list after subjects heard and free recalled a distractor list and again after a 20-minute non-verbal distractor task.

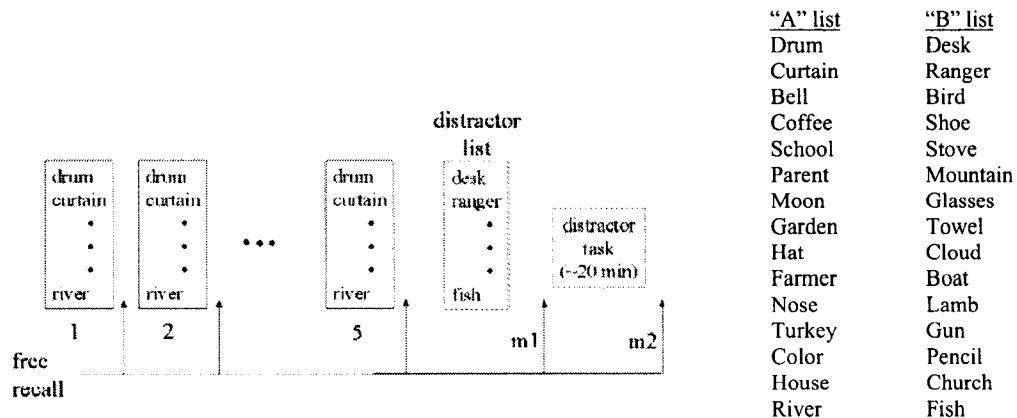


Figure 3.1 Rey's Auditory Verbal Learning Test (AVLT). There are five presentations of the same (“A”) word list and one presentation of a new distractor (“B”) word list. On each trial, subjects hear the full list of 15 words before being prompted to recall. Subjects are asked to free recall the original list of words again without additional presentation immediately after the distractor list (m1) and after a distractor task (m2) lasting approximately 20 minutes.

In one condition subjects heard the word lists in a standard, spoken fashion. In the other condition subjects heard the word lists in a musical-rhythmic context, with the word list presented as lyrics for a novel song (see Figure 3.3). The spoken and musical conditions used identical word lists of equal overall duration. All stimuli were presented at 80 dB sound pressure level (SPL) through a pair of speakers behind the subject (i.e., free field). The sound files were recorded using the same female voice for both conditions. One-syllable words were assigned one quarter note of 1 sec duration, while two-syllable words were assigned one eighth note of 0.5 sec (500ms) per syllable to generate melodic-rhythmic phrasing and to keep the sung condition at 15 seconds duration (with one second rest at the end). The song was sung by a female vocalist and included a keyboard accompaniment. The originally composed melody was not familiar but was simple and repetitive in structure, with measure pairs organized into an ABAB' form.

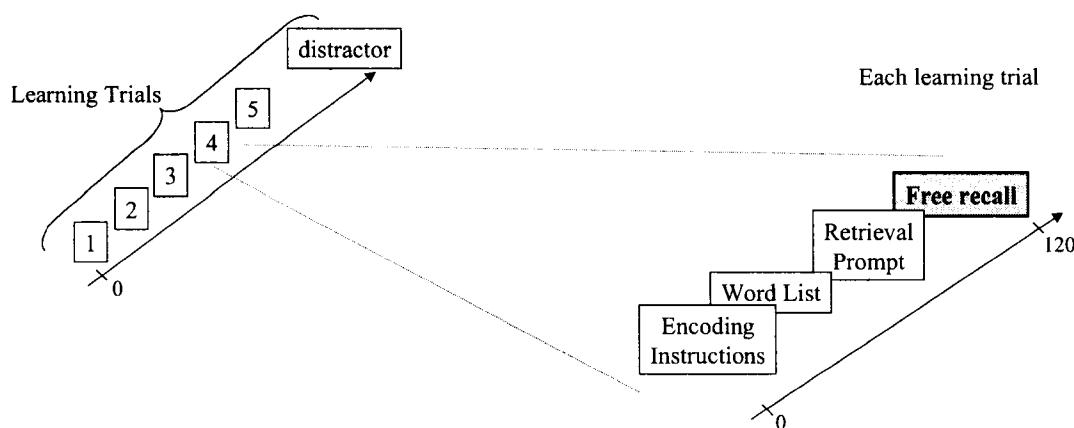


Figure 3.2 AVLT procedure. On each of the five learning trials (1-5), as well as the following distractor trial, subjects are given instructions for learning the list, then given the actual word list, then instructed to free recall the words. Each such trial takes an average of approximately 120 sec.

J. 140 G C D

Drum, cur-tain, bell, cof - fee, school, par - ent, moon and gar - den,

G D7 G

hat, far - mer, nose, tur - key, co - lor and house and ri - ver.

(A)

J. 120 D G D A7

Desk and ran - ger bird and shoe and stove and moun - tain glass-es, towel

D Emin/G A7 D

cloud and boat and lamb and gun and pen - cil and church and a fish.

(B)

Figure 3.3 Musical scores for the words lists. (A) is the “A”-list, (B) is the “B”-list.

Equipment

The AVLT is typically administered in person without simultaneously recorded EEG. In the present study, the AVLT was administered using pre-recorded sound files and remotely recorded voice responses with the subjects isolated in a recording chamber. This has two advantages. First, by automating the stimulus presentation, it maximizes consistency between trials for each subject, and also across subjects. Second, it avoids the increased risk of artifacts in the simultaneously recorded EEG that would normally accompany personal interaction. The recording chamber consisted of a Faraday cage enclosed by a sound-proof booth. Subjects sat in a recliner. A 17" diagonal CRT monitor displaying a fixation point was placed approximately 5 feet directly in front of the subject. The fixation point consisted of a white "+" approximately 6" wide on a black background. Auditory stimuli were presented via speakers positioned

approximately three feet behind and two feet to either side of the subject. A microphone positioned approximately one foot in front of the subject's mouth recorded all verbal responses. A serial response box (Psychology Software Tools, Inc., Pittsburgh, PA, USA) was placed on a 1'x4' board that straddled the sides of the recliner and provided a comfortable location for the response box over the subject's lap. Subjects used button presses on the response box to start the experiment and indicate when they were done recalling words on each trial.

Stimuli and verbal per-trial instructions were recorded using a microphone and saved to both stereo channels in audio (“.wav”) files using GoldWave (GoldWave, Inc., St. John’s, Newfoundland, Canada). The audio files were loaded into E-Prime (Psychology Software Tools, Inc., Pittsburgh, PA, USA), which was also used to program the sequence of stimuli and response contingencies used in the procedure. One Microsoft Windows PC ran E-Prime. A separate Microsoft Windows PC ran Acquire (Neuroscan, El Paso, TX, USA) software, which was used to record EEG. The E-Prime PC sent “trigger” signals to the EEG PC via a serial cable. The Acquire software detected the trigger signal so that the continuously recorded EEG would include markers indicating trial onsets with approximately 1 ms resolution. Neither the E-Prime PC nor the EEG PC could be simultaneously used for digital voice response recording, and the laboratory did not have an extra computer available, so subjects’ verbal responses were recorded on a cassette tape recorder manually-operated by the laboratory technician.

The EEG was continuously recorded throughout the experiment with a 32-electrode “QuikCap” cap (Neuroscan, El Paso, TX, USA) and “SynAmps” amplifiers (Neuroscan, El Paso, TX, USA). The positions of the electrodes are shown in Figure 3.4. There are actually 37 physical electrodes in the cap, including 30 scalp electrodes, 1 electrode for each mastoid, 1 ground electrode, and 4 electrodes used for EOG channels. The mastoid electrodes are physically linked and serve as a reference for the scalp electrodes. The EOG “channels” are bipolar and are used to monitor blinks and eye movement artifacts. The VEOG channel measures the vertical electrooculogram by taking the difference between electrodes above and below the left eye, and

the HEOG channel measures the horizontal electrooculogram by taking the difference between electrodes placed on the outer canthus of each eye (i.e., just lateral to both eyes). The signals were analog band pass filtered 1-100 Hz before digital sampling at 1 kHz. Although much higher than the 200 Hz required by Nyquist, signals were sampled at 1 kHz for the mere convenience that in subsequent time-domain analyses and plots, samples are equivalent to milliseconds.

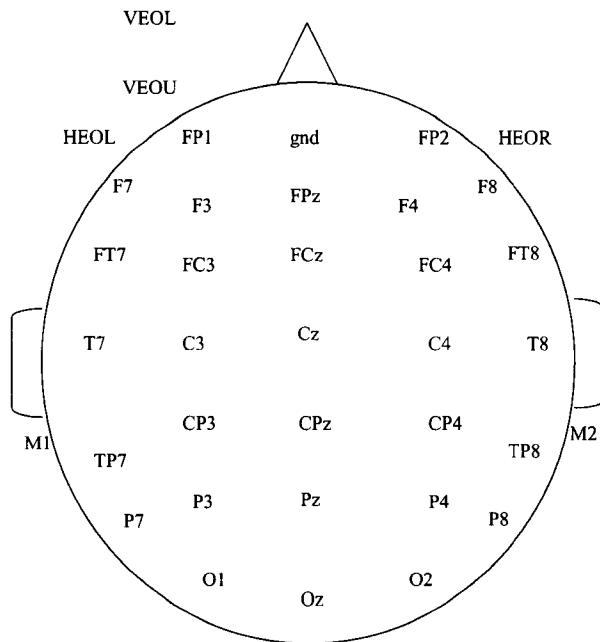


Figure 3.4 Layout of electrodes in the 32-channel QuikCap.

Procedure

After providing informed consent and removing obtrusive accessories such as glasses, jewelry, and hair appliances, subjects were fitted with the appropriately sized electrode cap. Various reference points on the cap and facial electrodes for recording ocular artifact are positioned then all cap electrodes are filled with the electrolytic gel and adjusted until impedances fell below 8 kOhm. Subjects participate in a simple demonstration of the effect of eye blinks and eye movement on the EEG. Then they are led into the recording chamber, positioned comfortably in the recliner, and briefed on how to use the response box and microphone. They

are also given general instructions for minimizing artifacts. Finally, they are given condition-specific instructions to learn the words, asked to confirm that they understand, and the experiment began. After the experiment was complete, the EEG cap was removed and the subject formally and informally debriefed on the experiment. Full details of the procedure for preparing the subjects and applying the electrode cap are provided in Appendix B.

3.2 Data Acquisition

Section 3.1 described the subjects, task design, equipment, and procedures used for physically acquiring the raw data. This section describes the collating and translation of the physically recorded responses and signals into a data format used in subsequent data analysis.

Behavioral

Subjects' verbal responses were replayed and manually scored for their content. A list of correctly recalled words was noted for each trial. The responses were translated to a binary "recall" matrix of 15 rows and 8 columns. The rows corresponded to words in the ordered word list and the columns corresponded to trials (1-5 learning trials, 6 distractor trial, 7 and 8 later memory trials). Trial-to-trial dynamics during the learning phase were evaluated by pair-wise evaluation of the first 5 columns of the "recall" matrix. The transition from not being able to recall to being able to recall a word that is repeatedly presented served as the operational definition of verbal learning. Specifically, this referred to the transition from a trial in which the word is not correctly recalled to the first trial in which the word is correctly recalled (see Figure 3.5). Thus subsequent analysis of EEG activity focused on newly recalled words from second or later presentations of the word. Analogously, repetition without learning was represented by trial-to-trial pairs in which the word is not recalled in both trials.

		Trial				
		1	2	3	4	5
Word	1					
	2		→			
3						
14			●			
15			●			
			→			
				→		

Figure 3.5 Operational definition of verbal learning. Learning, denoted by the arrows, occurs the first time a given word is successfully recalled (shaded) after having been presented at least twice. Thus, trial pairs used to evaluate learning consist of an unrecalled trial followed by a first-time recall during the very next trial (i.e., next list presentation).

Physiological

Digital EEG recordings were manually examined off-line for excessive artifacts.

Electrodes FC4 and FCZ exhibited occasional railing due to sporadic technical problems with the corresponding channels in the amplifier and were excluded from further analysis. Neuroscan's ocular artifact reduction was used to regress out ocular artifacts from non-EOG electrodes (Semlitsch, Anderer, Schuster, & Presslich, 1986). One subject from each group exhibited excessive ocular artifact and their data was excluded from further analysis.

Independent components analysis (ICA) was applied to the remaining 30 electrodes of the continuously recorded digital EEG data from the beginning of the first trial to the end of the last. The general framework for ICA includes m sources (**s**) and n observations (**p**), and the algorithm iteratively finds an $n \times m$ mixing matrix **W** under the constraint that the sources have maximally independent time courses.

$$\mathbf{p} = \mathbf{Ws}$$

In the application of ICA to EEG, the observations are the time samples of the signals (e.g. one observation every msec), the k^{th} column of **W** gives the scalp projection of source k , and the j^{th} row of **W** gives the weighting of the m sources to electrode j .

The Matlab (The MathWorks, Inc., Natick, MA, USA) implementation of the ICA procedure called Infomax, available as part of the EEGLAB software (Delorme & Makeig, 2004), was used. ICA first sphered the data, which decorrelated the electrodes. This simplified the ICA procedure to finding a rotation matrix which has fewer degrees of freedom (Hyvärinen & Oja, 2000). Except for the convergence criteria, all of the default parameter values for EEGLAB's Infomax algorithm were used. To make the subsequent per-electrode and per-component analyses comparable, the same four quadrants depicted in Figure 3.6 below were used for per-electrode analyses. The spatial organization of topographic EEG into quadrants was motivated by previous EEG research in working memory (Sarnthein, Petsche, Rappelsberger, Shaw, & von Stein, 1998), which has been associated with widely distributed anatomical substrates not unlike those associated with verbal learning. Four electrodes, specifically chosen to represent spatially distinct regions on the scalp and to avoid both sagittal and coronal midline electrodes, defined each of the four quadrants. The four independent components with the strongest average projection to the electrodes in that quadrant were identified for each of the four quadrants. Thus, subsequent spectral analysis of the left frontal quadrant, for example, reflected spectra in the four sources with the strongest projection to the left frontal quadrant.

The trigger signal from E-Prime marked the beginning of each trial. The onset of each word in each trial was calculated by adding to the per-trial trigger the relative delays of word onsets measured in the audio .wav files. Per-word epochs were constructed by selecting the EEG (and independent component time series) from a time window commonly used in verbal learning studies: 500 ms starting 250 ms after each word's onset.

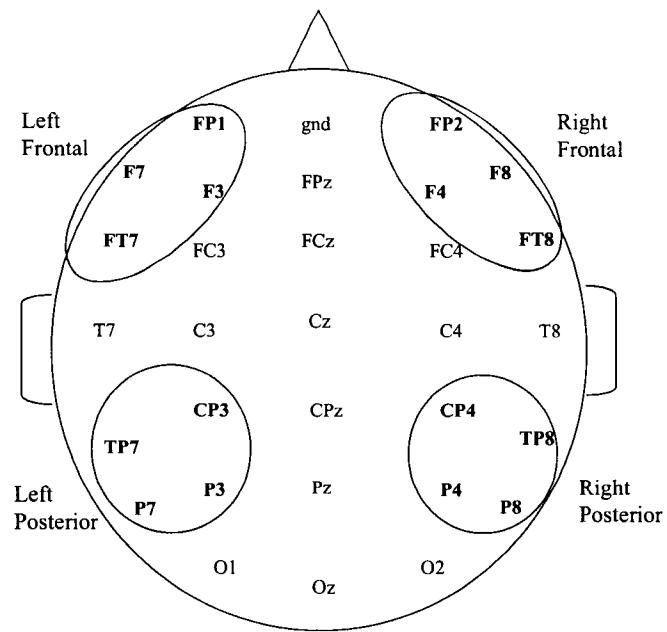


Figure 3.6 Topographic quadrants. Each of the four quadrants is defined by four electrodes as denoted above.

“Per-electrode spectral power” was computed for each epoch in each of the 16 electrodes included in the four topographic quadrants. Analogously, the “per-source spectral power” was computed for each epoch in each of the 16 independent components with projections to each of the four quadrants. In both cases, spectral power was computed with Welch’s periodogram method, which uses the average spectra from overlapping windows of the epoch. Then the average spectral power was calculated in each of the delta (2-5 Hz), theta (5-7 Hz), alpha₁ (7-9 Hz), alpha₂ (9-11 Hz), alpha₃ (11-13 Hz), beta₁ (13-20 Hz), beta₂ (20-33 Hz), and gamma (34-50 Hz) frequency bands. These spectral power measures were, in turn, log-transformed and outliers were clamped at +/- three standard deviations. The results were averaged over the four electrodes (or independent components) in each quadrant. Thus, there are single “per-electrode spectral power” and “per-source spectral power” measures for each frequency band for each epoch and each quadrant.

The four quadrants are also used in computing inter-electrode coherence. Inter-electrode coherence over each epoch was computed for all pairs of the 16 electrodes in the quadrants in each of the theta (5-7 Hz), alpha₁ (7-9 Hz), alpha₂ (9-13 Hz), beta (13-30 Hz), and gamma (34-50 Hz) frequency bands. These frequency bands are slightly different from and a subset of the eight frequency bands used in per-electrode spectral measures because the coherence metric involves lower frequency resolution.

Coherence C_{ij} between each pair of electrodes i and j is defined as the magnitude squared of the cross spectral density between electrodes i and j normalized by the product of the two electrodes' respective power spectral densities:

$$C(f)_{ij} = \frac{|P_{ij}(f)|^2}{P_{ii}(f)P_{jj}(f)} = \frac{\left| \sum_{i=1}^N F_i(f) \cdot F_j^*(f) \right|^2}{\sum_{i=1}^N |F_i(f)|^2 \cdot \sum_{i=1}^N |F_j(f)|^2},$$

where $C_{ij} \in [0,1]$, P_{ij} is the cross spectral density between electrodes i and j , P_{ii} and P_{jj} are the power spectral densities of electrodes i and j , respectively, N is the number of trials, * denotes complex conjugate, and $F_i(f)$ is the Fourier transform of the EEG signal from electrode i at frequency f . Although investigators in various subfields of neuroscience have employed different definitions of coherence, this specific definition was chosen because it is the variant most commonly used in the most closely related research (Weiss & Rappelsberger, 2000; Summerfield & Mangels, 2005).

Two forms of aggregated coherence measures were considered. “Intra-quadrant coherence” was defined as the mean coherence among all six ($\frac{4 \times 3}{2}$) pairings of electrodes within each quadrant. “Inter-quadrant coherence” was defined as the mean coherence among all 16 inter-quadrant pairings of the two sets of four electrodes defining two quadrants. Thus inter-quadrant coherence was defined for frontal, right, posterior, and left quadrant pairs.

Trial-to-trial changes were computed for all four metrics (“per-electrode spectral power”, “per-source spectral power”, “intra-quadrant coherence”, and “inter-quadrant coherence”). As a result, for every subject/metric/“channel”/frequency band, the 15 word x 5 trial matrix of encoding-related EEG was converted to a 15 word x 4 “trial-to-trial change” matrix. Here “channel” refers to spatial dimension, such as electrode, independent component, and, in the case of coherence, quadrant or quadrant pair. The changes were then normalized on a per-subject, per-metric basis by dividing each of the trial-to-trial change metrics by the mean change over all 60 trial-to-trial changes of the subject’s change metrics. This normalization mitigates strong inter-subject differences in EEG dynamics, thereby facilitating the aggregation of the metrics across subjects within each group and the subsequent within and between group analyses.

3.3 Data Analysis

Behavioral

Rows were summed in the first six columns of the “recall” matrix (described in Section 3.2) to determine the total number of words correctly recalled on each trial. The corresponding learning curves were plotted to illustrate how the number of words correctly recalled on each trial increased over time. To determine whether the groups exhibited learning, the first and last trials’ performance was subjected to two-tailed T-tests with $\alpha= 0.05$. The groups’ total recall counts were compared with two-tailed T-test with $\alpha= 0.05$ on each trial to determine whether one group outperformed the other.

Physiological

Repetition and learning were quantitatively evaluated and compared using changes in the four EEG metrics described in Section 3.2: per-electrode spectral power, per-source spectral power, intra-quadrant coherence, and inter-quadrant coherence. For each metric, trial pairs were divided into two types based on behavioral data: repetition and learning. As described in Section 3.2, “repetition” refers to a pair of consecutive trials of the same word in which the word is not

recalled on either trial. “Learning” refers to a pair of consecutive trials of the same word in which the word is not recalled on the first trial and is recalled on the second. Because there is stimulus repetition in both cases, comparing the “learning” condition to the “repetition” condition primarily elucidates the incremental effects of learning alone. Means and standard errors were plotted for each metric in three comparisons: repetition vs. learning in spoken verbal learning, repetition vs. learning in musical verbal learning, and learning in spoken vs. musical verbal learning, each corrected for repetition by subtracting the mean repetition metric.

Despite reducing the spatial dimension to a quadrant-level analysis, the EEG metrics still involved a very high number of dependent variables. Because of this and because of the inherent noise in EEG metrics, resampling statistics were used to quantitatively evaluate the physiological markers of repetition and learning. Furthermore, when compared to conventional statistical approaches such as analysis of variance (ANOVA), resampling statistics are more robust with respect to violations of normality, homoscedasticity, and outliers (Sarnthein et al., 1998; Nichols & Holmes, 2002; Maris, 2004; Hoogenboom, Schoffelen, Oostenveld, Parkes, & Fries, 2006).

Pseudocode for the resampling approach is given below:

```
for each metric
    for N iterations (N = 10000)
        randomly reassign trial pairs to condition ("repetition" or "learning")
        for every frequency band and spatial "channel",
            compute Hotelling's T2 statistic
            find the T2max

        sort the T2max scores in decreasing order
        for every frequency band and spatial "channel",
            T2actual = T2 statistic using the original (actual) condition assignments
            p(channel, frequency band) = the % of sorted T2max scores > T2actual
```

Hotelling's T^2 statistic is a variant of the student's t-statistic generalized to multivariate statistical testing. Comparisons were considered significantly different when $p < 0.05$. Qualitative follow-up analyses included an examination of the topography of the "per-electrode spectral power" averaged across subjects in each condition by interpolating the metric among all 28 of the non-artifactual scalp electrodes. This was done for those frequency bands where significant differences existed between conditions and/or groups. Post-hoc analyses motivated by the topographies are presented and discussed in Chapter 4.

Chapter 4. Results

The behavioral results that illustrate the actual learning curve of the task are presented in Section 4.1. The physiological changes that correspond to learning are presented in sections 4.2-4.4. Section 4.2 presents the physiological results for spoken verbal learning and Section 4.3 presents the physiological results for musical verbal learning. In both sections, the changes associated with learning are directly compared to the changes associated with repetition. In Section 4.4, the physiological changes associated with learning are “corrected” for the effects of repetition for each type of verbal learning and the spoken and musical modalities are compared directly. The results are organized by EEG metric in a similar sequence in Sections 4.2, 4.3, and 4.4: per-electrode spectral power, the topographic differences in per-electrode spectral power, per-source power, intraquadrant coherence, and finally interquadrant coherence. The entire chapter’s results are summarized in Section 4.5.

4.1 Verbal Learning – Behavior

Verbal learning performance, as measured by number of correctly recalled words over the course of the learning trials, is depicted in Figure 4.1. Subjects in the spoken condition recalled an average of 11.0 words on the last learning trial and 4.9 on the first, corresponding to a statistically significant improvement in performance, $t(16) = 9.6$, $p < 0.0001$. Subjects in the music condition recalled an average of 9.7 words on the last learning trial and 4.3 on the first, corresponding to a statistically significant improvement in performance, $t(16) = 6.3$, $p < 0.0001$. Most of the improvement in recall performance occurred in trials 2 and 3, with only minimal improvement in trials 4 and 5. Performance returned to baseline level on the distractor trial. Recall was not significantly different between the spoken and musical groups on any trial, all $t(16) < 1.4$ and $p >$

0.1. However, the mean performance averaged about one word higher in the spoken condition than in the musical condition.

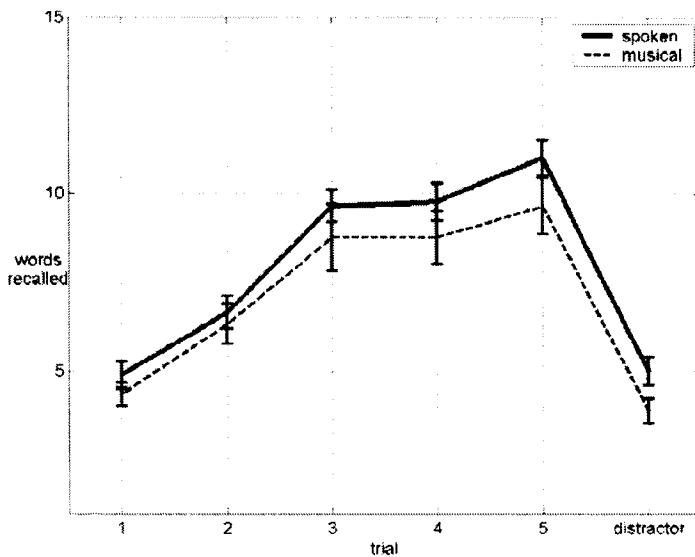


Figure 4.1 Verbal learning performance. Mean number of words correctly recalled on each trial for both groups. Error bars are standard error. Both groups demonstrate learning, recalling significantly more words on the last learning trial than on the first, with the most learning occurring early in the task (trials 2 and 3).

4.2 Physiology of Spoken Verbal Learning

In this and subsequent sections on physiological results, the data is provided in two formats. The first format is a collection of four bar plots organized in a roughly topographic fashion. Each bar plot shows the mean and standard errors of the normalized metrics for each of the frequency bands. Frequency bands are labeled in the figures as “d, t, a1, a2, a3, b1, b2, and g” for delta, theta, alpha₁, alpha₂, alpha₃, beta₁, beta₂, and gamma, respectively. For the per-electrode spectral power, per-source spectral power, and intraquadrant coherence metrics, the topographic organization reflects the relative position of the four quadrants. Left frontal is placed in the upper left, right frontal in the upper right, etc. The quadrants are also labeled on every plot: LF = left frontal, RF = right frontal, LP = left posterior, and RP = right posterior. For the inter-quadrant coherence metric the four bar plots are shifted to reflect the quadrants they link. For example, the coherence between the left and right frontal quadrants is depicted with a bar plot in

the upper center of the figure. Likewise, the coherence between the right frontal and posterior quadrants is depicted with a bar plot in the middle right of the figure. Thus the panels in the inter-quadrant coherence figures are F = between left and right frontal, R = between right frontal and right posterior, P = between left and right posterior, and L = between left frontal and left posterior. The second format shows the topographic distribution of per-electrode spectral power for individual frequency bands. The metric's values at the 28 non-artifactual electrodes are interpolated.

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Per-electrode spectral power

Figure 4.2 illustrates the changes in per-electrode spectral power, averaged over electrodes in each of the four scalp quadrants. With the exception of slight decreases in high frequency bands in some quadrants, repetition generally involved an increase in spectral power. In contrast, learning involved a mix of spectral power decreases and increases, depending on the quadrant and frequency band. Delta power increased in posterior areas, whereas β_1 power decreased in frontal areas. The only case in which there was a statistically significant difference between learning and repetition occurred in right posterior alpha₁, in which repetition was associated with an increase in spectral power and learning was associated with a decrease in spectral power.

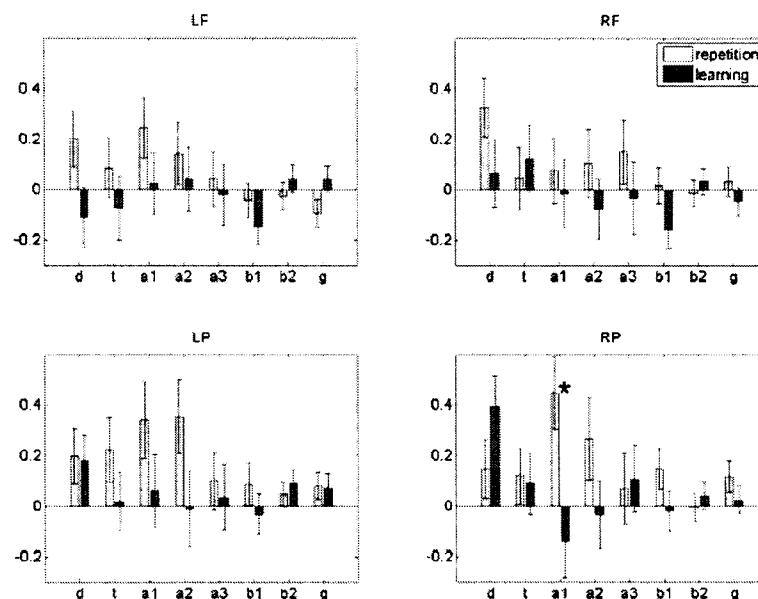


Figure 4.2 Changes in per-electrode spectral power associated with repetition and learning. Y-axis is normalized change in $\log_{10}(\text{spectral power})$. * $p < 0.05$

Figure 4.3 depicts the topographic distribution of α_1 spectral power changes for repetition and learning. The statistically significant difference in the right posterior quadrant is evident, with repetition involving increased spectral power, and learning involving decreased spectral power. Other patterns also emerge. Learning involved a decrease in spectral power relative to repetition over most of the scalp. Also, whereas right hemisphere spectral power increased going from anterior to posterior during repetition, an opposite trend emerged in learning, with right hemisphere spectral power decreasing in the anterior-to-posterior direction.

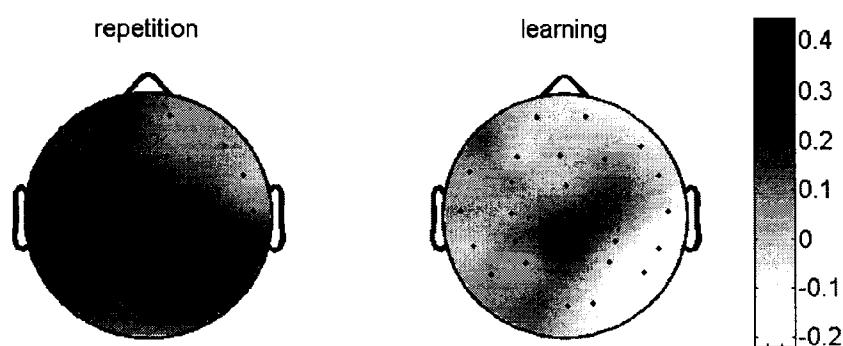


Figure 4.3 Topographic distribution of α_1 spectral power changes for repetition and learning. Anterior is top (nose), left is left. Same scale as Figure 4.2.

It should be noted that this and the later two figures showing the topographic distribution of spectral changes are designed to provide a qualitative picture of the effect. Statistical tests on the corresponding effects were only planned a priori for the per-quadrant analyses depicted in the immediately preceding figures because of the poor spatial resolution of EEG. The noise levels implied by the standard error bars in the immediately preceding plots are representative of the standard errors one would expect for each electrode in the topographic representation. The topographic distribution of only the frequency band exhibiting statistically significant differences between learning and repetition is depicted.

“Per-source” spectral power

Spectral power changes of independent sources are shown in Figure 4.4. As with per-electrode spectral power, the spectral power of independent sources increased with repetition. However, the exception to this, decreases in power in upper frequency bands, was more pronounced in beta and gamma frequency bands of the independent sources. This effect was isolated to sources with frontal projections. In contrast, in per-electrode spectra, upper frequency power decreases were less consistent among bands and distributed among 3 of the 4 quadrants.

Although learning involved a mix of increased and decreased spectral power in independent sources, the strongest effects were decreases in alpha₃ and beta₁ frequency bands in sources projecting to the right hemisphere. This also resulted in the only statistically significant difference between repetition and learning, which occurred in alpha₃ in right frontal quadrant. Independent sources with projections to the right frontal scalp quadrant exhibited increased alpha₃ power for repetition and decreased alpha₃ power for learning.

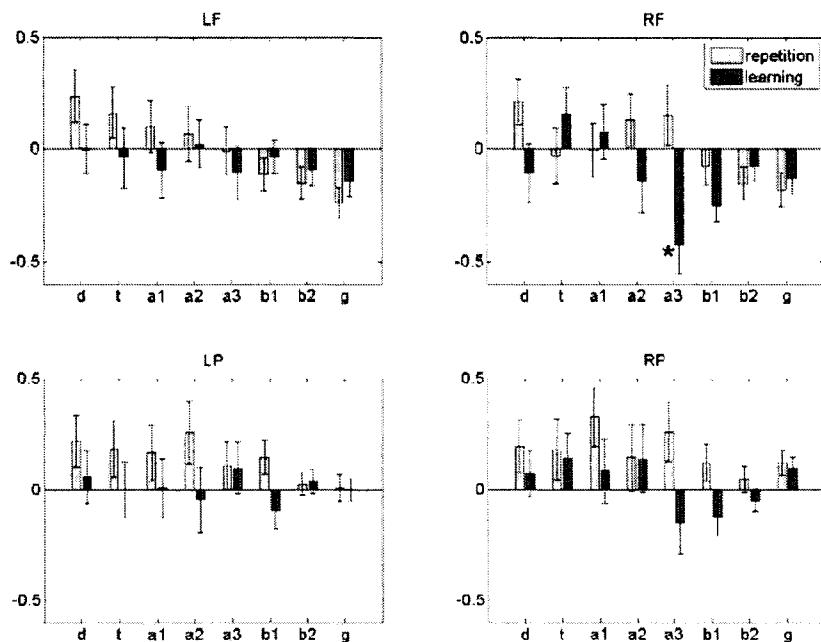


Figure 4.4 Changes in per-source spectral power associated with repetition and learning. Y-axis is normalized change in $\log_{10}(\text{spectral power})$. * $p < 0.05$

Intra-quadrant coherence

The effects of repetition and learning on coherence, shown in Figure 4.5 below, are mixed and exhibit no clear pattern. In most frequency bands in most quadrants, both conditions showed minimal if any change in strength of coherence. Although not statistically significant, alpha₂ coherence in the left frontal quadrant decreased during repetition and increased during learning. Similarly, theta coherence in the right posterior quadrant was essentially unchanged during repetition, but increased substantially during learning. As with the alpha₂ result, this effect was not statistically significant.

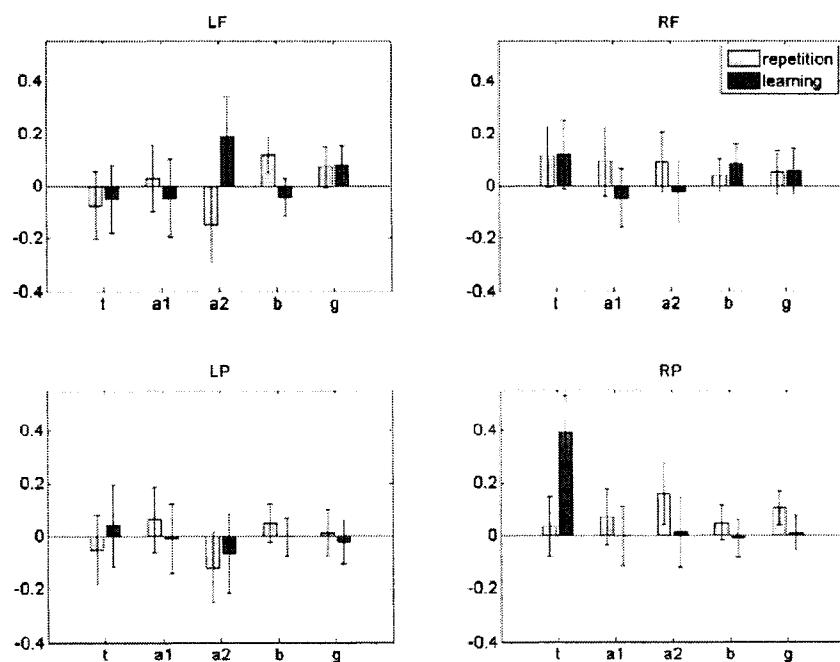


Figure 4.5 Changes in intra-quadrant coherence associated with repetition and learning. Y-axis is normalized change in coherence. * p< 0.05

Inter-quadrant coherence

Figure 4.6 illustrates changes in the strength of coherence between the four quadrants.

As with the intra-quadrant measures described earlier, in most quadrant pairs and in most frequency bands, repetition and learning exhibited minimal changes in coherence strength individually, and there were minimal differences in coherence changes between the two conditions. A few notable exceptions exist. With the exception of alpha₂, repetition involved no coherence strength decreases in the other frequency bands in all quadrant pairs. The only significant difference between the two conditions occurred in the gamma band in the coherence between right frontal and right posterior quadrants. In that case, repetition involved increased coherence strength whereas learning involved decreased coherence strength.

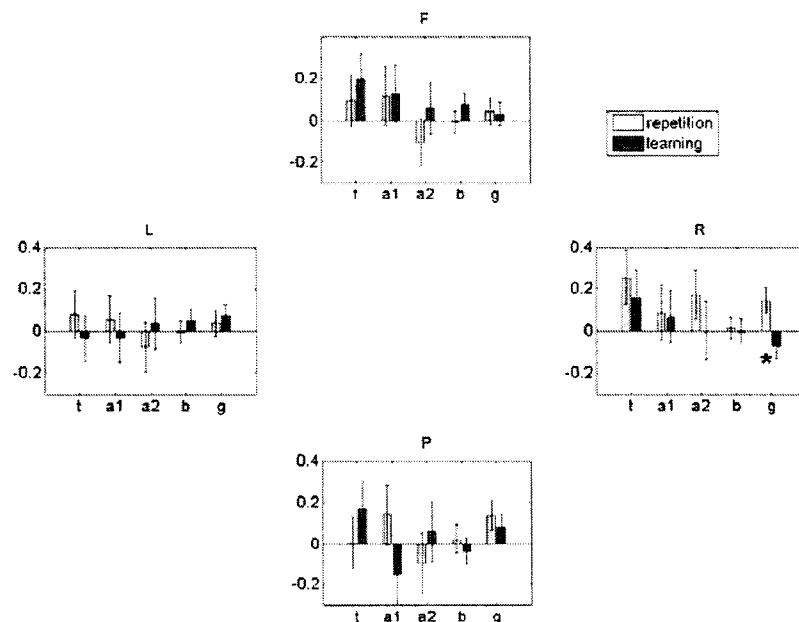


Figure 4.6 Changes in inter-quadrant coherence associated with repetition and learning. Y-axis is normalized change in coherence. * p< 0.05

4.3 Physiology of Musical Verbal Learning

Per-electrode spectral power

Figure 4.7 illustrates the changes in per-electrode spectral power, averaged over electrodes in each of the four scalp quadrants. As was the case with spoken verbal learning, repetition generally involved an increase in spectral power, particularly in upper alpha bands in posterior quadrants. In contrast, learning involved a mix of spectral power decreases and increases, depending on the quadrant and frequency band. There were notable decreases in delta and theta power in left frontal and right posterior quadrants, and in theta and alpha₁ power in the right frontal quadrant. The contrast between repetition and learning was statistically significant for left posterior alpha₃ power and approached significance for frontal theta power. In each of these cases, repetition was associated with power increases and learning with power decreases.

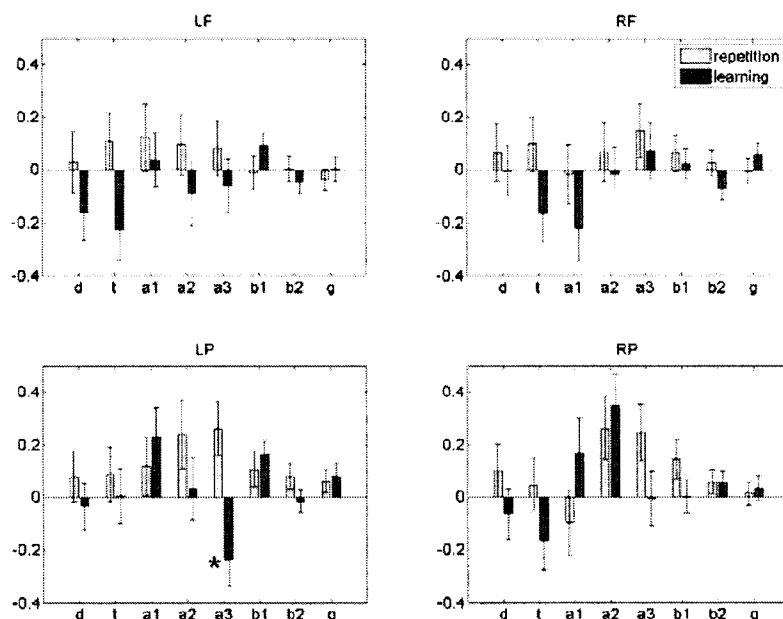


Figure 4.7 Changes in per-electrode spectral power associated with repetition and learning. Y-axis is normalized change in $\log_{10}(\text{spectral power})$. * $p < 0.05$

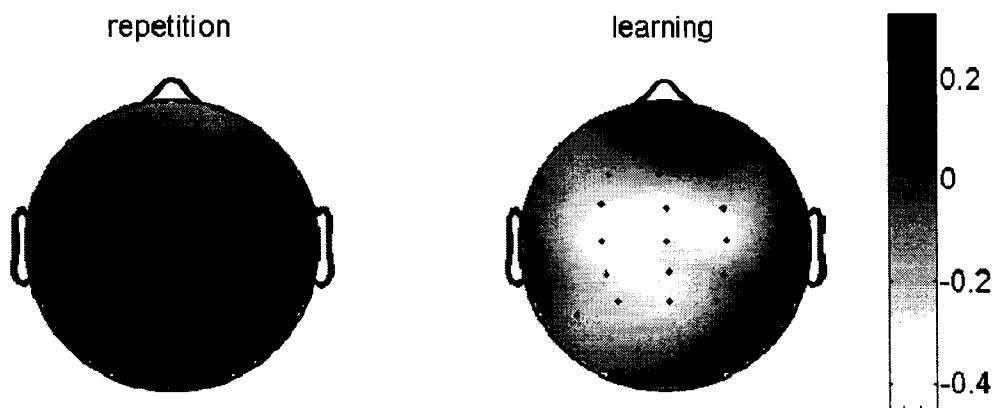


Figure 4.8 Topographic distribution of alpha₃ spectral power changes for repetition and learning. Anterior is top (nose), left is left. Same scale as Figure 4.7.

As seen in Figure 4.8, the topographic distribution of alpha₃ spectral power changes was qualitatively very different for repetition and learning in the case of musical verbal learning. Repetition involved increased spectral power over most of the scalp, strongest in centromedial areas. Conversely, learning involved widespread decreases in spectral power, strongest in centromedial areas. The planned comparisons in the four quadrants did not detect differences in centromedial areas. Thus, a significant alpha₃ difference between repetition and learning was detected only in the left posterior quadrant, where the strong centromedial effects extend to scalp areas in that quadrant. Post-hoc analysis of alpha₃ spectral power changes at Cz, the centromedial electrode, showed a strong effect of learning versus repetition, with a $p < 0.005$.

“Per-source” spectral power

Changes in the spectral power of independent sources are shown in Figure 4.9. In contrast to per-electrode spectral power, the increased spectral power of independent sources associated with repetition was more predominantly posterior in distribution. Similar to the per-electrode spectral power, learning was associated with a mix of per-source increases and decreases in spectral power, depending on frequency band and quadrant. However, none of the per-source spectral power differences between repetition and learning were statistically significant.

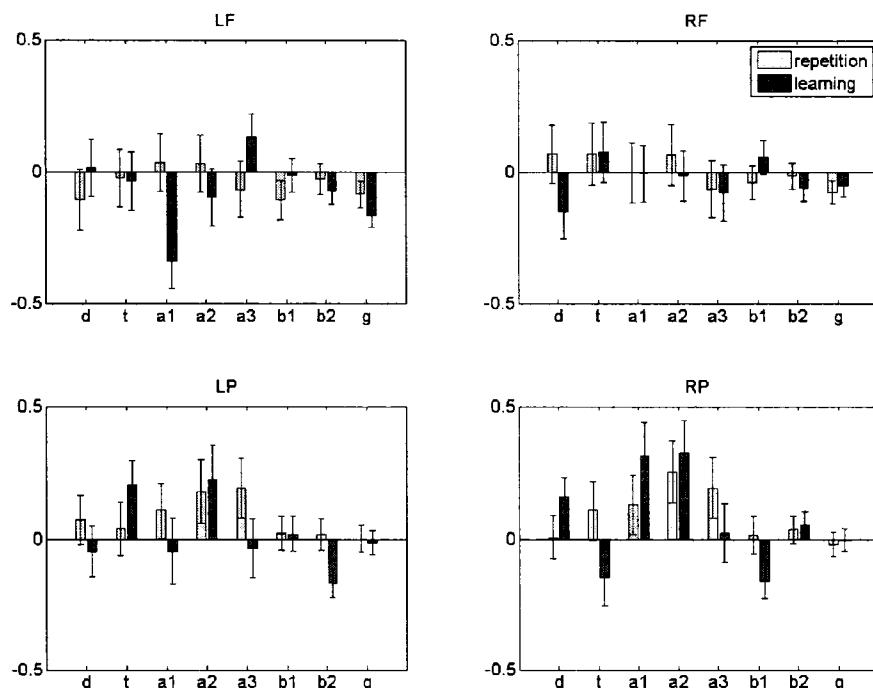


Figure 4.9 Changes in per-source spectral power associated with repetition and learning. Y-axis is normalized change in $\log_{10}(\text{spectral power})$.

Intra-quadrant coherence

The effects of repetition and learning on coherence, shown in Figure 4.10 below, are mixed and exhibit no clear pattern. In most frequency bands in most quadrants, both conditions showed minimal if any change in strength of coherence. Exceptions were the notable decreased strength in alpha₂ coherence in left quadrants and the increased strength in right posterior alpha₁ coherence, both associated with musical verbal learning. However, none of these effects were statistically significantly different from their repetition counterparts.

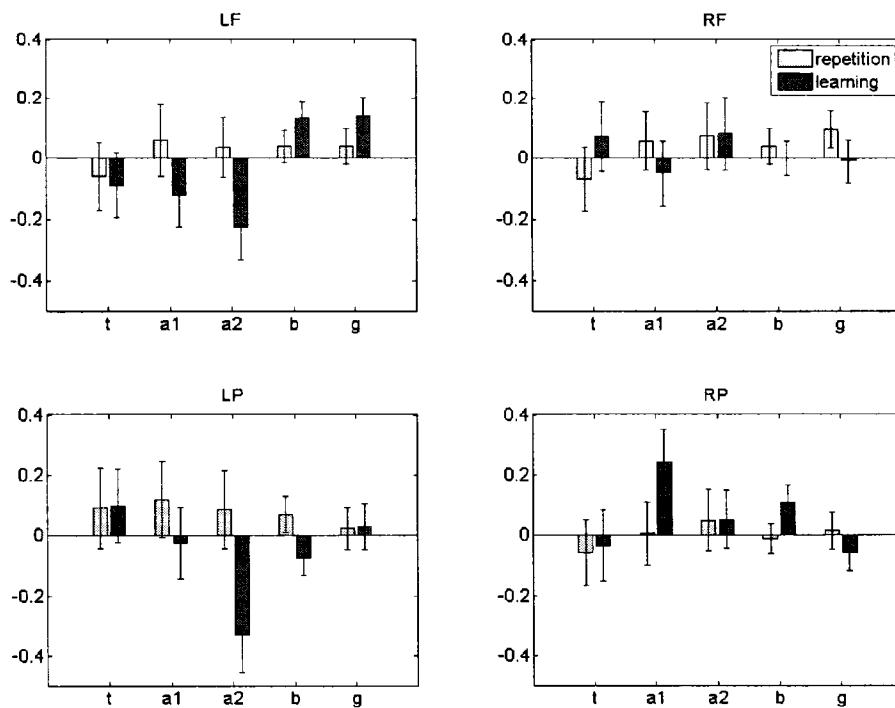


Figure 4.10 Changes in intra-quadrant coherence associated with repetition and learning. Y-axis is normalized change in coherence.

Inter-quadrant coherence

As with the intra-quadrant measures described earlier, in most quadrant pairs and in most frequency bands, individually repetition and learning exhibited minimal changes in coherence between the four quadrants (Fig. 4.11). There were minimal differences in coherence changes between the two conditions, with a few notable exceptions: learning was associated with increased coherence between frontal quadrants in every frequency band. The strongest effects occurred in the theta and alpha₁ bands, although this effect was not statistically significant. The difference between repetition and learning was most noticeable in the coherence between posterior quadrants. Repetition evoked increased coherence in theta and alpha₂; learning was associated with an opposite pattern of decreased coherence in those two frequency bands, and increased coherence in alpha₁. This effect was nearly significant ($0.1 > p > 0.05$) for each of the three individual bands.

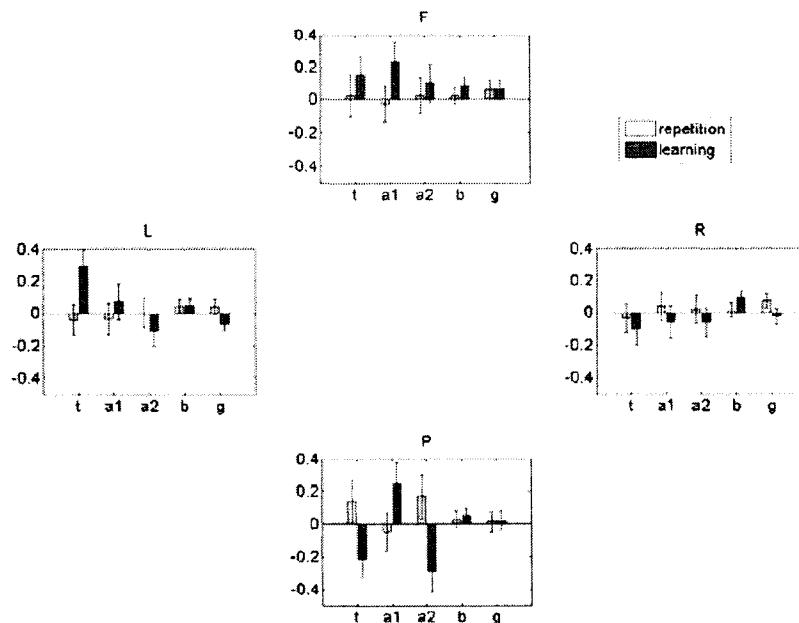


Figure 4.11 Changes in inter-quadrant coherence associated with repetition and learning. Y-axis is normalized change in coherence.

4.4 Comparing Spoken and Musical Verbal Learning

Verbal learning in the spoken and music groups was compared by first subtracting the mean effect of repetition from each group's individual learning metrics on a per-metric basis. The results for each metric are presented below.

Per-electrode spectral power

In general, the music group exhibited either less of a decrease, or an actual increase, in per-electrode spectral power compared to the spoken group (Figure 4.12). This difference was most notable in the alpha₁ band in posterior quadrants, and reached significance in the right posterior quadrant. One notable exception was the alpha3 band power in the left posterior quadrant, where the musical group exhibited a much stronger decrease in power than the spoken verbal learning group.

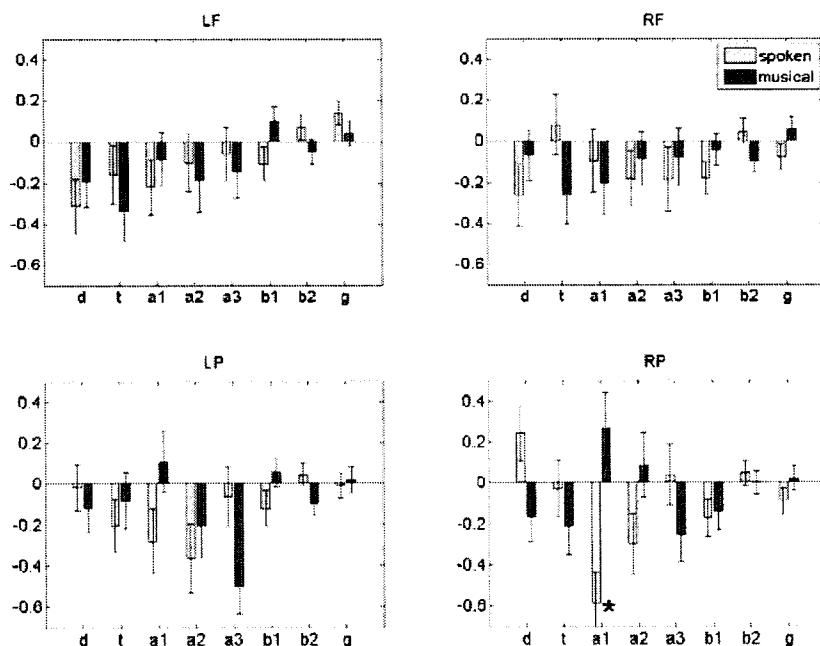


Figure 4.12 Changes in per-electrode spectral power associated with learning, corrected for repetition. Y-axis is normalized change in $\log_{10}(\text{spectral power})$. * $p < 0.05$

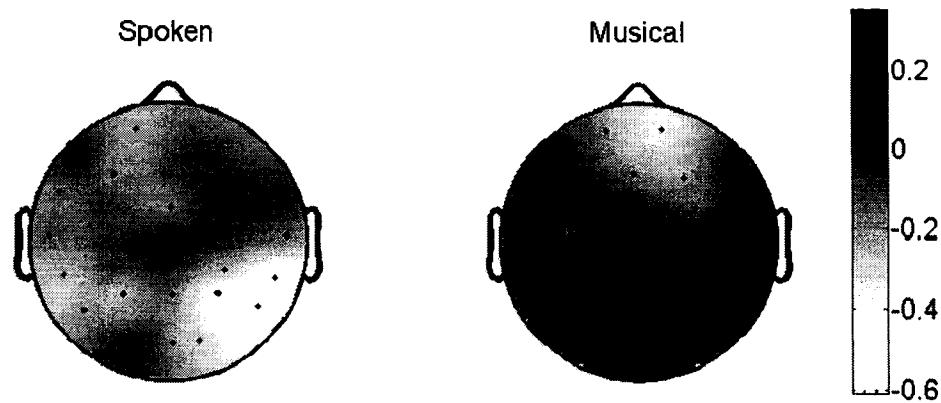


Figure 4.13 Topographic distribution of α_1 spectral power changes for spoken and musical learning, corrected for repetition. Anterior is top (nose), left is left. Same scale as Figure 4.12.

As seen in Figure 4.13, the topographic distribution of α_1 spectral power changes was qualitatively very different for spoken and musical verbal learning corrected for repetition.

Spoken verbal learning involved decreased spectral power over most of the scalp, strongest in right posterior areas. Musical verbal learning involved decreased spectral power in frontomedial areas, and increased power in posterior areas. The most notable difference between the two conditions was in the right posterior area, as detected in the planned per-quadrant analysis shown in Figure 4.12. Considering the frontal/posterior double dissociation between the two groups in conjunction with the right posterior quadrant differences, one could hypothesize that the two groups were best dissociated by their relative difference in right frontal/right posterior α_1 power changes. Post-hoc analysis of right-frontal – right-posterior metrics indeed showed a strong effect between the groups, with a $p < 0.005$. The same analysis on the left side was not significant, $p > 0.05$.

“Per-source” spectral power

Figure 4.14 shows that the groups’ repetition-corrected learning also differed in spectral power changes in independent sources. As with per-electrode spectral power, there was a general trend for the musical verbal learning group to exhibit either less of a decrease in spectral power or in some cases an increase in spectral power relative to the spoken verbal learning group. This difference reached statistical significance in α_3 spectral power in sources projecting to the right frontal quadrant, where the spoken group exhibited decreased power and there was no change in power for the music group. Exceptions to the pattern were seen in α_1 in sources projecting to frontal quadrant and in theta in sources projecting to the right posterior quadrant.

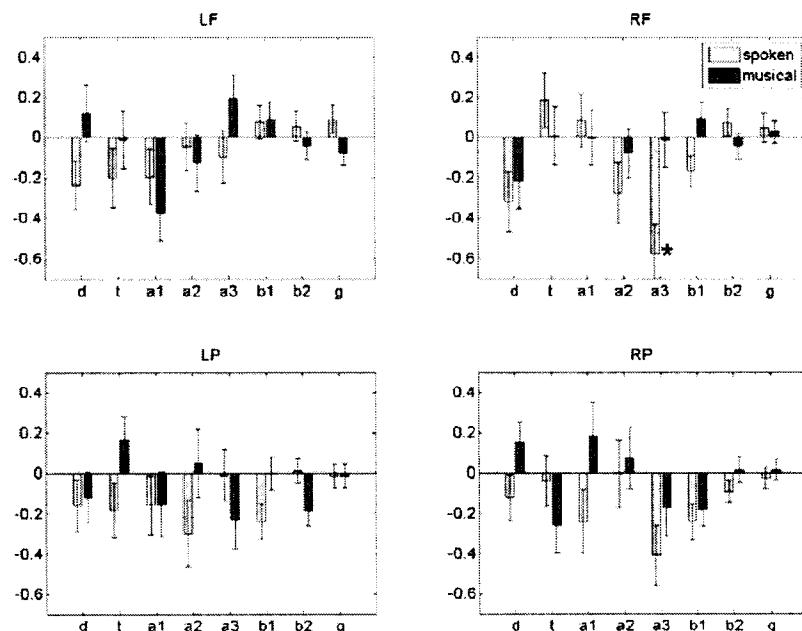


Figure 4.14 Changes in per-source spectral power associated with learning, corrected for repetition. Y-axis is normalized change in \log_{10} (spectral power). * $p < 0.05$

Intra-quadrant coherence

The within quadrant coherence changes associated with the two group's repetition-corrected learning are shown in Figure 4.15 below. The spoken group exhibited increased α_2 coherence, and the musical group decreased coherence, in both left quadrants, reaching significance in the left frontal quadrant.

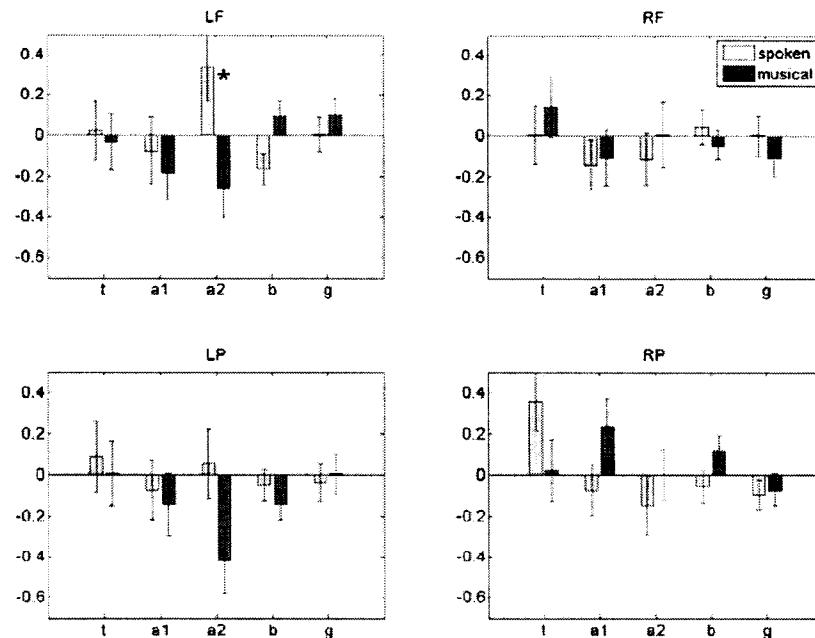


Figure 4.15 Changes in intra-quadrant coherence associated with learning, corrected for repetition. Y-axis is normalized change in coherence. * $p < 0.05$

Inter-quadrant coherence

Figure 4.16 below shows the changes in coherence between quadrants associated with repetition-corrected learning for both groups. The two groups' inter-quadrant coherence measures did not differ significantly when corrected for repetition. However, the differences did approach significance in coherence across the posterior hemispheres in the theta, alpha₁, and alpha₂ frequency bands. There was a double dissociation, in which spoken learning involved increased coherence in theta and alpha₂ bands and decreased coherence in alpha₁, whereas musical learning involved just the opposite pattern.

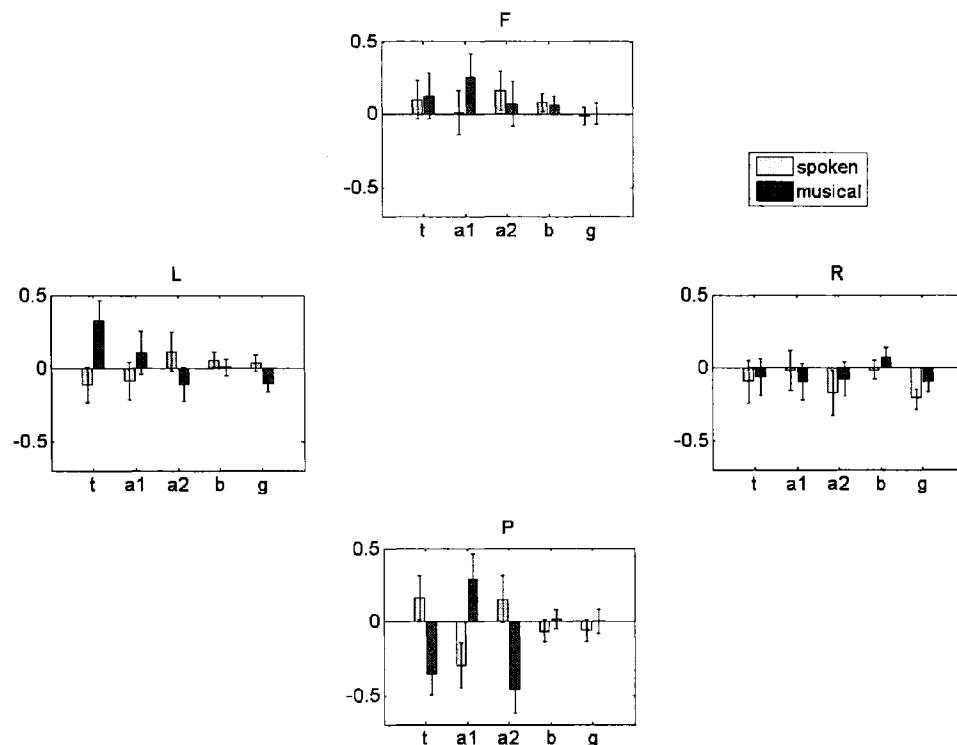


Figure 4.16 Changes in inter-quadrant coherence associated with learning, corrected for repetition. Y-axis is normalized change in coherence.

4.5 Controlling for Time-on-Task

If instances of repetition and learning do not share similar temporal distributions over the course of the task *and* if oscillatory metrics exhibit systematic changes over the course of the task, there is a possibility that differences between repetition and learning trial pairs could be measured “time-on-task” effects in addition to differences between repetition and learning per se. This issue was addressed in two ways. First, both repetition and learning were defined by the *changes* in oscillatory EEG metrics from one trial to the next. Thus, *linear* “time-on-task” changes in those metrics would be automatically controlled for by the definitions of the metrics, as depicted in the top part of Figure 4.17.

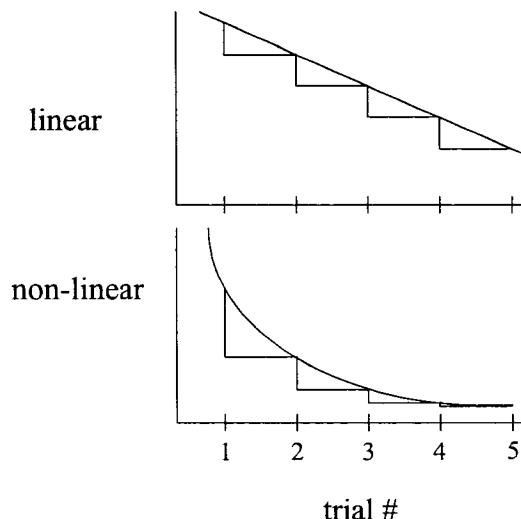


Figure 4.17 Interaction between linearity (or lack thereof) in physiologic metric and trial number for “time-on-task” effects.

However, if the “time-on-task” changes in oscillatory metrics were non-linear, trial-to-trial dynamics would vary with time. As depicted in the bottom part of Figure 4.17, for example, earlier trial pairs would exhibit a greater decrease than later trial pairs. Thus, the second way in which the “time-on-task” issue was addressed was by investigating the relative temporal distribution of repetition and learning trial pairs, as shown in Figure 4.18. In the spoken verbal learning condition, there is a slight trend for repetition trial pairs to occur earlier than learning

trial pairs (mean trial 3.1 vs. 3.4). However, this distinction was not statistically significant ($p > 0.05$, Student's t-test after Bonferroni correction). Although not visibly apparent from the figure, a similar trend was found in the musical verbal learning condition (mean trial 3.2 v. 3.3), but was also not statistically significantly different ($p > 0.05$, Student's t-test after Bonferroni correction).

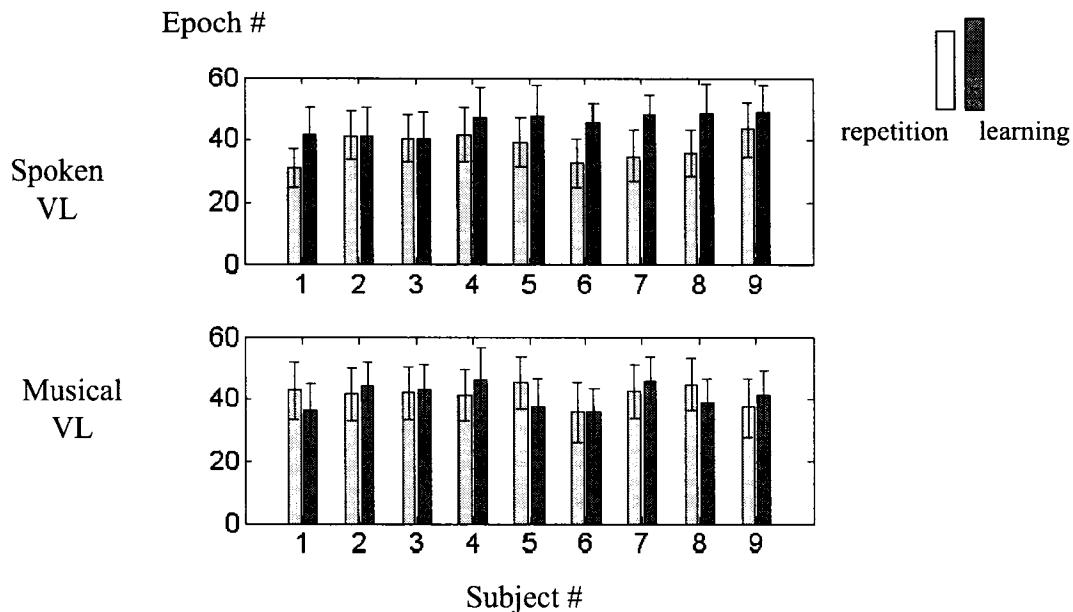


Figure 4.18 Distributions of repetition and learning trial pairs, defined by epoch number of the second trial, for each subject and each group (means +/- standard error). Epochs 1-15 correspond to trial 1, epochs 16-30 correspond to trial 2, etc.

4.6 Results Summary

Both groups exhibited successful verbal learning, as demonstrated by significant increases in the number of words correctly recalled over the course of the five learning trials. Although the mean music group performance was slightly lower than that of the spoken group, the difference was not statistically significant.

For the spoken group, repetition was generally associated with increased per-electrode spectral power, whereas learning was associated with either lower increases or decreases in spectral power. The distinction reached statistical significance in the case of right posterior

alpha₁ power. Similarly, spectral power was generally increased for repetition and, relatively, decreased for learning in the independent sources projected to the same four quadrants used to characterize the actual per-electrode spectral power. This reached significance in the right frontal quadrant for alpha₃ power. There were no significant differences between repetition and learning in intraquadrant coherence, although the pattern was for lower coherence in repetition and higher coherence in learning, most notable in left frontal alpha₂ and right posterior theta coherence. Conversely, repetition was associated with increased, and learning with decreased, gamma coherence between right quadrants.

For the music group, as with the spoken group, repetition was generally associated with increased per-electrode spectral power, whereas learning was associated with relatively lower spectral power. This effect was only statistically significant in left posterior alpha₃, and it approached significance in frontal theta band. There were no significant differences between repetition and learning in per-source spectral power, intraquadrant coherence, and interquadrant coherence. However, there was a relative decrease in alpha₂ coherence within both left quadrants comparing learning to repetition. There was also a broadband increase in coherence between frontal quadrants associated with learning, and a simultaneous decrease in coherence between right quadrants, and between posterior quadrants, in theta and alpha₂ frequency bands.

Verbal learning in the spoken and music groups was compared after subtracting the mean effect of repetition from their learning metrics. In general, the music group exhibited either less of a decrease, or an actual increase, in per-electrode spectral power compared to the spoken group. This difference was most notable in the alpha₁ band in posterior quadrants, and reached significance in the right posterior quadrant. Post hoc comparison of power spectral topographies suggested that the strongest difference between the groups was in their relative distribution of spectral power increases or decreases between frontal and posterior regions. The groups' repetition-corrected learning also differed in spectral power changes in independent sources: whereas the spoken group exhibited decreased alpha₃ spectral power in sources projecting to the

right frontal quadrant, the same sources exhibited no change in power for the music group. In terms of intraquadrant coherence, the spoken group exhibited increased coherence in left frontal alpha₂, and the music group exhibited decreased coherence. Although there were no significant differences between the groups' interquadrant coherences, their differences in coherence between left and right posterior quadrants approached significance for low frequency bands. Specifically, the spoken group exhibited increased theta and alpha₂ coherence and decreased alpha₁ coherence, whereas the music group exhibited the opposite pattern.

Chapter 5. Discussion

Section 5.1 provides a discussion of the behavioral results of the study and possible reasons why the musical mnemonic did not improve verbal learning performance. Whereas the oscillatory changes associated with learning were organized in a methodological fashion in the Results chapter, the implications of the results are organized by themes in the subsequent four sections of this chapter. Section 5.2 provides a discussion of the general finding that verbal learning involves desynchronized oscillations relative to repetition. Section 5.3 elaborates on this finding by discussing how learning involves changes in the coupling between brain regions. Section 5.4 includes discussion of how verbal learning with a musical mnemonic involves less desynchronization than spoken verbal learning, and Section 5.5 discusses this difference in the context of the topographic differences between the two learning modalities.

5.1 Verbal Learning – Behavior

The overall pattern of performance agrees with normative data (Lezak, 1995; Mitrushina, Boone, & D'Elia, 1999). That recall performance returns to baseline level on the B-list trial demonstrates that the learning is not merely a general time-dependent effect. Recall performance improves significantly in both the musical and spoken verbal learning conditions. We hypothesized that the musical mnemonic would lead to improved verbal learning performance. A variety of previous studies described in the Background chapter were suggestive of such an outcome. In summary, we expected that the temporal structure inherent in the musical mnemonic would provide a template for associative binding between the mnemonic and the words and, relatedly, help subjects to “chunk” the list of words into groups that could more easily be recalled. Chunking has been used to increase digit span substantially (Chase & Ericsson, 1982). In

contrast to expectations, the musical mnemonic for verbal learning does not confer a performance advantage relative to the spoken condition. There are several possible explanations for this finding. The explanations put forth below are neither exhaustive nor mutually exclusive.

One possible explanation is that in the music condition the recall modality differs from the encoding modality. The word list is presented in song but subjects are asked to recall in speaking. Thus, according to the notion of “transfer appropriate processing”, recall would be impaired for the music group relative to the spoken group. The relationship between the way items are encoded and the way they are retrieved (Morris, Bransford, & Franks, 1977) influences recall performance. In general, performance is enhanced if the way items are retrieved is similar to the way in which they are encoded. Conversely, performance can be degraded if items are recalled in a fashion different from the way in which they are encoded. Transfer appropriate processing theory would then predict that, everything else being equal, the spoken group would perform better than the musical group. Jellison and Miller (Jellison & Miller, 1982) tested conditions in which a stimulus was given in a spoken condition, and response was requested in the same context. This experiment was also done in two other conditions consisting of a sung stimulus with spoken recall, and a sung stimulus with sung recall. With word recall, there was equal performance in both sung and spoken conditions. However, the mixed condition resulted in lower recall performance. Indeed, subjects may subconsciously tend toward recalling words in a fashion similar to the way they were heard. There was anecdotal support for this in the present study. Subjects that recall the spoken list often use a similar inflection and rhythm as to the voice that presented the list. Thus, verbal recall may improve when not having to translate sung to spoken in the recalling process, for instance. In future experiments, one could mitigate this issue by having subjects recall the word list in the same manner in which it was presented (spoken – spoken recall, sung – sung recall).

Second, the relationship between the order in which words are presented and the order in which they are recalled may have also played a role in performance. Subjects are not asked to

recall the words in any particular order. If asked to recall the words in the order in which they are presented, this might give the musical group an advantage by drawing on the natural sequencing embedded into the temporal structure of the musical mnemonic.

Third, perhaps there is an implicit increased demand on verbal learning systems when words are learned with a musical mnemonic. Music may divide attentional resources and attention is generally considered an important precursor to recognizing and encoding information, both in the brain and in artificial systems (Draper & Lionelle, 2005). There are models of memory and consciousness describing how reduced attentional resources could interfere with processes of memory encoding (Richardson-Klavehn & Bjork, 1988; Moscovitch & Umiltà, 1991). In the present study, the spoken group has only words to learn. The musical group has both words and music that can be processed and learned. Although they are not asked to learn the music *per se*, the musical mnemonic may recruit attentional resources that are not recruited in the spoken condition. Thus, the musical condition may induce (albeit implicitly) divided attention, reducing the attentional resources available for processing and encoding the words themselves.

Fourth, Claussen and Thaut (1997) suggest that familiar music may be more efficacious at aiding learning and memory than unfamiliar music because in the latter case subjects have to learn a new melody simultaneously (Gfeller, 1983). This interpretation was also considered in a study using spoken and musical conditions for learning phone numbers (Calvert & Billingsley, 1998). As Wallace has shown, unless the melody is one that has been previously learned, the musical structure does not serve as a helpful device, but can in fact actually detract from learning of the text (Wallace, 1994). Yet perhaps even an unfamiliar tune may become helpful with sufficient repetition (Wallace, 1994). Even with familiar music, successful encoding may depend upon repetition of the stimuli (Rainey & Larsen, 2002). Furthermore, a familiar tune (e.g., jingle bells, ABC song, etc.) may introduce competing bias from words more commonly associated with that tune, producing an unwanted confound. Relatedly, a musical mnemonic may modulate the semantics of verbal material. Melodic factors such as pitch or inflection can influence meaning to

words and phrases (most notably in some Asian languages). The modulated semantic information may require more or different processing, recruiting not only verbal but also other processing systems in the brain.

Finally, verbal learning with a musical mnemonic may be more successfully probed with recognition tests than with free recall as in the present study. Music is known to induce strong associations, as evidenced by Yalch's study in which brand slogans were better remembered when accompanied by a "jingle" (Yalch, 1991). Strong associative memories, while helping both recognition and recall forms of retrieval, generally give a stronger enhancement to recognition. Thus the stronger retrieval demands of uncued recall in the present study may dilute potential advantages that a musical mnemonic provides in recognition memory. Nevertheless, free recall is the generally preferred protocol for probing the physiological subsequent memory effect (SME) that is of central interest in the present study (Rugg & Allan, 2000).

5.2 Verbal Learning Involves Desynchronized Cortical Oscillations

In this and all subsequent sections discussing physiological results, it should be remembered that the key measures are *changes* in brain oscillations associated with the transition from hearing a word on one trial to hearing the same word in the next trial. Verbal *learning* is operationally defined to be the transition from not recalling the word to recalling it on the next trial and *repetition* as the case in which the word is not recalled on either of the two sequential trials. In summary, *learning* is viewed as a change of brain state from not having encoded to having encoded the word. Correspondingly, the physiological correlates of learning, and the non-learning control *repetition*, are measured as changes (plasticity) in brain oscillations. As discussed in Chapter 2, increases in spectral power in individual electrodes are interpreted as increased oscillatory "synchronization" even though it is a single signal, because, in order to be measurable at the scalp level, it relies on the synchronized oscillatory activity of a large population of neurons in a circumscribed mass of neural tissue in underlying cortex (Nunez, 2000).

Verbal learning involves alpha subband desynchronization

Across most of the spatial and spectral domains, repetition is associated with synchrony and learning with desynchrony. However, the detailed manner in which this is manifest differs for the two types of verbal learning. This difference between repetition and learning reaches statistical significance in right posterior alpha₁ oscillations for spoken verbal learning and left posterior alpha₃ for musical verbal learning. In both of the specific cases, repetition is associated with strong synchronization and learning with desynchronization. It is interesting that the significant differences between repetition and learning in the present study occur in different alpha subbands. Different EEG laboratories do not all use the same subdivision of alpha into separate subbands, and some do not subdivide alpha at all. However there is growing consensus that activity in the alpha band is not a unitary phenomenon and that subdivisions are useful (Klimesch 1999). The results of the present study support this notion not only because changes in the alpha subbands are not consistently correlated, but also because different subbands provide significant dissociations between the repetition and learning conditions. Thus present study's results are consistent with recent evidence that the alpha subbands become more distinct with increasing task demands (Fink et al. 2005). The results are also consistent with another study investigating word encoding in the auditory modality, which found that encoding was associated with decreased alpha₁ power in bilateral posterior regions (Weiss & Rappelsberger, 1998). Thus the picture that emerges is that auditory verbal learning involves a predominantly posterior alpha desynchronization whose specific subbands and laterality depend on whether or not the learning is accompanied by a musical mnemonic.

The present study's results in frequency bands other than alpha are consistent with previous studies on the subsequent memory effect (SME) but the repetition-controlled effects are not statistically significant. For example, multiple laboratories have found that encoding is associated with increased theta synchronization (Klimesch et al., 1996; Gevins et al., 1997;

Sederberg et al., 2002). The present study shows the same result in 3 out of 4 quadrants, although the effect is not statistically distinguishable from the effect of repetition. A similar consistency between the present and other studies is found in delta (Weiss & Rappelsberger, 2000) and gamma frequency bands (Sederberg et al., 2002; Schack & Weiss, 2005), again with a broad spatial distribution in the present study but non significant effect compared to repetition. It may be that the synchronization in the delta, theta, and gamma frequency bands in the present study are not significant because the study involves repeated stimulus presentation and these other studies do not. Another explanation is that the other studies involve visual rather than auditory word stimuli. Such an explanation is consistent with previous research (Weiss & Rappelsberger, 1998) suggesting that learning-related changes in oscillatory synchronization are sensitive to the specific sensory modality used to encode the word.

Another possible reason for the slight difference in results between the present and previous studies is the subtle differences in metrics. In both the present and other studies, EEG from the period of interest (i.e., when the stimulus is being presented) is compared to some other, “baseline” period. Other studies typically use a pre-stimulus period of time during which no stimulus is presented. The resultant change in spectral power is typically referred to as event-related synchronization (ERS), or its inverted counterpart, the ERD (Pfurtscheller, 1999). In contrast, the baseline period in the present study is the previous presentation of the same word. Although less conventional, this latter method is a direct result of the conventional implementation of the AVLT in which words are presented auditorily one right after another. Thus there is no consistent pre-stimulus baseline period that is free of stimuli in the AVLT. However, the AVLT has two advantages: 1) it allows for comparison with normative data from widespread application of the AVLT in neuropsychological assessment, and 2) it provides a tighter control because the differential effects of learning involve comparing two instances of the exact same word rather than different words as is usually the case in the typical SME paradigm.

As discussed in Chapters 2 and 3, the present study's task design should control for most non-learning related effects. Nevertheless, it is possible that other factors systematically covary with whether or not words were subsequently recalled. One such possible factor is the differential level of attention, which is known to modulate EEG oscillations (Nieber 2002). However, in order for gross attentional changes to account for the results in the present study, attention levels changes in the trial-to-trial transitions would have to differ in the two trials *and* this pattern would have to be consistent across most instances of the two types of trial pairings and across subjects. This scenario is not entirely implausible, because attention can be viewed as necessary but not sufficient for encoding. Thus an account that at least includes the effects of attention cannot be entirely ruled out from this and, for that matter, other similar studies of explicit verbal learning. Although alpha band synchronization was originally thought to reflect an "idling" state in the brain during decreased levels of arousal and attention, it has in the past several years also been associated with internal mental operations (Klimesch, 1999; Buzsâaki, 2006). The results of the present study, demonstrating that verbal learning is associated with changes in alpha synchronization, lend further empirical support to the notion that alpha oscillations subserve cognitive and memory-related functions and are not simply a general reflection of the level of arousal and attentional state of the brain.

Relatedly, as with any study of the encoding phase of memory, one cannot exclude the possibility that subjects sometimes properly "encode" a word but fail to recall it. Thus, although brain oscillations are evaluated during the encoding period, the operational definition of learning actually relies on accurate recall, for which encoding is necessary only at some earlier instance, possibly including trials prior to the current trial.

Repetition in verbal learning

In tasks such as the AVLT used in the present study, the subject is explicitly instructed to try to remember words for subsequent retrieval. This is sometimes referred to as "intentional"

learning, as opposed to the incidental learning that occurs in most studies of the effect of word repetition on the EEG. For example, most such repetition studies use lexical decision tasks wherein subjects are simply asked to indicate whether or not the presented stimuli are legitimate words. Incidental learning is demonstrated when subjects' responses are influenced by occasional word repetition. One result is the well-studied effect known as repetition priming, whereby item recognition is improved with repeated presentation (Tulving & Schacter, 1990). One physiological correlate of this behavioral phenomenon is the notion of "repetition suppression"; EEG oscillations become desynchronized with repeated presentation of the stimulus. However, this effect can be reversed if the stimuli are unfamiliar, resulting in synchronizing EEG oscillations with stimulus repetition (Gruber & Muller, 2005) and concomitant increased activation in regional activation measured with fMRI (Henson, Shallice, & Dolan, 2000).

In a study with visual word stimuli, repetition evoked more left frontal delta and theta synchrony, and more central low alpha, than new words (Van Strien et al., 2005). The effect decreased with subsequent repetitions (i.e., repetitions two through nine). Similarly, (Fiebach et al., 2005) found that unfamiliar word repetition produced increased gamma synchrony but familiar word repetition produced gamma desynchrony. The emerging picture, then, is that repetition of unfamiliar words and "initial repetitions" of familiar words evoke oscillatory synchrony, but repetitions of familiar stimuli evoke oscillatory desynchrony. By this account, one would expect repetition of words in the present study, which are certainly "familiar", to evoke desynchrony. Although this is true in some frequency bands and some cortical regions, the predominant effect is instead oscillatory synchrony. Recall, however, that these other repetition studies did not explicitly instruct subjects to learn the words. They were, rather, typically given a lexical decision task, i.e., instructed to merely indicate whether or not the stimulus was a legitimate word. In contrast, in the present study, subjects are explicitly instructed to try to learn the list of words. Thus, one interpretation of the results from both types of studies is that when

subjects are processing *or* trying to encode a word, cortical oscillations become synchronized.

On trials where subjects are trying to encode a word *and are successful*, cortical oscillations become desynchronized. This account hints at the possibility of an exciting general principle of brain encoding: that evaluating previous encodings involves synchronized oscillations, and that forming new encodings involves desynchronized oscillations.

In an alternative account, Gruber et al. have theorized that decreased synchronous oscillations correspond to “sharpening” of object representation and that increased synchronous oscillations correspond to cell assembly formation for new object representation (Gruber, Malinowski, & Muller, 2004; Gruber & Muller, 2005). This account would be consistent with the results of the present study if unsuccessful but repeated attempts to encode a word involve cell assembly formation for representing the word and that the word’s representation is “sharpened” when it is properly encoded.

Independent sources

When evaluating quadrants based on projections of sources produced by ICA, the statistically significant effect for the spoken verbal learning group shifts to the right frontal region and the α_3 subband. Although the generalization of relative desynchronization associated with learning compared to repetition still exists in the case of independent sources for the music group, none of the differences reach statistical significance.

Theoretically, changed synchronization of sources produced by ICA should more accurately reflect the true brain activity underlying learning. This is because ICA can, in principle, be used to separate independent brain activity that would otherwise remain mixed in the original per-electrode EEG signals. These expectations should be tempered, however, by assumptions underlying ICA that cannot be verified. It is reasonable to assume that the sources projecting to the scalp mix linearly and have fixed spatial projections. However, it is less tenable to assume that the sources are non-Gaussian and that both the sources and the matrix characterizing the

manner in which they are mixed are stationary. Furthermore, the theoretical argument for using ICA with EEG in cognitive studies has, thus far, only limited empirical support. Some have suggested that ICA is particularly good for studying complex cognitive functions with lower signal-to-noise ratios than functions closer to sensory processing, such as perception (Tang & Pearlmuter, 2002). Peterson showed that spectral power analysis used in conjunction with ICA provides a stronger dissociation than spectra of the original EEG signals in a visual imagery task (Peterson et al., 2005). By distinguishing spoken verbal learning from repetition in a quadrant and alpha subband that differ from the non-ICA result, the present study lends further empirical support to the potential value of ICA in cognitive neuroscience research using EEG.

5.3 Verbal Learning Involves Modified Interregional Oscillatory Coupling

As discussed in Chapter 2, coherence provides an explicit measure of oscillatory activity that is synchronized over cortical networks that are more widely distributed than the focal phenomena usually attributed to per-electrode spectral measures. Therefore coherence reflects spatial coordination among cortical regions and can begin to address the question of how brain regions interact through oscillations. Although conceptually related, per-electrode spectral power and inter-electrode coherence are not necessarily correlated (Nunez et al., 1997). In some studies, researchers have found a learning-related change in EEG coherence but *not* spectral power (Weiss & Rappelsberger, 2000; Fell et al., 2003). We adopt the interpretation that coherence is a measure of functional, oscillatory coupling among cortical regions (Weiss & Rappelsberger, 1998). Because verbal learning involves the coordinated network activity of many widely distributed brain regions, we expected that verbal learning would be associated with changes in oscillatory coupling.

The relative coupling of cortical regions depends on the condition and specific brain regions involved. In general, repetition is associated with coupling and learning with uncoupling. This distinction reaches statistical significance for the spoken verbal learning group in gamma

oscillations connecting right frontal and right posterior regions. This result is in direct contrast with a previous study in which associative learning involved gamma coupling (Miltner et al., 1999). Associative learning requires one to learn an association between items. Because gamma coupling has long been associated with the related function of “feature binding” in sensory perception, it may be that the Miltner et al. result reflects a similar role for gamma coupling “item binding” in some forms of associative learning. The present study’s verbal learning task does not explicitly involve an associative component and this may explain why we find the opposite effect of gamma uncoupling associated with learning. Perhaps gamma uncoupling represents a “release” of otherwise unhelpful item bindings that free up network resources for encoding the previously un-encoded word.

Consistent with the general principle put forth in the previous section, perhaps cortical regions remain coupled when subjects are processing or trying to encode the word, then uncouple when the attempt to encode the word is successful. However, this account is inconsistent with the earlier study by Fiebach et al. (Fiebach et al., 2005) that found gamma decoupling with familiar word repetition and coupling with unfamiliar word repetition. Furthermore, two separate laboratories (Weiss & Rappelsberger, 2000; Summerfield & Mangels, 2005) found increased theta coupling associated with successful verbal encoding. It is possible that the discrepancy could be explained by differences between the present and these previous studies in methodological details, because, for example, (Summerfield & Mangels, 2005) and (Fiebach et al., 2005) used visual word stimuli, whereas we used auditory word stimuli. Also, (Summerfield & Mangels, 2005) used recognition rather than the free recall used in the present study. Nevertheless, it is interesting that verbal learning involves modified coupling in the gamma band. Coherent gamma oscillations were initially primarily associated with perceptual binding processes (Engel et al., 2001). However, the functional roles with which they have been associated have been expanded to include a variety of cognitive functions beyond perception. Similarly, the regions of the brain in which gamma has been explored have extended from initial

reports in neocortex to implicating gamma in medial temporal lobe-mediated encoding processes, as reviewed in (Traub, Whittington, Buhl, Jefferys, & Faulkner, 1999; Wagner et al., 1999). The results of the present study provide further evidence that the spatial extent and functional roles of gamma oscillatory coupling may be richer than originally thought.

For the musical verbal learning group, repetition involves enhanced coupling in theta and alpha₂ oscillations connecting the left and right posterior regions and learning involves uncoupling, a difference that is nearly statistically significant for each band. Both groups exhibit the opposite effect in coupling between the left and right frontal regions: musical verbal learning is associated with enhanced coupling in all frequency bands and spoken verbal learning is associated with enhanced coupling in all frequency bands except gamma. However this result also falls short of statistical significance. Nevertheless, the nearly significant coupling between left and right frontal regions is consistent with a growing body of evidence implicating prefrontal cortical areas in verbal encoding (Fletcher et al., 1997; Buckner, Logan, Donaldson, & Wheeler, 2000; Eldreth et al., 2006; Matsui, Tanaka, Yonezawa, & Kurachi, 2007).

5.4 A Musical Mnemonic Involves Less Desynchronization in Cortical Oscillations than Spoken Verbal Learning

To facilitate a direct comparison between spoken and musical verbal learning, changes associated with learning were compared after subtracting the mean effects of repetition for each group. As a result, musical verbal learning is seen to involve generally less desynchronization than spoken verbal learning. Indeed, musical verbal learning is actually associated with relative synchronization in posterior alpha₁, rising to statistical significance in the right hemisphere.

It is unclear why the musical mnemonic would lead to less desynchronization than spoken verbal learning. One possibility is that learning in both cases involves desynchronization, but that other additional processes specific to the musical case involve synchronization that partially counteracts the learning-related desynchronization. Music may synchronize alpha oscillations during cognitive processes even after the music has stopped (Jausovec, Jausovec, & Gerlic,

2006). Subjects whose scalp EEG alpha synchrony is strengthened when exposed to binaural beats also perform better on working memory tasks than do subjects whose EEG does not respond with higher alpha synchrony (McMurray, 2006). Thus, although subjects in the present study do not receive the same kind of temporally-offset interaural stimuli involved in the binaural beats paradigm, the musical mnemonic may provide similar temporal structure that could facilitate some alpha synchrony that would reduce the net alpha desynchrony during verbal learning. Thaut (2005) has postulated that music's inherent perceptually aesthetic properties would tend to synchronize oscillatory brain activity. If this effect is consistent across all trials in the present experiment, the effect would cancel out in the trial-to-trial change metrics. However, if this effect is differentially expressed on trials in which subjects are successfully encoding words for subsequent recall, it would have a net synchronizing effect consistent with the results of the present study. Although the musical mnemonic did not confer an advantage for learning in the present study, if learning relies on desynchronizing brain oscillations and music tends to synchronize them, a musical mnemonic may facilitate learning by strengthening the synchronous oscillatory template from which learning-related desynchrony evolves.

Another possibility is that the musical mnemonic naturally evokes some associative processes, in which the subjects implicitly associated specific words with aspects of the mnemonic's structure. Associative processes typically involve differential activity in medial temporal lobe that has been shown to recruit theta oscillations for associative encoding (Burgess & Gruzelier, 1997). Thus it is possible that, although insufficiently strong to improve word recall performance, sub-efficacious associative processes in the musical verbal learning group lead to enhanced cortical synchronization that contribute to the net decrease in overall desynchronization.

The temporal sequence of the musical mnemonic might also induce an implicit sequencing to the word encoding process. In the motor domain, sequencing has been shown to evoke increased oscillatory synchrony in the EEG (Pfurtscheller & Lopes da Silva, 1999). Thus if the musical

verbal learning condition evokes processes involved in sequencing it could produce some synchrony that would counter other encoding-related desynchronizing processes.

5.5 The Spatial Organization of Oscillatory Desynchronizations Differs between Spoken and Musical Verbal Learning

The distinction between spoken and musical verbal learning becomes clearer when one more explicitly considers the spatial aspects of the changed oscillations. First, the two conditions differ in the topography of their local synchrony changes, as depicted in Figure 4.13. In a global sense, spoken verbal learning is associated with desynchrony and musical verbal learning with synchrony. But the differences in the detailed topographic distribution are more marked, consistent with our earlier results (Thaut et al., 2005). The areas of strongest desynchrony are the right posterior region for spoken and medial frontal for musical verbal learning. In contrast, the musical verbal learning's posterior region includes the areas of strongest synchrony, particularly in the right hemisphere. Thus, whereas spoken verbal learning involves greater desynchrony going from frontal to posterior right regions, the opposite transition is seen in musical verbal learning.

Differences in topographies of scalp EEG oscillatory changes may be due to differences in underlying brain regions involved. Speech and music recruit different frontotemporal brain regions, even when they are controlled to be acoustically similar (Tervaniemi et al., 2006). Phonological elaboration, which may result from mapping words to a musical mnemonic, has been shown with positron emission tomography (PET) to increase activity in left prefrontal areas (Zurowski et al., 2002). Also, the hemispheric specializations that have been documented in music processing may have homologues in verbal memory encoding: the left side appears to be involved in lexical processing and the right side in processing of sensory detail (Gazzaniga, 2000). The richer sensory detail in the musical mnemonic condition would, therefore, be expected to recruit greater right hemispheric activity than the spoken verbal condition. Because the metrics used in the present study involve the *change* in EEG activity from one presentation of

a word to the next, the general sensory and perceptual processing of stimuli has been controlled for. Thus, differences in brain activity can be attributed to a hemispheric specialization for richer sensory detail in the musical condition only to the extent that the differences in sensory detail influence the actual encoding process.

Second, the two types of learning differ in the amount of oscillatory coupling within the left frontal region. Spoken verbal learning involves relative coupling in left frontal alpha₂, whereas musical verbal learning involves relative decoupling in left frontal alpha₂. In conjunction with a related study demonstrating the opposite effect in alpha coupling within the right frontal region (Peterson & Thaut, 2007), the present result suggests a double dissociation between the frontal hemispheres for the two modalities of verbal learning. That the distinction in the present study occurs in left frontal areas is particularly intriguing because of the purported role of that area not only in verbal production but also in verbal working memory, a likely constituent of the verbal encoding process.

Third, the two types of learning differ in the nature of their posterior interhemispheric oscillatory coupling. The spoken group exhibits increased theta and alpha₂ coupling and decreased alpha₁ coupling, whereas the music group exhibits the exact opposite pattern. Because changes in the three bands are not all the same, and because the group differences approach statistical significance for each of these three individual frequency bands, a multivariate composite including all three bands would likely produce a strong statistically significant difference between the groups. Such a post hoc conclusion suggests further experiments to test this particularly intriguing possibility of multiband interactions dissociating different types of verbal learning. One interpretation of this multiband effect is that the low-frequency (e.g., theta) reflects “state-dependent” processes and the higher frequency (e.g., alpha₂) reflects “item-dependent” processes that work jointly to meet the task demands (Duzel et al., 1999). Another interpretation is that the theta-alpha interaction reflects the interplay between shorter and longer-

term memory systems (Sauseng et al., 2002). If so, it is reasonable to expect that their interaction would also influence encoding for the duration of memory required in the present study.

The results of the present study support the notion that spatial and spectral dimensions cannot be evaluated independently, as implied by Pfurtscheller's suggestion that, for example, there are many functionally distinct alpha phenomena that are differentiated by their topographies (Pfurtscheller, Neuper, & Krausz, 2000). The finding that there are topographically distinct changes in oscillations associated with spoken and musical verbal learning is also consistent with the accumulating evidence that music processing involves a broad, distributed network of brain regions that only partially overlaps with regions involved in verbal function. Studies using lesion (Halpern, 2001; Peretz, 2002), functional imaging (Zatorre et al., 1996; Platel et al., 1997; Parsons et al., 1998), EEG (Peterson & Thaut, 2002) and MEG (Tecchio et al., 2000; Maess et al., 2001) have suggested that music-related processing in the brain involves cortical and subcortical networks that are more widely distributed than non-musical verbal function. Melody and text are encoded in different areas of the brain (Samson & Zatorre, 1991). Different aspects of music can be ascribed to the brain hemispheres (Baeck, 2002). The left hemisphere is active in rhythm discrimination, pitch familiarity, interval structure, and temporal and sequential aspects of music. The right encodes tone pitch, melody, timbre and harmony. The topographic differences in oscillatory neural plasticity between spoken and verbal learning suggest that the unique brain networks involved in music processing may also be involved in learning with a musical mnemonic, independent of music's differential demands on sensory/perceptual processing.

Chapter 6. Conclusions

After summarizing the study's key results and contributions in section 6.1, the significance of the research for basic and applied science is discussed in section 6.2. Section 6.3 highlights implications of the study's results for both biological and machine learning. The study's limitations and future work are described in section 6.4.

6.1 Key Results and Contributions

Subjects demonstrate successful verbal learning in the study, whether they hear the words in a conventional spoken format or with a musical mnemonic. Although we hypothesized that the musical mnemonic would improve learning performance relative to the spoken condition, the musical group did not perform better. A number of theoretical reasons for this are put forth in Chapter 5. In summary, the musical condition may have been made more difficult because the task involves an inherent change in modality between stimulus presentation (musical) and word retrieval (spoken). Also, perhaps the musical mnemonic would have conferred an advantage if the subjects were asked to recall the words in order, because the structural aspect of music may lend itself to better order memory. This was in fact demonstrated in a subsequent study with multiple sclerosis patients (Thaut, 2005). Although a musical mnemonic did not improve the patients' overall learning performance, it did lead to an approximate doubling of the percentage of word pairs recalled in the correct order (from 17% to 39%). Another possibility is that the musical mnemonic inadvertently diverted attentional resources from the primary task of learning the words. Given these reasons to expect degraded learning and memory performance in the music group, it is surprising that they performed almost as well as the spoken group. Perhaps the potentially deleterious effects in the music condition were counteracted by its mnemonic benefits.

One operational advantage of the nearly equivalent learning performance in the two conditions is that differences in their corresponding physiological measures cannot be attributed to gross differences in performance. Thus, differences between the spoken and musical verbal learning in EEG oscillatory measures can be directly attributed to differences between the two learning modalities.

The primary objective of the study was to determine the changes in brain oscillations associated with ecologically salient verbal learning. By incorporating repetition in an auditory verbal learning task, we explicitly used a design that was more ecologically salient than other previous studies of the brain activity associated with verbal learning. Repetition is an inherent part of most forms of learning. It is paramount in practice and rehearsal. Although repetition is such an important part of everyday learning, the brain activity associated with repetition and verbal learning have traditionally been studied in isolation. In previous EEG studies of verbal memory function, words to be remembered are presented only once and tested only once. The author is not aware of any other studies that investigate repetition and verbal learning jointly while simultaneously recording the EEG.

Some tests of verbal memory that examine simultaneous EEG do not isolate encoding and retrieval phases, because they use continuous performance methods that require subjects to engage in retrieval processes that overlap with the time course of encoding a new word on the list. In the present study, the encoding and retrieval phases are kept separate, allowing us to focus on the putative learning aspect, the encoding phase.

Mnemonics are also an important aspect of learning. They are used extensively to memorize long lists of words in a wide variety of domains. Music in particular provides a very efficient template for remembering long lists of words. When cued with a short portion of a song, people can recite the lyrics even if they have not heard the song for many years. While this anecdotal evidence is compelling, the influence of music in memory has undergone limited scientific

evaluation. The present study sought to take a first step in addressing this issue by investigating the influence of music not only on memory performance but also on the associated brain activity.

There are three key results of this study, summarized below. Unless stated otherwise, the neural plasticity associated with learning is characterized as the changes in brain oscillations *relative* to the control condition of repetition.

1. Verbal learning involves oscillatory desynchronization, local coupling, and global uncoupling.

When individuals are repeatedly presented with the same list of words that they are attempting to learn but do not recall, their brain oscillations become more synchronized. However, when they demonstrate learning by correctly recalling the word, the same brain oscillations (during the immediately preceding encoding phase) become desynchronized. This effect is significant in the right posterior region of the cortex in the alpha₁ frequency subband.

Oscillations within left frontal and right posterior cortical areas become more coupled in alpha₂ and theta bands, respectively. However, the oscillations between frontal and posterior cortical regions on the right become uncoupled in the gamma frequency band.

2. Verbal learning with a musical mnemonic involves desynchronization, local uncoupling, and global uncoupling and coupling.

As with the spoken verbal learning, when individuals are repeatedly presented with the same list of words that they are attempting to learn but do not recall, their brain oscillations become more synchronized. However, when they demonstrate word learning by correct recall, the same brain oscillations become desynchronized. This effect is significant in the left posterior regions of the cortex in the alpha₃ frequency subband.

In terms of coupling, the story is more complex in musical verbal learning. Although none of the effects are significant, the trends suggest that learning is associated with: a) uncoupling

within left cortical regions in alpha₂ band, b) uncoupling between left and right posterior regions in theta and alpha₂, c) coupling between left cortical regions in theta and between posterior regions in alpha₁, and d) coupling between frontal regions in all frequency bands.

3. Verbal learning with a musical mnemonic involves less desynchronization than spoken verbal learning and a markedly different spatial organization.

In terms of quadrant-based regions, the musical mnemonic is associated with less desynchronization than spoken verbal learning in right posterior cortex in the alpha₁ band. However, the difference between the two learning conditions becomes markedly spatial when comparing the scalp topographies of their alpha₁ changes. Spoken verbal learning evokes a pattern of desynchrony going from frontal to posterior regions on the right side. In contrast, musical verbal learning evokes the opposite frontal-to-posterior pattern on the right side.

Whereas spoken verbal learning involves relative coupling in left frontal alpha₂ oscillations, musical verbal learning involves relative uncoupling. Also, the two conditions involve opposite patterns of coupling between left and right posterior cortical regions: spoken involves theta and alpha₂ coupling and alpha₁ uncoupling, while musical learning involves the exact opposite pattern. Collectively, the results suggest that the two learning modalities draw upon markedly different brain networks to implement verbal learning.

6.2 Significance

The present study is significant in the cognitive neuroscience of verbal learning and memory because it represents the first line of research investigating brain plasticity associated with ecologically salient verbal learning. It elucidates the changes in brain oscillations associated with learning in the context of, and after controlling for, the effects of repetition. It also evaluates the effect of a musical mnemonic on the brain oscillations associated with verbal learning. As discussed in section 5.2, the results of the present study can be reconciled with previous studies

through a proposed unifying account of the functional role of synchrony and desynchrony in brain oscillations. Specifically, the results support the notion that synchronized oscillations result when subjects are processing or attempting to encode words, but that the actual encoding process corresponds to a desynchronization of those same oscillations. This account is consistent with the notion that cortical function relies on population phase coding for object representation. Such an account has implications beyond verbal function to models of synaptic plasticity as well as machine learning models. But the present study has a number of implications for applied neuroscience as well.

Verbal learning tests can serve a diagnostic role in neurologic disorders, as has been found with the specific verbal learning test used in the present study, the AVLT. The AVLT is particularly well suited to differential diagnosis of what might otherwise present as confounded disorders (Mungas, 1983). Verbal memory function can also be a reliable, early diagnostic for Alzheimer's disease (Barrett, 2000). Multiple sclerosis patients exhibit selective verbal learning and memory deficits on the California Verbal Learning Test (Defer, Daniel, & Marie, 2006), which is very similar to the AVLT. Pending further research with more normal and patient subjects, the physiological analysis methods used in the present study could be used in conjunction with behavioral testing with the AVLT to further refine neurologic diagnoses.

Music has long been used in a variety of capacities for ameliorating memory deficits in neurologically impaired individuals. Post-traumatic amnesics have better recall for events during a music therapy session than for events outside of that session (Baker, 2001). Studies have found that music can induce cortical plasticity (Pantev et al., 2003) and that musical mnemonics can be used for memory rehabilitation (Wilson, 1987). Yet the rehabilitative results have been mixed (Aldridge, 2005). Dementia patients unable to learn new verbal material can learn new song material (Prickett & Moore, 1991). Furthermore, although a musical mnemonic did not improve recognition memory after the AVLT in multiple sclerosis patients, it did seem to provide a stronger aid to those patients with less cognitive impairment than those with stronger cognitive

impairments (Sena, 2006). Regardless of the behavioral influence of a musical mnemonic on verbal function, the physiological measures used in the present study could provide a helpful adjunct for determining whether and how the mnemonic may be affecting brain substrates for a given behavioral function.

More importantly, the results suggest that a musical mnemonic could allow individuals to recruit potentially compensatory pathways in the brain for verbal learning and memory functions. The finding that the topographic distribution of neural plasticity associated with verbal learning differs when a musical mnemonic is employed supports this possibility. While the investigation of the potential for music to assist with learning and memory proceeds, what remains even less clear is the neurobiological basis for such effects. Music may help facilitate verbal learning not only as a mnemonic device that strengthens associations in normal verbal memory pathways, but also by recruiting complementary brain networks for encoding and retrieving words from memory. Also, to the extent that music likely invokes stronger associations than spoken verbal learning, musical verbal learning may differentially recruit specialized neural systems that are particularly well suited to associative memory formation. Associative memory functions have long been attributed to the hippocampus. The hippocampus is a central component of the medial temporal lobe (MTL), and the MTL can play a compensatory role in verbal memory function if the prefrontal cortex is impaired (Castillo et al., 2001).

Despite the possible rehabilitative merits of musical mnemonics, their applicability may be limited. Most cases in which musical mnemonics improve learning and memory are demonstrated in specific contexts, and generalization of the benefit to other information and contexts is generally considered to be limited (Ponsford, 2004). The results of the present study are, by definition, limited to the scope of this study and may not generalize to other learning tasks (Glisky & Glisky, 2002). However empirical research into musical mnemonic strategies for rehabilitating memory shows early promise in the context of broader cognitive rehabilitation (Thaut, 2005). And there is evidence that the brain plasticity associated with learning may be

persistent. EEG measures such as the alpha desynchronization associated with cognitive tasks including memory demonstrate intersession stability over two years (Neuper, Grabner, Fink, & Neubauer, 2005). And when encoding-related activity is sorted for subsequent memory after delays of up to 20 minutes, musical verbal learning was associated with increased oscillatory coupling relative to spoken verbal learning (Peterson & Thaut, 2007). Thus, despite the current relative lack of data about the efficacy and neurobiological basis of musical mnemonics, further investigation is merited. Such approaches to rehabilitation can be used in conjunction with other rehabilitative strategies such as external aids or environmental adaptations. Furthermore, although pharmacological agents such as amphetamines have been shown to enhance verbal learning (Soetens, Casaer, Dhooge, & Huetting, 1995), the wide array of potentially deleterious side affects of pharmacological approaches deem mnemonic strategies worthy of further investigation.

6.3 Implications for Biological and Machine Learning

Sources of oscillatory modulation

It is generally accepted that the scalp-recorded EEG measures activity primarily in cortical regions (Nunez, 2000). Yet there is a wide and growing array of evidence suggesting that cognitive functions, including various types of learning and memory, rely not only on cortex but also on subcortical structures such as thalamus and basal ganglia. Indeed it appears that interactions between cortex and these subcortical structures may lie at the heart of many cognitive functions. Although the contribution of these structures can be studied with functional neuroimaging such as fMRI and PET, scalp EEG is ill suited for detecting their direct contributions. Nevertheless, oscillations in these subcortical structures are often closely associated with oscillations in cortical areas. For example, recurrent circuits linking posterior cortex and thalamus are likely the source of some alpha-band EEG oscillations found predominantly in posterior scalp regions (Klimesch, 1997). Although less well studied, there is

emerging evidence of similarly scalp-recordable oscillations arising from circuits recurrently linking frontal cortical areas, basal ganglia, and anterior thalamic nuclei (Brown, 2003; Fogelson et al., 2006; Sarnthein & Jeanmonod, 2007). The results of the present study, indicating learning is associated with modulated brain oscillations, are consistent with the possibility of subcortical involvement in modulating cortical oscillations, even though such a link cannot be unequivocally determined with scalp-recorded EEG alone.

In Parkinson's disease, the loss of dopaminergic input to the basal ganglia has been implicated in patients' degraded learning capabilities, not only in motor function but in cognitive function as well. In parallel with this dopaminergic loss, there is increased oscillatory synchrony in frontal cortical and basal ganglia nuclei. Dopaminergic and chronic deep brain stimulation therapies for Parkinson's ameliorate some of the cognitive symptoms and also act to desynchronize the apparently pathologically synchronized oscillations. Although it remains unclear whether modulations of synchronized oscillations play a causative role in the learning-related plasticity of the system, the evidence suggests that oscillations are at least correlated with that plasticity. The next section discusses how oscillations may relate to the synaptic-level plasticity that is likely at the heart of behavioral-level plasticity and learning.

Network oscillations and synaptic plasticity

Cellular-level studies have suggested a functional role for network oscillations in neural plasticity. Oscillations control the timing of activity in individual human neurons (Jacobs, Kahana, Ekstrom, & Fried, 2007). Oscillations may also provide a functional link between network- and synaptic-level plasticity by providing a temporal framework for organizing pre- and post-synaptic activity (Paulsen & Sejnowski, 2000). Two of the most well studied forms of synaptic plasticity are long-term potentiation (LTP) and its more recent extension spike-timing dependent plasticity (STDP). LTP reflects strengthened synaptic transmission as a result of synchronized pre- and post-synaptic neuronal firing. LTP in the hippocampus has been shown to

be dependent upon theta oscillations and the timing of inputs relative to the phase of the theta cycle (Pavlides, Greenstein, Grudman, & Winson, 1988; Holscher, Anwyl, & Rowan, 1997; Kahana, Seelig, & Madsen, 2001). There is also evidence that the synchrony of gamma oscillations influence LTP in neocortex (Wespatat, Tennigkeit, & Singer, 2004). Theoretical research has specifically tied gamma oscillations to recurrent inhibition in spiking neuron models and demonstrated the central role of gamma rhythms in facilitating spatiotemporal encoding through STDP (Yoshioka, 2002). STDP further refines the phenomenon of LTP by explicitly emphasizing the importance of the exact relative timing of pre- and postsynaptic neurons. Thus the relative synchrony of oscillations in a population of neurons defines a rhythmic template against which the relative timing of inputs influences the extent and pattern of synaptic plasticity. There is currently a dearth of empirical support for this notion in human cognitive functions. However, the continued expansion and adoption of *in vivo* microelectrode recordings in support of intraoperative neurosurgical procedures in humans will likely provide a unique opportunity to investigate the relationship between oscillations, synaptic plasticity, and cognitive function.

Implications for neurobiologically-inspired machine learning

There is a long history of synergy between animal and human intelligence and artificial intelligence (Freeman, 2000). Some of the most prominent outcomes of that synergy are in the domain of learning. The results of the present study have implications for the development of neurobiologically-inspired machine learning. The present study illustrated that learning is associated with modulations of oscillatory brain activity. This suggests that machine learning systems incorporating oscillatory constructs may provide a better substrate for learning than systems without oscillatory constructs. One such construct is recurrent connections in artificial neural networks. Although recurrent neural networks pose greater analytic challenges than their nonrecurrent counterparts, the results of the present study on the human learning system suggest that recurrent networks may be better suited for implementing learning. Recurrent neural

networks have been around for decades (Hopfield, 1982) and there is a recent surge of interest in a form referred to as echo state networks (ESNs) (Jaeger, 2003). ESNs involve recurrent internal connections and have demonstrated remarkable performance in engineering applications such as communication channel optimization (Jaeger & Haas, 2004). ESNs can be characterized as dynamical systems with stable oscillatory attractors and bifurcations that lead to changes in oscillatory regimes. Thus, because one of the present study's key results is that learning is associated with changes in the brain's oscillatory regimes, the present research gives further biologically-based empirical support for machine learning systems like ESNs. Continued research on the relationship between oscillations and learning in the biological domain will likely benefit the machine learning domain, and vice-versa.

Because learning was generally associated with desynchronization in the current study, and because of the theoretical importance of phase relationships in synaptic plasticity discussed in the previous subsection, algorithms that incorporate oscillatory constructs may benefit from explicit use of population phase coding (Lisman, 2005). In such a scheme, object representations and/or errors that drive learning could be instantiated by the relative phase of "firing" in each of a neural network's population of individual units relative to a separate "master" oscillator or oscillations in another subpopulation of the network providing a rhythmic template. This approach has intuitive appeal because it has long been recognized that in many everyday-learning problems the human nervous system outperforms our most advanced machine learning systems. The usual reason put forth for this discrepancy is that, although the biological system operates at time scales several orders of magnitude slower than its artificial counterparts, the biological system has a much greater number of constituent units with which to compute. If such a large population of neurons learns and represents by a code based on relative firing phase in each of its constituent units, an ideal substrate for that code would be a dynamically modulated oscillatory network. This idea is supported by recent theoretical work (Freedman, 2006) illustrating that the

information transmitted by an individual neuron's actions potentials is proportional to how far the spike is out of phase relative to the population oscillation.

6.4 Limitations and Future Work

Behavioral

As discussed earlier, there are numerous possible reasons why the present study did not demonstrate a beneficial effect of the musical mnemonic on verbal learning. Because the primary objective of the study was to investigate the electrophysiology associated with verbal learning, only one experimental implementation of a musical form of verbal learning was used. A more rigorous evaluation of whether and what aspects of a musical mnemonic can improve verbal learning would require a different line of investigation. One could evaluate, for example, the many experimental design parameters involved in such tasks. According to the theory of transfer appropriate processing, one might hypothesize that subjects would recall more words if they were explicitly instructed to recall them by singing them rather than saying them. Alternatively, perhaps a modified cued recall could be used in which the non-vocal part of the musical mnemonic is replayed in order to cue recall of the associated words. However, this raises the challenge of how to design an appropriate cued recall for the non-musical, spoken verbal learning control condition. Furthermore, one could evaluate different specific musical mnemonics, as perhaps a more familiar tune would serve as a better mnemonic. Note that these independent variables are purely behavioral and could be varied independent of simultaneous measures of brain activity. From a purely pragmatic standpoint, pure behavioral research into this issue would proceed much more quickly without, for example, concurrent EEG, because subjects could be run faster and/or for longer periods of time, and data analyses would take much less time.

Astute consideration of memory tasks such as the one used in the present study will reveal an important subtlety that is rarely discussed: we are actually probing the conjunction of encoding and retrieval phases rather than just encoding. We dissociate epochs during *encoding*

based on whether or not subjects subsequently *retrieve* the words. Although encoding is necessary for retrieval, it is not sufficient. It is quite possible that a word is “encoded” on a given trial but for some reason the subsequent recall on that same trial is not successful. Thus the word may have been “learned” but not retrieved. This is a common issue in memory research. One way to begin to tease apart this subtlety is through manipulations of the retrieval phase of the task. If the retrieval phase is made easier than free recall, it should reduce the proportion of trials on which an “encoded” word is subsequently not correctly retrieved. There are several ways of implementing this, as for example by cueing recall or through use of a recognition test. Dramatic improvements in retrieval performance would suggest that the words were encoded but that the demands of the free recall test made retrieval more difficult. In some studies with the AVLT, the usual free recall test is followed by a recognition test. Subjects usually recognize about 3-4 more words than they recall (Savage & Gouvier, 1992). In the absence of such manipulations, attributing results to the encoding phase should be tempered by the realization that the effects actually reflect the conjunction of encoding and retrieval aspects of memory. Thus, although we analyzed brain activity during the encoding phase, the operational definition of learning that we employed requires both successful encoding and recall. Note that a subject's brain processes may be "closer" to successful encoding on a 2nd trial even though it is also unrecalled (i.e. higher "activation" than previous unrecalled trial, but still just slightly below recall "threshold"), whereas this might not be the case for another subject, so their physiological results might be very different, yet their behavioral results look the same.

Although of course learning need not involve feedback (Hergenhahn & Olson, 1997), many learning settings do. Indeed rewards can serve as a powerful motivator for learning. Verbal learning tasks including the AVLT implementation used in the present study generally do not include feedback or rewards. Nevertheless, feedback and/or reward mechanisms could be added to such a task, and the concomitant effects on performance and brain activity studied. Much of the animal learning research involves reward-based learning and great strides have been

made to elucidate the neural substrates for that learning. Although homologues of verbal function are difficult to study in animals, that body of research could provide a baseline against which neurobiological studies of human verbal learning could be compared if the studies were to include mechanisms for reward.

Finally, future research could build on the results of the present study without changing the tasks simply by including more subjects and more trials. If demographic characteristics of the subject population are appropriately controlled, increasing the number of subjects or the number of trials or both could strengthen the statistical significance of the results. This applies not only to the behavioral but also to the physiological effects found in the present study.

Physiological

The results of the present study suggest that spatial and oscillatory aspects of scalp EEG do not vary independently. Thus, the study of verbal learning, and many other cognitive functions for that matter, would likely benefit from analysis methods that explicitly take into account the interdependencies between spatial and spectral measures in the EEG. Most studies in the field, including the present one, do not evaluate dependent measures of space and frequency jointly. Yet results commonly point to their interaction. Although evaluating their interaction substantially increases the dimensionality of dependent variables, it may also lead to deeper insights into the neurobiological basis of the functions under study. Similarly, even just within the spectral domain, the various frequency bands are typically treated independently of each other. Yet, again in this and other studies, the results suggest that this might not be the case. In terms of the coupling between left and right posterior regions, spoken verbal learning involved increased theta and alpha₂ coupling and decreased alpha₁ coupling. The exact opposite pattern was observed in musical verbal learning. Thus a multivariate metric including all three frequency bands might have provided a better signature of the distinction between the two types of learning.

With the trend toward higher-density EEG recording, a full multivariate characterization of the interaction between spatial and multi-band spectral dependent measures poses a severe analytic challenge. Consideration of functional oscillatory coupling among brain regions by use of coherence further exacerbates the problem. For example, although 8 frequency bands in a 30-electrode cap will yield 240 dependent variables, coherence in the same frequency bands in the same cap will yield 3,480 features. Clearly, the number of dependent variables quickly far surpasses the number of trials available for analysis in most EEG studies. However this general problem is not unprecedented and has received extensive attention in other domains such as molecular biology. For example, with microarrays one can assay the expression level of many thousands of genes simultaneously. However, there are usually only 100 or fewer samples. Various machine learning methods have been used to address this problem, typically under the umbrella of “feature selection”. In stark contrast to the domain of molecular biology, feature selection of this sort has received minimal attention in the cognitive neurosciences. Yet the results from the present study suggest that we can gain greater insight into the neural basis of cognitive function by evaluating the interdependencies among these high-dimensional dependent variables in the EEG. As we (Anderson & Kirby, 2003; Peterson et al., 2005) and others (Yom-Tov & Inbar, 2002) have begun to demonstrate with EEG studies outside the realm of verbal learning, feature selection may be a fruitful first step.

The coherence analysis in the present study used only a subset of the electrode pairs and only gross topographic coupling within and between four quadrants on the scalp. This approach mitigates the issue of high-dimensionality in the number of dependent variables because a relatively small number of comparisons are being made. The approach is common in verbal learning research (Weiss, Muller, & Rappelsberger, 2000; Schack & Weiss, 2005). However, the approach also runs the risk of missing changes in coupling that may prove to be functionally significant for verbal learning. Nevertheless, there are likely diminishing returns to having additional details about the spatial aspects of oscillatory coupling in the EEG. The method’s poor

spatial resolution makes it difficult to draw plausible inferences about how scalp activity is related to underlying sources.

Although of ecological significance, the auditory modality for providing word stimuli in verbal learning tasks poses some significant challenges. In the present study, words were presented at a rate of approximately one per second and the auditory waveforms of many of the multi-syllabic words in the lists are almost one second long. The time window usually associated with encoding processes, approximately 250-750 ms after the stimulus, is not entirely after the completion of the stimulus delivery. Indeed the time window is passed before some of the word stimuli are completely delivered. While it is not clear at what midpoints during the auditory waveform of the words different individuals would recognize the word, it is quite possible that those points in time would extend well into the time window used for EEG analysis, and in some cases even fall after the 750 ms threshold. Thus the EEG analyzed in the present study may partially reflect earlier sensory and perceptual processes that, although certainly prerequisites to encoding, do not reflect the encoding process alone. Of course, this issue is at least partly mitigated by comparing epochs with identical stimuli, as was the case in the present study. However, we cannot exclude the possibility that the point in time at which subjects recognized words varied from one trial to the next. Indeed it is plausible that subjects would recognize words faster with successive presentations of the same word, thereby increasing the relative proportion of the analysis time window that includes post-perceptual processes such as encoding. Of course, these issues do not arise in the visual modality, in which case stimulus presentation is nearly instantaneous and sensory/perceptual processing does not have to wait for protracted stimulus delivery. Nevertheless, auditory verbal function is central to our daily lives. Furthermore, the auditory modality is of course critical for implementing a musical mnemonic. Thus technical issues related to the temporal overlap between stimulus delivery and the processes used by the brain to analyze and encode the stimulus merit further attention.

At a broader time scale, there is a possibility that the distinctions found between learning and repetition in the present study could result from the two cases having different distributions over the four possible trial pairings (i.e. 1-to-2, 2-to-3, 3-to-4, and 4-to-5). Learning and repetition EEG dynamics would appear different if, for example, the learning trial pairings tended to occur later than the repetition trial pairings *and* the oscillatory EEG changes from one trial to the next varied systematically over the course of the experiment. This explanation seems unlikely because the mean trial of the learning and repetition cases for both the spoken and musical verbal learning were all within a range of 0.4 and exhibited no significant differences under parametric and non-parametric statistical tests. Nevertheless, this issue is also relevant to verbal memory studies without repetition and should be more explicitly addressed in future studies.

Finally, the present study used only EEG to assess brain activity associated with verbal learning. As alluded to in Chapter 2, other methods for measuring brain activity could be brought to bear on this topic. For example, EEG's magnetic field counterpart the MEG shares the temporal resolution of EEG but has slightly better spatial resolution. It is also more sensitive than EEG to cortical activity in sulci that are orthogonal to the scalp. One example area of particular interest in the auditory domain is the superior temporal lobe, which includes auditory sensory cortical areas. Although most of the sensory processing should be the same for learning and control conditions, the superior temporal lobe may contribute to word encoding, as some evidence has suggested it contributes to very short-term memory for auditory patterns (Kropotov et al., 1995).

In addition, the experimental design used in the present study could be readily adapted for use in functional neuroimaging such as fMRI or PET. Although unable to measure the electrophysiology of the brain, these methods provide a gross measure of "activation" in specific brain regions based on the regions' metabolic requirements and corresponding hemodynamics. Although the noise in fMRI scanners has posed problems for auditory stimulus delivery and response recording in the past, those problems have now been largely overcome. PET and fMRI

provide much better spatial resolution than EEG and MEG and would allow one to identify specific neural structures at the millimeter level that are differentially involved in verbal learning and how it is affected by a musical mnemonic. This would be of particular interest to confirm the hypothesis generated in the present study that musical verbal learning involves different brain regions than those involved in spoken verbal learning. It would be particularly interesting to also use functional neuroimaging to determine if patient populations with well-known, focal brain lesions benefit from musical mnemonics for verbal learning and use different brain regions for its implementation. Recent strides in EEG technology and signal processing have also made it viable to measure EEG inside the fMRI scanner (Debener, Usperger, Siegel, & Engel, 2006). Obviously, this would be particularly exciting because one could simultaneously record electrophysiological oscillations and the hemodynamic activity of specific brain regions involved in verbal learning. With further improvements in functional imaging and the fusion of data from both functional imaging and EEG/MEG, the field will be able to address the questions of not only *what* areas of the brain are involved, but also *how* they interact to give rise to verbal learning and other important cognitive functions.

Appendix A. Subject Forms

A.1 Informed consent form (one signed copy retained; one copy given to subject)

INFORMED CONSENT TO PARTICIPATE IN A RESEARCH PROJECT

TITLE OF PROJECT: The Cognitive Neuroscience of Auditory Rhythms

NAME OF PRINCIPAL INVESTIGATOR: Carol A. Seger, PhD.

NAME OF CO-INVESTIGATOR: David A. Peterson

CONTACT NAME AND PHONE NUMBER FOR QUESTIONS/PROBLEMS: David A. Peterson, 491-5291, petersod@cs.colostate.edu

SPONSOR OF PROJECT: None

PURPOSE OF THE RESEARCH:

The purpose of this project is to study how humans perceive and interpret music. In particular, we are investigating the biological and psychological bases of rhythm perception. By measuring your brain activity while you respond to auditory rhythms, we gain insight into how the brain processes rhythm.

PROCEDURES/METHODS TO BE USED:

You will complete one roughly two and one-half hour experimental session. It will take approximately one hour to prepare you for brain activity monitoring using the electroencephalogram (EEG). The EEG is a method for non-invasively measuring your brain's electrical activity. The activity is measured with gel electrodes placed at the surface of the scalp at several standard locations around your head. The electrodes and procedures for their application and removal are sanitary. Also, the EEG is a passive procedure; the electrodes only measure electrical activity, they do not produce it.

The experiment, involving the cognitive tasks, will also take approximately one hour. All tasks involve listening to computer-generated sounds and providing responses via a push-button computer response box. If at any time you wish to discontinue the experiment, it will be terminated. After the experiment, you will be given a copy of the debriefing sheet, and will have answered any questions you have about the experiment.

RISKS INHERENT IN THE PROCEDURES:

There are no known psychological or social risks to the participant associated with the research procedure. EEG is a passive technique for measuring electrical potential on the surface of the scalp, not a technique for inducing electrical potentials. As with any routine visit to an EEG

Page 1 of 2 Subject initials _____ Date _____

laboratory in a hospital and/or research facility, however, there is a slight, although limited, risk of infection. Sites on the scalp are prepared for electrode application with an abrasive gel similar to a skin cleanser. Although use of the gel rarely results in breaking the skin, this possibility exists. To mitigate this risk, any persons applying electrodes to the subject will wear sterile disposable latex gloves during the application procedure. Any sign of skin breaking during the electrode site preparation will result in sterile cleansing and no further abrasion of that electrode site.

If you have an allergy to latex, you should not participate (as indicated in the Research Information Sheet).

It is not possible to identify all potential risks in research procedures, but the researcher(s) have taken reasonable safeguards to minimize any known and potential, but unknown, risks.

BENEFITS:

You may benefit by gaining a greater understanding of how psychology experiments are performed. The benefits of the research in a wider context are greater understanding of rhythm perception in particular, and human cognition in general.

CONFIDENTIALITY:

Data from the experiments will be kept confidential. Participants will remain completely anonymous; at no time will your data be linked with your name.

LIABILITY:

The Colorado Governmental Immunity Act determines and may limit Colorado State University's legal responsibility if an injury happens because of this study. Claims against the University must be filed within 180 days of the injury. Questions about participants' rights may be directed to Celia S. Walker at (970) 491-1563.

PARTICIPATION:

Your participation in this research is voluntary. If you decide to participate in the study, you may withdraw your consent and stop participating at any time without penalty or loss of benefits to which you are otherwise entitled.

Your signature acknowledges that you have read the information stated and willingly sign this consent form. Your signature also acknowledges that you have received, on the date signed, a copy of this document containing 2 pages.

Participant name (printed)

Participant signature

Date

Investigator or co-investigator signature

Date

A.2 Participant debriefing form

The experiments you just completed are used to investigate the perception of auditory rhythms. By simultaneously recording your brain's electrical activity, we collect indirect information about how the brain processes auditory information. The timing and accuracy of your responses will be studied in conjunction with the EEG data to seek correlations between the overt behavioral interpretation of the stimuli and the underlying brain activity. By improving our understanding of how the brain processes auditory information, this study will provide new insights into the neural basis of music and language. Note that your data will be identified using an arbitrary participant number. At no time will your name be connected with your data.

Several chapters in Myer's textbook are relevant to this research, including Chapters 14, 24, 29, and 47. Of most direct relevance, however, is chapter 14 on auditory perception. If you are interested in learning more about this specific field of research, good summary references are (Naatanen and Winkler, 1999) and (Basar and Schurmann, 2001). If you have any questions or concerns about this research, or would like to discuss the results, please feel free to contact David Peterson at the following:

David A. Peterson
(970) 491-5291
A-22g Clark
Department of Psychology
Colorado State University
Fort Collins, CO 80523
petersod@cs.colostate.edu

Thank you for your participation!

References

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Naatanen R, Winkler I (1999) The concept of auditory stimulus representation in cognitive neuroscience. *Psychol Bull* 125:826-859.

Appendix B. Subject preparation and electrode cap application

- 1) Preliminaries
 - a) Describe the experiment to the subject.
 - b) Have subject read and sign the informed consent form.
 - c) Suggest subject use restroom, remove chewing gum if any, and get drink of water if need to (overall duration of setup and experiment about 90 minutes).
 - d) Have subject remove glasses, jewelry on head, and hair things (if applicable)
 - e) Measure head circumference, choose and document cap size:
 - i) medium: 54-62 cm (most participants)
 - ii) large: 62-68 cm
 - f) Prep skin for mastoid and VEOG electrodes by using NuPrep on a q-tip and scrubbing the skin. (This helps reduce impedance.)
 - i) Inform subject that NuPrep "is like facial scrub".
 - ii) For the mastoid electrodes, scrub the skin on the bone behind the ear.
 - iii) For the VEOG electrodes,
 - (1) the lower one gets attached to face under the eye, toward the outer part of the cheek
 - (2) the upper one gets attached above the eyebrow (vertically in line with the center of the eyebrow)
- 2) Apply the cap
 - a) Put cap on head, front first—FP1 and FP2 should be centered at top of forehead; pull the net down over the participant's ears.
 - b) Measure from the center of FP1 and FP2 down to the nasion (bone in between eyebrows), should be approximately 4 cm.
 - c) Make sure back of cap is pulled snug (yet still comfortable).
 - d) Check that HEOL and HEOR are near the outside of the eyes.
 - e) Tape the red cord from the net to the subject's shirt (L side).
- 3) Apply mastoid sensors
 - a) Get at least 4 pieces of tape ready.
 - b) Take syringe without metal tip and fill with electrode gel. Wipe off the outside and reattach the metal tip. Show the subject it is blunt.
 - c) Fill mastoid sensor (M1, blue) with gel, put on bone behind ear where you scrubbed, and then tape down securely. Do the same for the mastoid on the other side of the head.
 - d) Attach the chinstrap as snug as possible (while still comfortable) and recheck mastoids to make sure they are intact.
- 4) Apply eye sensors
 - a) (red: VEOL (lower) and VEOU (upper)). Use 1020 paste and put the sensors on with tape.
- 5) Apply all other sensors
 - a) Attach connector on red cords to head box—grab by plastic, match rectangular piece to hole—squeeze sides and slide in until get close enough to lock plastic tabs on sides.
 - b) On EEG PC, go to acquisition>Impedance (can change range by clicking on the range button, put at 5 to 25). Achieve impedances < 8 kOhm on all electrodes, although HEOG and VEOG can be higher.

- c) Start with the ground sensor.
- d) For each sensor:
 - (1) Begin filling each sensor with gel. Press sensor down and apply gel by squeezing out a little at a time by putting the needle on the scalp.
 - (2) After injecting gel, put in stick and twirl (and use bigger circles); may need to supplement with more gel. (Be sure to let subject know he/she should report pain)
 - (3) [Remember, if need to refill the syringe with gel, remove needle tip, take Kimwipe and wipe off needle.]
- e) Document final impedances on the Subject Data Sheet.
- 6) Give Subject a Demonstration
 - a) Start EEG acquisition on Scan machine.
 - b) Select VEOG and maximize to show eye blink.
 - c) Have the subject watch how a few blinks influence the brainwaves that we measure.
 - d) Emphasize that they should try to minimize blinking during the experiment.
- 7) Setup subject in sound booth
 - a) Have subject put glasses back on (if applicable).
 - b) Have subject hold head box.
 - c) Wind up head box cable while walking with subject to sound booth.
 - d) Drape wound-up head box cable over hook behind recliner.
 - e) Ensure subject is comfortable and not sitting against interface cable .
 - f) Provide "general" task instructions.
 - (1) Show response box, confirm they see the "Yes" and "No" and the "1" and "2" labels. (Subject may wish to have response box on lap or on that board if it would be more comfortable.)
 - (2) Show microphone, swing into place.
 - (3) Give total time estimate of experiment: 45-50 minutes.
 - (4) Remind to minimize all body movement, except as needed for response box.
 - (5) Remind to relax muscles, especially neck.
 - (6) Remind to minimize swallowing and blinking.
 - (7) Reduce eye movement: fixate on center of screen (will be a plus sign most of the time)
 - g) Dim light in subject room.
- 8) Initiate EEG recording and start the experiment.
 - a) Depending on which condition was randomly selected by E-Prime, give subject condition-specific instructions:
 - i) Spoken: "You will hear a list of words. Listen carefully, because after the list, you will be asked to say back as many words as you can remember. It won't matter in what order you will repeat them. Just try to remember as many as you can."
 - ii) Sung: "You will hear a list of words sung with a tune. Listen carefully, because after the list, you will be asked to say back as many words as you can remember. It won't matter in what order you will repeat them. Just try to remember as many as you can. It is ok if you learn the tune but remember that it is more important that you learn the words."
 - b) Before proceeding with rest of experiment, ask the subject: "Do you understand the instructions? Do you have any questions? After I close the door, press "1" to begin."
- 9) After task completion
 - a) Stop EEG recording.
 - b) Remove subject from recording booth.
 - c) Remove EEG cap.
 - d) Give subject debriefing information.
 - e) Answer any questions about the procedure and the disposition of their data.

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