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Alberto Filgueiras

Neural basis of phonological working memory: testing theoretical models using fMRI meta-analysis

TESE DE DOUTORADO

Thesis presented to the Departamento de Psicologia, PUC-Rio, as partial fulfillment of the requirements for the degree of Doutor em Psicologia in the Departamento de Psicologia do Centro de Teologia e Ciências Humanas da PUC-Rio.

Advisor: Prof. Jesus Landeira-Fernandez
Co-advisor: Prof. Lisa Archibald

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Abstract

Filgueiras, Alberto; Landeira-Fernandez, Jesus (Advisor). **Neural basis of phonological working memory: testing theoretical models using fMRI meta-analysis.** Rio de Janeiro, 2015. 99p. Ph.D. Thesis - Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro

Phonological working memory can be defined as a set of mental processes that encode, store, maintain, manipulate, and retrieve auditory information. It is the foundation for other complex and higher cognitive functions, such as planning, task switching, logical and abstract reasoning, and language. Some evidence shows a relationship between the development of phonological working memory and further language acquisition and general fluid intelligence. Current neuroscience discusses the networks and brain regions that account for working memory. Working memory relies on a parietal-frontal network that is divided according to memory and attention. It has been hypothesized that the prefrontal cortex plays an important role in working memory tasks. Working memory is a relatively recent psychological discovery, and several authors suggest different theoretical models to explain it. Among the most important are those proposed by Alan Baddeley, Nelson Cowan, and Adele Diamond, which have been the most studied and implemented in attempts to test their hypotheses. Studying the neural basis of phonological working memory will help shed light on the organization and location of mnemonic and attentional functions in the brain. The present study comprised a meta-analysis of functional magnetic resonance imaging studies on phonological working memory that were published between 2000 and 2014. The results showed that one region in the temporal lobe and another region in the fronto-polar cortex were clustered intersections of phonological working memory, suggesting that these brains regions may account for sensorial memory and the central executive, respectively.

Keywords

Neuroscience; Working Memory; Functional Magnetic Resonance Imaging; Meta-analysis.

Resumo

Filgueiras, Alberto; Landeira-Fernandez, Jesus (Orientador). **Bases neurais da memória de trabalho fonológica: testando modelos teóricos usando meta-análise de RMf.** Rio de Janeiro, 2015. 99p. Tese de Doutorado - Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro.

A memória de trabalho fonológica pode ser definida como um grupo de processos mentais usados para codificar, guardar, manter, manipular e recuperar informações auditivas. É o alicerce de outras funções cognitivas superiores e mais complexas como o planejamento, mudança do foco da tarefa, raciocínio lógico e abstrato e linguagem. Algumas evidências mostram a relação entre o desenvolvimento da memória de trabalho fonológica e mais tarde a aquisição da linguagem e inteligência global fluida. A antropologia contemporânea discute o papel da memória de trabalho como uma forma rudimentar de pensamento e suas consequências para o desenvolvimento de ferramentas e cultura entre os hominídeos. Têm sido aceito que a expansão da região frontal do crânio abre espaço para novas formações corticais no cérebro, especialmente no lobo frontal. Crê-se que o córtex pré-frontal tem um importante papel em tarefas de memória de trabalho. Ao mesmo tempo, a memória de trabalho é uma descoberta psicológica recente e diversos autores sugerem diferentes modelos teóricos para explicá-la. Dentre os mais importantes, Alan Baddeley, Nelson Cowan e Adele Diamond são aqueles cujas teorias são as mais estudadas e implementadas pelos pesquisadores que testam suas teorias. Estudar a base neural da memória de trabalho fonológica pode ajudar a lançar luz sobre ambos os pontos: o papel do córtex pré-frontal na evolução humana especialmente no funcionamento da memória de trabalho, e qual modelo teórico é o mais confiável dentro de uma perspectiva neuropsicológica. Para fazer isso, conduzimos uma meta-análise usando o método de estimação de verossimilhança das ativações e discutimos os resultados alicerçados na psicologia evolutiva e cognitiva modernas.

Palavras-chave

Neurociência; Memória de Trabalho; Ressonância Magnética funcional; Meta-análise.

Summary

List of Abbreviations

WM	Working Memory
LTM	Long-term Memory
STM	Short-term Memory
SM	Sensorial Memory
CE	Central Executive
FA	Focus of Attention
fMRI	Functional Magnetic Resonance Imaging
EEG	Electroencephalography
MEG	Magnetoencephalography
PET	Positron Emission Tomography
PFC	Prefrontal Cortex
FPC	Frontopolar Cortex
CC	Cingulate Cortex
PL	Parietal Lobe
TL	Temporal Lobe
FL	Frontal Lobe
SAS	Supervisory Attentional System
ALE	Activation Likelihood Estimation

"I do not think that measurement is an activity that is celebrated in our school system, and measurement is the life and blood of all sciences. In fact, those sciences that have not yet achieved a system of measurement cannot claim themselves to be matured subjects. So, take a look at everything Freud wrote, you look at that and where are the measurements? There are not. So, this is why Psychology has lacked so far behind the other sciences. They have not developed methods of measurement. So you struggle, you struggle the way Physics struggled when it first began, but you come along. For Psychology, in a few more hundred years."

(Neil DeGrasse Tyson, *On the verge*)

1

Introduction

Working memory is one of the most intriguing concepts in modern cognitive sciences. Its complexity leads researchers to question its existence, and evidence supports either some or no theoretical model to explain it. Under these circumstances, several questions remain about the real structure and consequences of working memory function. The present work attempts to shed light on such a diverse and complex matter based on functional magnetic resonance imaging (fMRI) studies and neuropsychology.

Let us say that I need to hold a telephone number in mind until I dial it, or I need to understand and follow directions about how to go somewhere I have never been before, or I need to follow instructions in a manual to use a new gadget. These are few examples of a human ability that we call working memory (Cowan, 1999). Evolutionarily, it makes sense to think that our ancestors from the Stone Age also had this ability, and it was likely essential for their survival (Coolidge & Wynn, 2005; Read, 2008).

To hold and manipulate all sorts of information in mind, a set of mental processes, known as working memory, is required. A good example of working memory is how we perform multiplication in our mind. The ability to actively maintain numbers in our mind demands focusing attention on one piece of information at a time because of humans' inherent limits of attention (Cowan, 2010). Because we have such limitations, we developed other mental strategies to overcome these mnemonic and attentional limitations, including, for example, grouping separate descriptions of a jungle as a singular mental piece(also known as chunking), overtly or covertly repeating novel directions to avoid forgetting them (also known as rehearsing), and accommodating new descriptions into previously known codes (also known as encoding; Cowan, 1999). Such strategies are not initially used but rather learned through experience and neural maturity, and they can be trained because they rely on neuroplasticity (Diamond, 2013).

The examples above illustrate how this type of operational memory is used and limited by an individual's mnemonic and attentional capacity. Much evidence indicates that working memory comes before other superior cognitive functions, such as language, reasoning, thinking, and planning, during early development (Diamond, 2013; Garon, Bryson, & Smith, 2008). Most human activities also need working memory to be executed properly. Following instructions, reading texts, and cooking food are tasks that are structured by a series of steps that rely on an individual's ability to update what was already done and what still needs to be done. Because of this, problems in working memory can lead to several consequences that impair the functioning of individuals. For example, children with working memory deficits during early development are more likely to show language impairments, learning disabilities, and attention disorders than their peers (Baddeley, 2003; Diamond, 2013). Elderly adults who present impaired working memory because of neurodegenerative diseases tend to present procedural difficulties and impairments in daily activities (Filgueiras, Charchat-Fichman, & Landeira-Fernandez, 2013). Working memory is used in everyday activities. Any complex thought relies on the proper performance of this cognitive function. Its importance spreads through all human cognition and is one of the foundations of creativity, reasoning, and abstract imagery (Diamond, 2013). Despite such importance, working memory is still a mystery to most cognitive scientists, and several questions remain unanswered.

Understanding how the brain is activated during working memory tasks can shed light on how such tasks activate the brain's neural networks. For example, Rottschy et al. (2012) evaluated all modalities of working memory (i.e., verbal, non-verbal, and visuospatial) in a single meta-analysis. Their results showed core activation of distinct areas, including bilateral activation of the dorsolateral prefrontal cortex, supramarginal gyrus, and anterior intraparietal sulcus and bilateral activation of the cingulate cortex (anterior insula and pars opecularis, part of Broca's area). Parietal and frontal regions appear to be activated during working memory tasks. Other meta-analyses also reported similar results (Owen, McMillan, Laird, & Bullmore, 2005; Wager & Smith, 2003). Strong evidence shows fronto-parietal network activation during working memory tasks. The literature suggests that parietal regions are mostly integrative. While the brain is executing a working memory task, those regions integrate perceptive and sensorial inputs in a way that allows processing (Owen et al., 2005). Frontal regions are associated with motor control and thinking; thus, mental processing likely occurs in those regions (Rottschy et al., 2012). According to this view, working memory can be divided into two components within the same network: integration and processing.

Theorists generally agree that working memory has two divided subsystems: one that is domain-general and one that is domain-specific (Baddeley, 2003; Cowan, 2010; Diamond, 2013). The domain-specific subsystem is also divided into phonological and visuospatial domains. These are mirror subsystems. Thus, the mental process that an individual uses to retain serial instructions in mind is likely similar to the one that is engaged when imagining a group of visually different stimuli to mentally manipulate them. This means that both phonological memory and visuospatial working memory share the same functional structure (Baddeley, Allen, & Hitch, 2011). The present work focuses on phonological working memory because evidence supports the notion that it has stronger associations with reasoning, naming, and language (Baddeley, 2000, 2003; Baddeley, Allen, & Hitch, 2011), the last of which is our main interest.

The present thesis consists of a meta-analysis that is presented in five parts: (1) history of working memory and importance of understanding it from a neuroscientific perspective, (2) the presentation of three of the most important theories to explain working memory function: (*i*) Baddeley, Allen, and Hitch (2011), (*ii*) Cowan (1999, 2010), and (*iii*) Diamond (2013)—Chapter 2, (3) objective and methods of this thesis—Chapter 3, (4) meta-analysis of fMRI studies on phonological working memory and how such studies can help resolve some of the issues in Chapter 2—Chapter 4, (5) conclusions of the present thesis and future directions—Chapter 5. The main goal of the present study is to shed light on working memory, how it works in the brain, and how fMRI evidence supports or does not support one theoretical model or another. Our efforts were directed toward providing further knowledge about this subject and not necessarily providing answers to unanswered questions.

1.1

History of working memory

Modern psychological science has been through paradigm transformations since its inception in 1857 in Leipzig with Wilhem Wundt (Mills, 2000). Psychoanalysis, psychophysics, and behavioral sciences were some of the earlier approaches to explaining psychological phenomena. During the first half of the 20th century, North-American psychologists were thrilled by studies of respondent and instrumental conditioning by such authors as B.F. Skinner, John Watson, and Ivan Pavlov (Mills, 2000). According to psychology's behavioral approach, the mind is a blank slate, and behaviors are imprints of learning that are created through conditioning. For behaviorists, there is no cognitive predisposition. Men are products of their environment. Thus, there is no need to study the human mind. To understand the psychological aspects of an individual, psychology only needs to know the stimuli, the individual history of learning and conditioning, and the result of the stimuli in terms of behaviors (Mills, 2000).

Historically, cognitive sciences were the response of North-American psychologists to the behavioral approach. In the late 1950s, such researchers as Albert Bandura, Aaron Beck, and Albert Ellis suggested that learning can also occur without self-experience (Bandura, 1971; Beck, 1967; Ellis, 1958). Bandura (1971) provided strong evidence of vicarious learning (i.e., learning by observing someone else's experience). Beck (1967) and Ellis (1958) showed how rational thinking enables learning in psychotherapy patients. This evidence suggested that learning is also attributable to cognitive predispositions that can be explained by different mental processes rather than simply environmental influences.

During this historical period, another researcher also showed how it is not possible to learn anything. Human cognition is not limitless, and cognitive capacity is defined by innate limitations. To show how memory is limited, George Miller (1956) proposed an experiment in which the participants had to remember a set of stimuli in the same order in which they were presented. Miller (1956) showed that participants are able to retain an average of seven items for each set in the same dimension (e.g., numbers, words, or phonemes) with possible variations from five to nine items, depending on the person. According to Miller (1956), this "magical number" of seven (plus or minus two) is the product of the ability to chunk information (i.e., to create groups of items in the same dimension). For example, whenever one is trying to memorize a set of numbers, creating tens and hundreds (i.e., chunks of two or three digits) enables better retention then trying to remember number by number.

Several studies were conducted since Miller's "magical number" paper in 1956 to understand how short-term memory works and whether it is the only process that is recruited to retain and recall information. In 1964, Conrad and Hull performed a set of experiments using pitches and sounds and showed that acoustic variations and perception affect short-term memory span performance. Similar results were found by Baddeley (1966a, b), who suggested that articulation and rehearsal of the sound by the participant allowed better retention and repetition in span tasks. In fact, Murray (1968) also showed that the articulation or sub-vocalization of a sound or phoneme can cause confusion when chunking and rehearsing are needed in short-term phonological tasks.

Altogether, this evidence suggested that other mental processes play important roles in retention and retrieving information in span tasks. Baddeley and Hitch (1974) then proposed an innovative theoretical model—the working memory model—to explain how humans use novel information and process it to deal with challenges in the environment. According to these authors, short-term memory (i.e., the one that is accessed by direct span tasks) is modality-dependent (i.e., phonological or visual).The mental manipulation of novel information requires more than just short-term memory. Miller, Galanter, and Pribham (1960) created the term “working memory,” but it was Baddeley and Hitch (1974) who named this way these mental processes involving retaining and manipulating novel information.

Since Baddeley and Hitch (1974) introduced the working memory model, several researchers have sought to understand the mental processes that underlie this psychological construct. However, Baddeley’s studies (e.g., Baddeley, 1966a, b, 2000; 2003a, b; Baddeley, Allen, & Hitch, 2011; Baddeley, Gathercole, & Papagno, 1998; Baddeley, Papagno, & Vallar, 1988) started a new field within cognitive sciences: working memory tasks and processes. To date, although Baddeley’s model has been reviewed and discussed, a final form has not been reached, but it is still the most adopted theoretical model to explain behavioral results in psychology.

1.2

Neuroscience of working memory and fMRI meta-analyses

Neurosciences and neuropsychology are growing fields of research in modern psychology. Since the development of neuroimaging techniques, such as fMRI, positron emission tomography, and magnetoencephalography, from the 1990s until today, psychological researchers have investigated how humans process mental tasks in the brain (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011). The basic idea of neuropsychology is that each and every psychological construct (e.g., memory, attention, thinking, planning, motor preparation, and control) has a neurobiological basis (i.e., a neural network in the brain that is responsible for processing and executing a task or behavior; Damasio, 2006). Because all psychological constructs have a neurobiological basis, the same must be true for working memory.

D’Esposito and Postle (2015) defined working memory as a mental process that accounts for coordinating and processing information when multiple goals are active and guides behavior based on information that is not present in the immediate environment. According to recent data, working memory uses content that is already known from long-term memory to manipulate internal representations through attentional control that generates encoding. Encoding is the ability to convey sensory or semantic information into mental short-term representations that are ready to be mentally manipulated but not necessarily consolidated in long-term memory (Jensen & Lisman, 2005).

Working memory appears to be an embedded set of mental processes that are basically divided into memory and attention (Cowan, 1999, 2010; Cowan, Blume, & Saults, 2013). Memory is divided into three main processes: sensorial memory (sensorial information storage, which happens in ~250 ms),short-term memory (responsible for encoding sensorial information into mental representations), and long-term memory (responsible for activating and retrieving stored represented information). During working memory tasks, attention is divided into two main processes: attentional focus (responsible for activating specific parts of long-term memory where task-relevant represented information is stored) and the central executive or attentional control (responsible for holding in the mind the task’s goal and maintaining focused attention on the correct portion of long-term memory; Cowan, 1999).

Recent fMRI studies (e.g., Jensen & Lisman, 2005) have provided evidence that long-term memory storage in the brain is linked to the type of encoding that is represented in the mind (e.g., auditory information is stored in the auditory cortex, a part of the temporal lobe; semantic-encoded information is stored in regions of Wernicke’s and Broca’s areas). These encoding-dependent regions of storage also appear to be activated during working memory tasks. Long-term memory is likely used to represent and manipulate short-term information (D’Esposito & Postle, 2015). The prefrontal cortex plays an important role in working memory tasks. Evidence from fMRI studies suggests that activation of the prefrontal cortex is pivotal for attentional control. Some authors have suggested that parietal and temporal regions are responsible for encoding, representing, and retrieving mnemonic information and embedding mental processes. Frontal regions are responsible for focusing attention and maintaining or shifting it during working memory tasks (D’Esposito & Postle, 2015).

Despite the growing literature, fMRI studies have not yet determined whether the neural networks that are responsible for encoding the same sensorial input are similarly activated during working memory tasks using different types of representation. The aim of the present dissertation is to address this issue by relying on fMRI meta-analytical methods. This study sought to compare pitch and sound stimuli (non-vocalized) with letters or syllables and words/nonwords. Although such stimuli are similar in terms of encoding, they have an hierarchical organization. Words have both semantic meanings and phonological representations. Syllables and letters are restricted to phonological representations, with a few exceptions (e.g., one-syllable words).Sounds and pitches have only auditory representations and are difficult to vocalize and are thus difficult to rehearse. If fMRI results for each of these types of stimuli are subtracted from one another, then the result would reveal a pure region of auditory storage and pure region of the central executive. This research is unique because all other meta-analyses of working memory have sought to unveil the neurobiological foundations of working memory in terms of neural networks (e.g., Owen et al., 2005; Rottschy et al., 2012; Wager & Smith, 2003) and not the specific location of a single function.

2

Theoretical Models of Working Memory

Working memory can be defined as a cognitive function that is responsible for storing, holding, manipulating, and retrieving novel information. All theorists agree on this definition, despite disagreement regarding such aspects as limits, capacity, structure, and function. Currently, the most accepted model for explaining working memory is Alan Baddeley's model (Baddeley & Hitch, 1974; Baddeley, 2000; Baddeley, Allen, & Hitch, 2011). It is a complex model that can be tested under several conditions and using different experimental paradigms, which is in contrast to other models, such as Cowan's (1999, 2010). However, it does not explain certain phenomena, such as the enhancement of working memory by familiarity with stimuli (Cowan, 2010), the verbal encoding of olfactory, visual, and tactile stimuli (Jönsson, Moller, & Olsson, 2011), and the influence of mood in working memory tasks (Chan, Shum, Toulopoulou, & Chen, 2008).

Other theoretical models have been proposed to explain empirical data. In 1999, Akira Miyake and Priti Shah co-edited a book that gathered the main researchers in the working memory field at the time, including Alan Baddeley, Nelson Cowan, Randall Engle, Stephen Tuholski, Michael Kane, and Richard Lewis. Among these authors, Cowan's model is the second most well-known in the literature and the first option for explaining the effects of familiarity and attention (Cowan, 2010). However, Cowan's model (1999, 2010) lacks precision in explaining different types of encoding and strong empirical evidence of individual and group differences in phonological, olfactory, and visuospatial working memory.

Working memory is thought to be executed, like other executive functions, in the prefrontal cortex. Engle, Kane, and Tuholski (1999) provided evidence of how working memory can be explained as an integrative part of fluid intelligence. Their evidence does not necessarily exclude either Cowan's or Baddeley's model, but it suggests that fluid intelligence performance and prefrontal cortex activation are associated with complex working memory tasks.

Working memory is also considered an executive function. Executive functions comprise a set of superior mental processes that are needed for concentration and attention when behaving automatically or relying on instinct or intuition would be ill-advised, insufficient, or impossible (Diamond, 2009a, b, 2013; Diamond, Lee, & Hayden, 2003). They include three low-order functions (inhibitory control, working memory, and cognitive flexibility) and three high-order functions (fluid intelligence, rational reasoning, and logical reasoning). Based on this perspective, working memory is limited to storing, holding, and retrieving novel information, whereas manipulating, controlling, updating, and inhibiting predisposed responses and self-regulation are part of executive functions but not responsible for working memory itself.

Baddeley's model (Baddeley & Hitch, 1974; Baddeley, 2000; Baddeley, Allen, & Hitch, 2011) is used when researchers seek to study only the effects of a modality (e.g., phonological, visual, or any other sensorial input) or when they try to separate working memory into its four hypothesized components: phonological loop, visuospatial sketchpad, episodic buffer, and central executive. When researchers try to explain the effects of familiarity and working memory capacity, they tend to cite Cowan's work. Diamond's model of executive function is also widely used to explain the role of the prefrontal cortex in tasks that require novel solutions, self-regulation, decision making, and the inhibition of predisposed responses.

These different theoretical models represent different views of the same phenomenon. This means that we have the opportunity to study them in-depth and test them using empirical evidence. The objective of this chapter is to review behavioral evidence and further understand the crucial differences between these models so we can test their hypotheses using functional magnetic resonance (fMRI) data.

2.1

Baddeley's working memory model

Information processing theory is one of the most frequently used psychological hypotheses to explain behavior that arises from psychological processes. It was first proposed during the cognitive revolution in the 1950s by important names in the history of psychology, such as Donald Broadbent, George Miller, and Noam Chomsky (Mills, 2000). The cognitive revolution emerged as a counterpart to the behaviorism movement that was concerned with only the product of the process, without caring about how behavior is generated in the mind.

One of the main landmarks of the cognitive revolution was the celebrated work of George Miller (1956) entitled, "The Magical Number Seven, Plus or Minus Two." Miller proposed that one of the main mechanisms of human cognition, a memory subtype that was initially called short-term memory, was limited by the number of stimuli that could be retained at the same time (seven plus or minus two, from five to nine items). The experimental paradigm that was used and successfully replicated in numerous publications since then (Conway, Cowan, Bunting, Therriault, & Minkoff, 2002) was the digit span task. The participant listens to a random sequence of numbers and is asked to repeat them orally. Miller showed that other cognitive processes were associated with this limit in the capacity of short-term memory.

With advances in psychological sciences, Baddeley and Hitch (1974) developed the first theoretical model that allowed an explanation of various empirical data that were generated by various digit span methods that were developed based on Miller's work in 1956 (Figure 1). The theoretical foundation on which the model of Baddeley and Hitch was created was information processing theory. This theory posits that the human mind works like a computer that processes stimuli as inputs and generates outputs. At this point, no one thought in terms of a behavioral product but rather in terms of the process that generates it. These authors suggested that not only the span of digits was limited; span limitations also exist for other types of information, such as words, colors, and shapes and the ability to recall them in reverse order of presentation, a task known as reverse or backward span. They also realized that the stimulus modality also mattered. Some people could perform better when the stimuli were auditory and worse when the stimuli were visual, and *vice versa*. Finally, they found that this entire process of retaining and manipulating information in the mind demanded a sort of general cognition that manages the underlying processes, such as an executive in a company, and its overall processing was intrinsically linked to the participant’s limit of attention. Baddeley and Hitch (1974)suggested that these processes reflected Miller’s working memory model, which can be defined as the ability to retain and manipulate new information and provide the most appropriate response that is dictated by the environment.

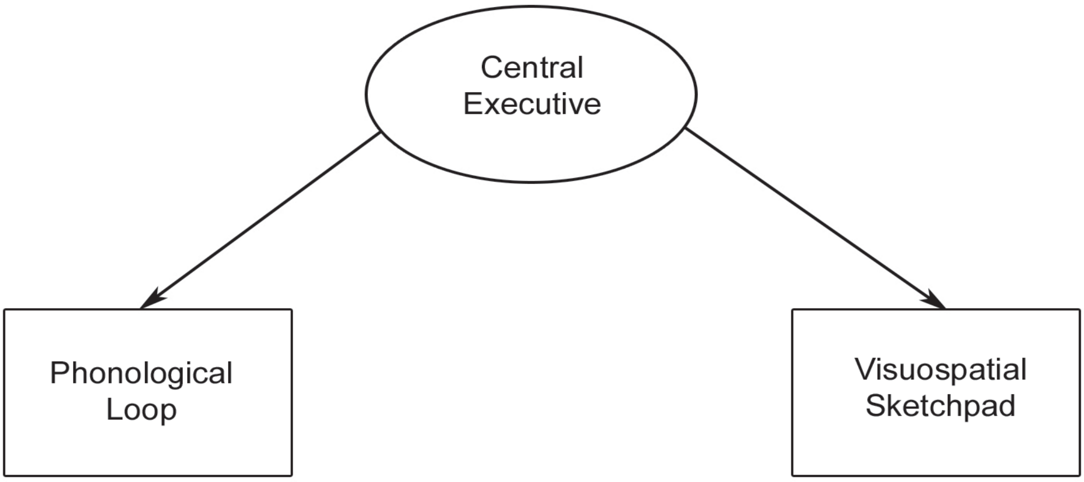

Fig 1. First working memory model adapted from the proposal of Baddeley and Hitch (1974).

The components of the theoretical model of Baddeley and Hitch are the phonological loop (responsible for retaining auditory and verbal information, such as words, letters, or sounds, while the central executive handles them), visuospatial sketchpad (which performs the same function as the phonological loop but with visual stimuli), and central executive (which serves to guide executive attention to the most relevant part of information at a time and manages the capacity of working memory according to task demands; Baddeley and Hitch, 1974).

When a person must remember a phone number, pick up the phone, and dial the number while repeating the numbers sequentially, he is relying on his own working memory. This also happens in other day-to-day activities, such as preparing a new recipe that was seen on television or trying to mimic a yoga teacher’s movements. These are all working memory tasks.

Since the model of Baddeley and Hitch in 1974, new hypotheses have emerged to explain the underlying processes and individual differences in working memory tasks. However, the most consistent model with much evidence to support it is Baddeley’s new model, revised in 2000. The independence of the modalities in domain-specific systems and presence of a general domain system comprise a more robust theoretical model to explain the processing of information using working memory (Baddeley, 2012). Baddeley included in the original model from 1974 a new component called the episodic buffer. The episodic buffer is a system that is responsible for integrating information from different modalities and sources into one, so an underlying component of the central executive serves as an interface between domain-specific systems and long-term memory to generate knowledge (Figure 2).

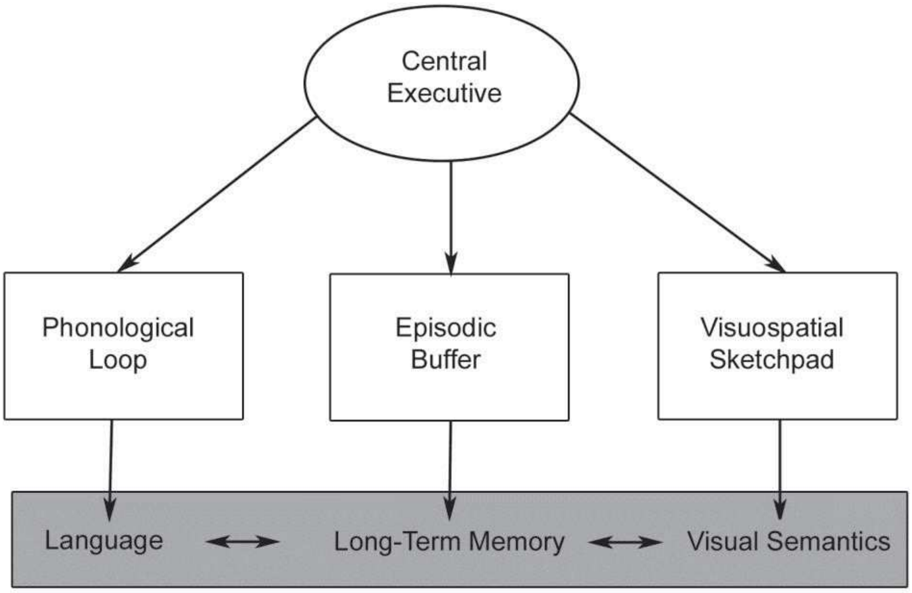

Fig 2. Second working memory model adapted from Baddeley (2000). Processes associated with fluid intelligence are in the white rectangles. The gray rectangle encompasses the processes associated with crystallized intelligence.

Since the new model was proposed, much evidence has emerged to support the hypothesis of an independent system of working memory and the importance of the episodic buffer as an integrative component. However, other empirical data indicated other subcomponents within slave-specific-domain working memory systems rather than just the phonological and visuospatial domains. After a series of experiments, Baddeley, Allen, and Hitch (2011) developed the latest version of the model, which includes the previously missing sensory modalities and importance of the episodic buffer in integrating modalities. In this latest model, the central executive is a general domain component that coordinates the episodic buffer only, so there are no connections between the central executive and other subsystems as previously thought. The episodic buffer integrates information and coordinates directly with the slave subsystems to execute whatever the central executive commands.

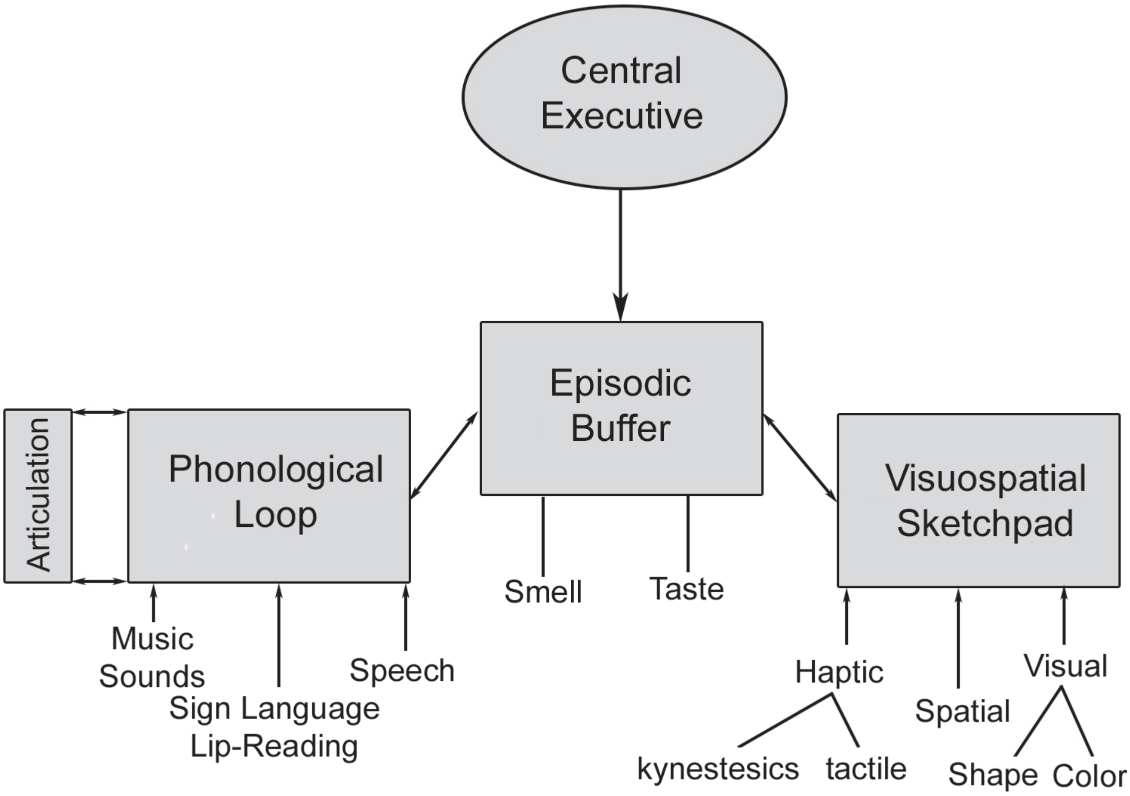

Fig 3. Latest working memory model adapted from Baddeley, Allen, and Hitch (2011). The episodic buffer became the only subcomponent that is directly controlled by central executive resources.

Recently, Allen, Baddeley, and Hitch (2014) suggested the presence of a double attentional component within the central executive to explain individual differences in visuospatial task performance. In their experiment, participants differed in the first three items from a serial working memory task in the presence of matched information in the same stimulus, such as color and shape at the same time. When the participant had to record that the square is always red, he could retain that duplicated information in the first three stimuli (e.g., red square, yellow rectangle, and green circle). The performance of the participants changed after the fourth stimulus, demonstrating the possible involvement of an attentional system for the first items but recruitment of a new system that is responsible for the latest information after the fourth item. This means that the central executive provides resources for the episodic buffer to work differently. The initial three items in short-term memory are privileged, but for the items that are subsequently presented, executive attention attempts to maintain their representation only when recall is needed. This new discovery by Allen, Baddeley, and Hitch (2014) allowed the development of new hypotheses of the functioning of the central executive.

2.1.1

Phonological working memory according to Baddeley’s model

The part of Baddeley’s working memory model that accounts for sounds, voices, language, and any kind of auditory input is phonological working memory. It is empirically defined as the integration between the central executive, episodic buffer, and phonological loop. Earlier in this chapter, we discussed the roles of the central executive: a domain-general system that manages the amount of attentional resources and coordinates the demand for the integration of modalities and the episodic buffer (a domain-specific slave subsystem that is responsible for integrating different modalities into one manageable piece of information, such as sound + speech, shape + color, and sound + color).

However, the phonological loop is another important slave subsystem. Understanding how it works can shed light on phonological working memory from Baddeley's point-of-view. The distinction between short-term memory and working memory is crucial. Baddeley (2003a) clarified that short-term memory is a system that is involved only in storing information, whereas working memory manipulates and retrieves stored information through mental processing. This means that the slave subsystems (phonological loop and visuospatial sketchpad) are in fact domain-specific short-term memories that are specialized with regard to their respective sensorial modality or input.

The structure and cognitive strategies that are used to store and maintain auditory and language information that is to be used in working memory tasks were explained by Baddeley (2003a). The first pivotal point regarding the phonological loop is that it is divided into two activities: temporary storage and rehearsal. It involves a subvocal rehearsal system that not only maintains information within the store but also records visual information within the store, provided a visual item can be named. What appears to happen is that sound similarity impairs immediate recall, likely because of sound discrimination. Although subjects can readily recall a sequence of letters (e.g., B,W,Y,K,R,X), they are likely to have considerable difficulty retaining sequences of letters with similarly sounding names (e.g., T,C,V,D,B,G; Conrad & Hull, 1964). A similar phenomenon occurs when words are used. A word sequence such as *man*, *cat*, *map*, and *cab* can be correctly recalled less than 20% of the time, whereas subjects will score above 80% with a dissimilar sequence, such as *pit*, *day*, *cow*, *sup*, *pen* (Baddeley, 1966a). The fact that this is a characteristic of short-term memory rather than long-term memory systems was demonstrated in a further study in which subjects were presented with lists of 10 words from each set and required to learn the sequence across a series of trials. Under these conditions, the similarity of meaning was important, and phonological similarity lost its effect (Baddeley, 1966b). This evidence indicates that familiarity does not help phonological working memory in simple span tasks.

Evidence of a rehearsal system is provided by the word-length effect, which involves presenting subjects with a sequence of items and requiring immediate serial recall. The memory of a five-word sequence drops from 90% when the sequence consists of monosyllables to ~50% when five-syllable words are used, such as *university*, *opportunity*, *international*, *constitutional*, *auditorium* (Baddeley, Gathercole, & Papagno, 1998). The word-length effect can be abolished by simply requiring the subject to utter a sequence of irrelevant sounds, such as repeating the word *the*. It impairs performance because it both blocks the maintenance of the memory trace through rehearsal and prevents the subject from using subvocalization to record the items in the phonological store when visual presentation is used. The episodic buffer appears to play an important role in trying to concentrate attentional effort in one modality of information rather than integrating the whole set of stimuli. Much evidence has shown that verbal encoding actually improves phonological working memory performance (Cowan, 2010; Jönsson, Moller, & Olsson, 2011); thus, Baddeley's (2003a) assumption of impairment has been faced with contradictory empirical evidence.

Some of this effect undoubtedly occurs because long words take longer to recall, leading to more forgetting (Cowan, 1999). However, the fact that a word-length effect occurs when the output delay is held constant, either by using a probe procedure or by recognition (Baddeley, 2003a), indicates that the effect operates at both the ongoing rehearsal level and through forgetting during responding.

Another important point regarding phonological short-term memory is that rehearsal relies on overall speech-motor programming and not articulation. The process of subvocal rehearsal does not appear to depend on the capacity for overt articulation. Baddeley (1966b)showed that dysarthric patients who lost the ability to articulate can show clear evidence of subvocal rehearsal, reflected by the word-length effect or an effect of acoustic similarity with visually presented items. In contrast, dyspraxic patients whose problems stem from a loss of the ability to assemble speech-motor control programs show no sign of rehearsal. This implies that the capacity to set up speech-motor programs underpins rehearsal rather than overt articulation.

Evidence supports the notion that the phonological loop is influenced by conceptual knowledge. This probably means that the working memory system is not dissociated from long-term memory. Mutual influences likely exist, depending on the task. Baddeley, Papagno, and Vallar (1988) tested the ability of one patient, who had a very pure phonological short-term memory deficit, to acquire the vocabulary of an unfamiliar foreign language: Russian. The experiment required her to learn eight items from the Russian vocabulary (e.g., *svieti*[rose]), and comparisons were made with her ability to learn to associate pairs of unrelated words in her native language (e.g., horse-castle). They found that such native language pairs were learned as rapidly by the patient as by normal control subjects, whereas she failed to learn any of the eight Russian items (Baddeley, Papagno, & Vallar, 1988). The phonological loop appears to be a useful aid in learning new words. In another study, they found that requiring subjects to suppress rehearsal by uttering an irrelevant sound disrupted foreign but not native language learning and that phonological similarity among the items to be learned also disrupted the acquisition of novel vocabulary, as did increasing the length of the novel items (Papagno & Vallar, 1992). Both of these variables impaired phonological loop performance.

Two alternative views can also explain the role of phonological short-term memory (clearly synonymous to the phonological loop) and language. Other authors suggested that phonological storage itself is merely a reflection of deeper phonological processing problems. This model by Brown and Hulme (1996) differed from our own by emphasizing the role of existing language habits in facilitating vocabulary learning. Gathercole and Baddeley (1993) found that sequences that were closer to English (e.g., stirple, blonterstaping) were indeed consistently easier than less familiar phoneme sequences (e.g., kipser, perplisteronk). This strongly suggests the influence of existing language habits on current nonword repetition performance, exactly as the Brown and Hulme (1996) model would predict. One way of explaining this pattern of results is by considering the division of the phonological loop into separate storage and articulatory components. The nonword repetition task might demand both of these, whereas only the articulatory output system might depend on earlier language habits, leaving the phonological store relatively language-independent. Baddeley (2003a) suggested that existing language habits have a major effect on performance in tasks that resemble the acquisition of vocabulary through their impact on output and rehearsal, rather than by directly influencing phonological storage.

The other alternative explanation is that language acquisition relies on general phonological processing and not on the phonological loop. Furthermore, whereas both the nonword repetition and phonological awareness models are capable of predicting reading performance, they appear to account for separable variance (Baddeley et al., 1998). Therefore, it can be argued that the greater specificity of the phonological loop hypothesis has a clear advantage over a general phonological processing interpretation.

In the case of short-term memory patients, their language deficits appear to be limited to the major disruption of short-term phonological storage while other phonological and linguistic skills appear to be preserved (Vallar & Shallice, 1990).

Phonological short-term memory clearly plays a pivotal role in language acquisition, regardless of other deeper or higher processes. Baddeley (2003a) suggested a neurobiological basis of the phonological loop that can be tested using fMRI meta-analysis, in which the temporary storage system is centered in Brodmann area 44 (predominantly in the left hemisphere), and the rehearsal system is centered in Brodmann area 40 (Broca's area, predominantly in the left hemisphere). These are the proposed structures for the phonological loop. Auditory information is analyzed and fed into a short-term store. Information from this system can pass into a phonological output system and result in spoken output or rehearsal. This, in turn, may recycle information, both subvocally into the short-term store and into the ears when rehearsal is overt. Visually presented material may be transferred from an orthographic code to a phonological code and thereby recorded within the phonological output buffer (Vallar & Papagno, 2002).

To test Baddeley's model (Baddeley & Hitch, 1974; Baddeley, 2000; Baddeley, Allen, & Hitch, 2011), activation in the following areas would be expected (Baddeley, 2003b): phonological loop (Brodmann areas 6, 40, and 44, predominantly in the left hemisphere), episodic buffer (Brodmann area 7), and central executive (Brodmannareas 9 and 46).

2.2

Cowan’s embedded-processes model

Working memory was defined by Nelson Cowan (1999, 2010) as a cognitive process that retains old and novel information in an accessible state that is suitable for manipulating and carrying out tasks with mental components. Nonetheless, working memory does not exist as a separate entity; it constitutes merely a practical and task-oriented label so researchers can discuss it. His hypothesis was that working memory is, in fact, a set of embedded-processes from both attention and long-term memory. It also means that if an entire process is invoked without facilitating a task, then it is still considered working memory (e.g., the verbal encoding of meaningless shapes). Cowan argued that his model does not deny the definition of processes that are found in other models, but he attempts to explain a single way of functioning, regardless of the type of stimulus or input.

The stimulus is stored for a brief moment (hundreds of milliseconds) in a sensory store to be further driven to either an activated portion of long-term memory or the focus of attention. An unchanged stimulus tends to go to the activated long-term memory, whereas a novel stimulus and voluntarily attended stimulus stay within the focus of attention. The activated portion of long-term memory is also known as short-term storage or short-term memory, which keeps the information that is needed to complete a task activated. The focus of attention is the enhancement of processing of one piece of information to the detriment of another. Finally, the process that is responsible for gathering those mental processes together in a way that can follow or be modified by instructions and incentives is called the central executive.

Four processes are used during working memory tasks: encoding, representation, maintenance, and retrieval. The processing of information is based on this set of mechanisms and relies on both long-term memory and attention to ease further processing. Individual differences in working memory tasks can be explained by limitations in both attention and long-term memory. The activated portion of long-term memory appears to present a time decay effect, whereas attention is limited by the amount of information that can be held in the focus of attention at a given time. If Cowan's hypothesis is correct, then there should be evidence that activated long-term memory (or short-term memory) gradually diminishes over time in tasks with a delayed response. Attention should be limited to a critical number of items or chunks in complex span tasks. He cites several experiments that showed that activated long-term memory indeed decays over time (10-20 s) in delayed-to-sample tasks when distractors are presented during maintenance. In different sets of experiments that use a stimulus that cannot be chunked or rehearsed, participants tend to show performance of 4±1 items in complex span tasks. Altogether, this evidence suggests that Cowan's model is indeed one of the closest ones that can explain working memory. Perhaps this indeed reflects an overlap of long-term memory and attention rather than a singular cognitive entity.

The subset of memory that is represented in long-term storage must be activated to be accessible to the focus of attention (e.g., in a number span, the long-term memory that is associated with all known numbers is activated and remains this way throughout processing). Only activated information may enter into awareness, but the opposite is not true, in which it is possible to access information from outside conscious awareness (e.g., when you are doing a number span task and someone calls your name).Cowan's model emphasizes the relationship between memory and attention. There are different processing limits for each cognitive domain: memory and attention. The focus of attention is controlled by two systems (voluntary and involuntary), and conscious awareness can be influenced during processing (Cowan, 1999, 2010).

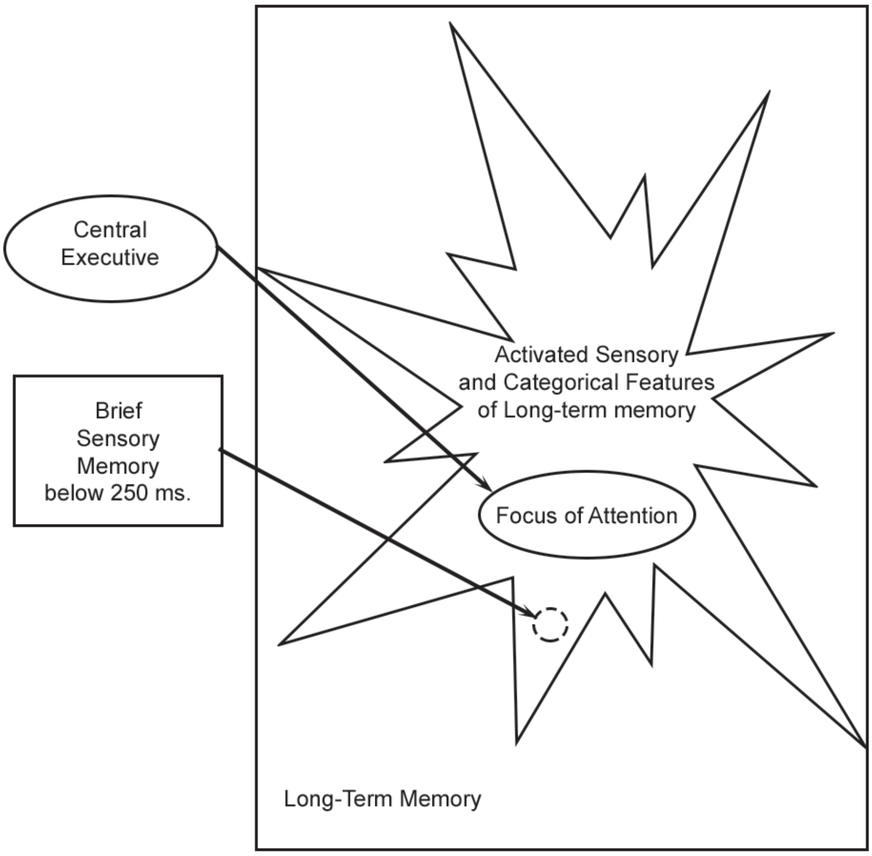

Fig 4. Cowan’s working memory model adapted from Cowan (2010). The central executive plays the role of a supervisory attention system with two components: one that is automatic and another that is voluntary. Long-term memory is constantly activated and remains this way while it is needed. Finally, one small portion of the activated memory is actually a brief sensory memory that lasts <250 ms and serves only to orient the focus of attention to particularly dangerous or predisposed stimuli.

Attention and awareness are coextensive. Attention is the enhancement of the processing of some information and exclusion of other currently available information, and awareness is the ability to be consciously aware of information. Involuntary attention is the automatic recruitment of attention (e.g., a fire alarm, the sound of a car horn, or someone calling your name) to detect physical changes in the environment or changes in an habituated stimulus. Voluntary attention is an effort-demanding process (e.g., searching for a stimulus within a set of items or saying a word list backward) that is controlled by the central executive. The central executive is “the collection of mental processes that can be modified by instructions and incentives" (Cowan, 1999, p.65). Cowan (2010) stressed that his model is not intended as a description of processing but rather as a simple summary and organization of pivotal features of attention and memory as embedded processes; without the coordination of both, processing is not possible.

The long-term memory portion of working memory is then described as a set of features in long-term memory that are used to encode the stimulus to make it more familiar, thus enhancing further memory representation. Encoding can be abstract or sensorial. Abstract codes include phonological codes (ba, bo, da, etc.), semantic codes (the meaning of a word or sign), spatial orientation codes (left, right, up, down, etc.), and so on. Sensory codes are the modality of the input, including visual codes (shape, color, size, luminosity, etc.), hearing codes (tones), tactile codes (textures), olfactory codes (smells), and gustatory codes (taste). Cowan (1999) argued that executive control circulates information that is currently within the focus of attention using rehearsal, but it is possible to use long-term memory if relevant information is available to deal with the task, such as using chunking as a strategy. The focus of attention is important to enhance encoding. In attention-shifting tasks (e.g., reading a text and responding to the sound of a specific syllable), when participants pay attention to one thing at a time (i.e., they stop reading to pay attention to a sound), they tend to make fewer mistakes than when they are immersed in reading. This suggests that phonological encoding demands the focus of attention at least at categorical levels. Cowan (2010) suggested that semantic encoding is limited if there is not an important part of attention and conscious awareness involved.

Working memory is also a valuable tool to represent a set of stimuli in long-term memory. According to Cowan (1999), representation appears to depend on the form in which an item is represented. Phonological short-term memory is influenced by auditory tasks but not by visuospatial tasks. Cowan argued that Baddeley's model neglects other types of representation, thus limiting his model to only phonological and visuospatial short-term memory. According to Cowan (2010), other modalities of representation appear to differ from auditory and visuospatial stimuli, such as tactile stimuli and nonverbal sounds. The properties of representation may vary accordingly to encoding properties. The verbal encoding of visual items is more suitable than serial recall if the items' names are known, whereas visuospatial encoding is more suitable when items are organized according to direction or position. This phenomenon can be clearly viewed in studies that used the olfactory modality with high and low demands of verbal encoding (Jönsson, Moller, & Olsson, 2011).

The maintenance of information in the focus of attention is the most important feature of the embedded-processes theory. Maintaining a set of items in activated memory requires strategies to keep the stimulus circulating in the focus of attention. Rehearsing is the most common strategy, but other strategies may apply, such as recirculating items in a search task. If a similar persistence of information is spread among all items, then individual differences between children could be explained by the rate of pronunciation rather than interword pauses. However, as lists of words increase in a word span task, silent periods between words also increase. Cowan (1999) suggested that once a child retrieves a particular item from activated memory, the focus of attention changes quickly to the next item. Thus, it is not only maintaining active information in short-term storage but also circulating this information in the focus of attention.

Finally, retrieving information accurately is pivotal in working memory tasks. This is defined as entering the correct items into the focus of attention. Retrieval from long-term memory is limited only by practical reasons, but retrieval from activated memory (i.e., short-term memory + attentional control) needs to be fast because information will disappear through memory decay. If sufficient episodic memory is represented and stored in long-term memory, then it is possible to retrieve items even after deactivation—loss of the novel information.

Cowan (2010) based his model on Anne Treisman's attenuation-filter theory of attention (1996). He extends Treisman's theory by adding the concepts of attended and unattended information. Thus, information activates certain portions of memory when the stimulus is relevant. An irrelevant stimulus does not fade away; it remains unattended but available in memory for the person to use if needed or demanded. Evidence suggests that unattended information is still able to be retrieved automatically by working memory if enough effort is given to orienting attention. Less effort is needed when physical changes occur in the stimulus, whereas more effort is needed when complex and semantic changes occur in unattended stimuli (Cowan, 2010). Both Cowan (1999) and Baddeley (1999) agreed about a passive storage component (activated memory/short-term memory) and an active processing component of working memory, but only Cowan took into account automatic activation during working memory tasks.

2.2.1

Working memory capacity

Cowan (1999, 2010) dedicated an important part of his work to explaining the capacity of working memory. Individual differences in capacity can explain differences in higher-order cognitive domains. "It seems unlikely that, say, seven items could be held in attention at once. Therefore, in addition to attended information, one needs activated sources outside attention and/or supplementary help from the long-term memory" (Cowan, 1999, p.79). Cowan conceded that he does not know if there is a limited capacity of activated memory, but because it is a part of long-term memory, there are likely no limitations. The time limit of activated memory seems to range between 10 and 30 s. Several discriminatory tasks show the decay of activated memory after this period of time.

According to Cowan (2010), the capacity of the focus of attention is the "magical number" 4 ± 1. Capacity is the number of items in the focus of attention at a given time. Different types of stimuli may have different limits (e.g., visuospatial or phonological), but differences are likely attributable to more or less effort that is demanded in attention switching or dual tasks. The time limit of attention is associated with vigilance tasks. Evidence suggest that this limit is around 1 h.

The capacity of working memory leads to the distinctive roles of embedded processes in either working memory or individual performance. According to Cowan (1999), working memory is a global workplace where the information that is needed to perform a task is especially accessible temporarily. Several pieces of memory must be combined and thus are concurrently activated, whereas individual performance can be explained by the mechanisms by which information becomes accessible, which may vary. Thus, performance varies because of activated mechanisms and not the use of working memory. "Thus, there is no single, separate theoretical entity that I would call working memory; that is a practical, task-oriented label" (Cowan, 1999, p.79).

Cowan's (2010) theory suggests that information in long-term memory is activated to allow a person to perform a task. Sometimes, if this information is insufficient, then additional long-term memory is activated. Other previously unused regions of long-term memory can be recombined or co-activated during the same task to complete it. If this happens, then a novel combination of information can be formed within activated memory, leading this new combination to build a new piece of long-term memory. This model of working memory includes attention as a pivotal piece of the puzzle. The focus of attention holds information within consciousness and deals with changes in stimuli. However, activated memory can be outside the attentional range and thus unattended by conscious awareness.

Cowan (2010) finally suggested a neurobiological basis for his embedded-process theory. Cowan's first assumption for a biological foundation of working memory was neuronal activation when the physical characteristics of a stimulus change, thus leading the focus of attention to move from one piece of information to another. Several regions are associated with each feature of working memory. Cowan suggested the following biological underpinnings of the major aspects of working memory: (1) brief sensory system (sensorial cortex; for phonological information, the auditory cortex in the temporal lobe), (2) long-term memory activated portion (association cortex in the parietal lobe), (3) storage and focus of attention (locus coeruleus, hippocampus, and anterior cingulate cortex), (4) central executive (prefrontal cortex),and (5) attentional intervention and entry into the focus of attention (thalamus).

2.3

Prefrontal cortex role and executive function

Executive function or executive control refers to a group of top-down mental processes on which an individual relies when he needs to concentrate and pay attention because doing a task automatically or relying on instinct or intuition would not be advised or sufficient (Diamond, 2013). When someone must deal with and respond to novel information and make the appropriate (not automatic) response, this is considered an executive function task. Using executive control demands effort. It is easier to continue doing what someone has been doing than to change. It is easier to give into temptation than to resist it. It is easier to go on *automatic pilot* than to consider what to do next (Diamond, 2013).

There is general agreement that there are three core executive functions (Miyakeet al., 2000): (1) inhibition (also called inhibitory control) that includes self-control (behavioral inhibition) and interference control (selective attention and cognitive inhibition), (2) working memory, and (3) cognitive flexibility (also called set shifting, mental flexibility, or mental set shifting, closely linked to creativity).Based on these, higher-order executive functions are built, such as reasoning, problem solving, and planning.

Executive control is a set of skills that are essential for mental and physical health, success in school and in life, and cognitive, social, and psychological development. For example, impaired executive functions are found in addictions, attention-deficit/hyperactivity disorder, depression, obsessive compulsive disorder, schizophrenia, and bipolar disorder. The same thing occurs with child development and educational readiness and performance (Diamond, 2013).

Understanding each executive function from a working memory theorist point-of-view is important. First, inhibition involves being able to control one's attention, behavior, thoughts, and emotions to override a strong internal predisposition or external lure and instead do what is more appropriate or needed in a given situation. Without inhibitory control, the brain would be at the mercy of impulses, old habitual thoughts or conditioned responses, and environmental stimuli that pull us in a given direction.

Inhibitory control allows us to change and choose how to react and behave rather than being unthinking creatures of habit. The classic tasks that are associated with inhibition include the Simon task, Flanker task, Go/No-Go task, stop-signal task, and Stroop task (Diamond, 2013).

Working memory, according to Diamond's (2013) model, refers to the ability to hold information in mind and mentally work with it (i.e., work with information that is no longer perceptually present). According to Diamond, only two types of working memory can be distinguished by encoding processes: verbal and nonverbal (visuospatial). Working memory is critical for making sense of anything that unfolds over time, which requires holding in mind what happened earlier and relating it to what comes later. Thus, to make sense of written or spoken language, one must determine whether it is a sentence, a paragraph, or something longer. Doing mathematics in your head, mentally reordering items, translating instructions into action plans, incorporating new information into thinking (updating), considering alternatives, mentally relating information to derive a general principle, and seeing relationships between items or ideas all require working memory. Reasoning would not be possible without working memory (Diamond, 2013).

Cognitive flexibility requires inhibition and working memory and comes much later in development (Garon, Bryson, & Smith, 2008). To change perspectives, we must inhibit our previous perspective and load a different perspective into working memory, one that can be already established in mind based on long-term memory or recently acquired based on short-term memory. Cognitive flexibility requires inhibitory control and working memory. One aspect of cognitive flexibility is being able to change perspectives spatially (e.g., looking at a dinner table from its longer side and then from its shorter side). Someone can also change perspectives interpersonally (e.g., assuming another person’s point-of-view in an argument). Another aspect of cognitive flexibility involves changing how people think about something (i.e., “thinking outside the box”; Diamond, 2013). For example, if one way of solving a problem is not working, then could someone come up with a new idea that taps into the solution that had not been considered before? Cognitive flexibility also involves being sufficiently flexible to adjust to changing demands or priorities, admitting you were wrong, and taking advantage of sudden, unexpected opportunities. For example, when a student is not understanding a concept that the teacher explains, then those teachers often blame the student. But we could think differently and try to figure out a way to teach the content to the student in another fashion so that he can follow and finally grasp the concept (Diamond, 2013).

2.3.1
Working memory and inhibitory control

One of the most important aspects of the theoretical model of executive function is that it separates the control of the focus of attention (considered here as inhibition) from the rest of the working memory system. In Diamond’s (2013) words:

> “They generally need one another and cooccur. One prototypical instance of when [executive functions] are needed is the class of situations where you are to act counter to your initial tendency on the basis of information held in mind. [Working memory] and inhibitory control support one another and rarely, if ever, is one needed but not the other” (Diamond, 2013, p. 143).

According to this view, whenever someone is executing a task, he must keep his goal in mind to know what is relevant or appropriate and what to inhibit. By concentrating especially hard on the information that one holds in mind, he increases the likelihood that the information will guide behavior and decrease the likelihood of an inhibitory error (i.e., giving the predisposed response rather than the correct one). This means that constantly holding, manipulating, and updating information in mind supports what someone should do and when he should inhibit a predisposed response to give the correct response. This leads to the conclusion that inhibition relies on working memory to be accurate.

Inhibitory control supports working memory. To relate multiple ideas or stimuli together, someone must be able to resist focusing exclusively on just one thing and recombine ideas and stimuli in new, creative ways. This means a person should be able to resist repeating old thought patterns and keep doing what is right rather than what used to be done. To keep the mind focused on something, one must inhibit internal and external distractions, thus voluntarily controlling the focus of attention. Many of us are familiar with suddenly realizing that we do not know what was in the passage we supposedly just read because our mind was elsewhere (i.e., a flight of thoughts or ideas; Diamond, 2013).

In fact, although inhibitory control and working memory appear to complement each other, some authors (e.g., Diamond, 2013; Wright & Diamond, 2014) believe they are in fact different domain-specific functions. However, other authors do not make a distinction between these two processes, rather considering them as one piece of the other (Baddeley, Allen, & Hitch, 2011; Cowan, 2010; Engle, Kane, & Tuholski, 1999). Diamond (2013) and Wright and Diamond (2014) suggested that three tasks provide evidence of this separation: Hearts and Dots task, spatial Stroop task, and complex span task. The Hearts and Dots task and spatial Stroop task require the person to hold only one rule in mind, meaning that there are low load or no load demands on working memory. Complex span tasks require almost no attentional control because there are no potential distractors that occur during the task (Diamond, 2013). The Hearts and Dots task and spatial Stroop task would be pure inhibition tasks, and the complex span task would be a pure working memory task.

Theorists of working memory models (Baddeley, 2000, 2003; Engle, Kane, & Tuholski, 1999) assert that inhibition is in fact a part of the supervisory attentional system (Norman & Shallice, 1986). According to this model, attentional control or executive control is divided into two subsystems. One system is responsible for processing environmental stimuli that involve perception, automatic attention, memory, and the updating of information. The other system controls and self-regulates actions in a way that keeps the mind constantly focused by inhibiting thoughts and ideas that are not related to the task at hand (Baddeley, 2000; Engle, Kane, & Tuholski, 1999; Norman & Shallice, 1986). According to Baddeley (2000), the supervisory attentional system is a proper model for the central executive and a domain-general set of mental processes that are responsible for maintaining the focus of attention in a task.

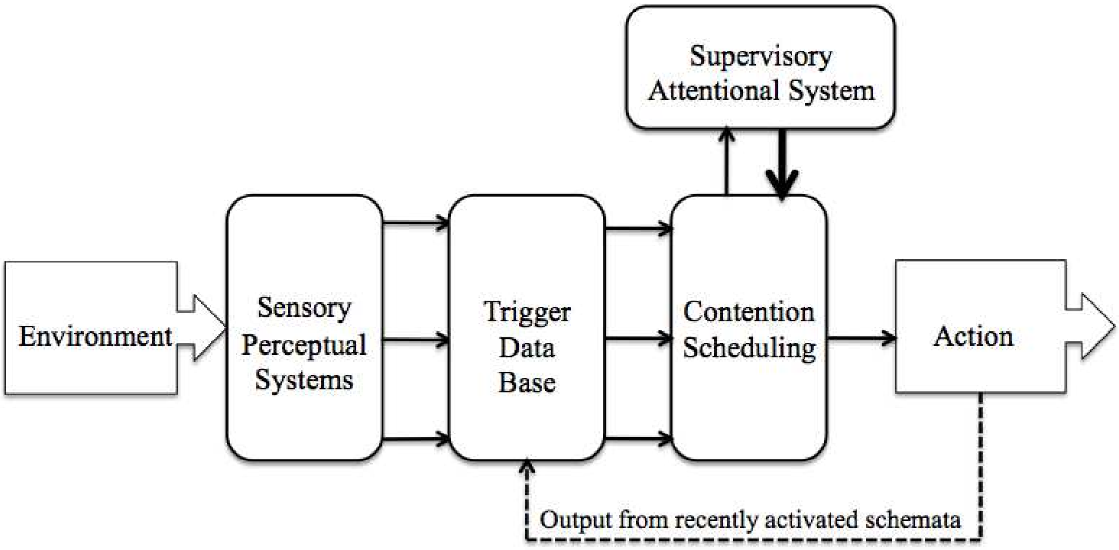

Fig 5. The supervisory attentional system according to and adapted from Norman and Shallice (1986). An environmental stimulus arrives in the mind through the sensory and perceptual systems, trigging long-term memory. To act or behave, consciousness brings from memory a set of thoughts or ideas and holds it in an organized and scheduled part of the consciousness. To behave accordingly, the mind should supervise the thoughts and ideas so they cannot escape from this organization. This is the work of the supervisory attentional system. Finally, the individual acts, and the outcome is judged, and memory is adjusting accordingly.

Baddeley (2000), Cowan (2010), and Engle, Kane, and Tuholski (1999), among others, agree that attentional or executive control is a part of the central executive. Something in dissonance with Diamond (2013) hypothesis of executive functions that suggests attentional control is an integrative part of the attentional system, but it does not influence on inhibitory control or working memory.

2.4

Working memory function and brain activation hypotheses

Based on the three theoretical models presented above (Baddeley's multiple-component model, Cowan's embedded-processes model, and Diamond's executive function model), we sought to test these models using fMRI studies.

To test each model using fMRI data, we must identify mixed and pure measures for each component. Based on several studies (e.g., Allen, Baddeley, & Hitch, 2014; Baddeley, 2003a; Baddeley et al., 1998; Cowan, 2010; Gathercole, Willis, & Baddeley, 1991; Wright & Diamond, 2014), we first separated tasks that are related to each component of the proposed theories. We then depicted regions that are associated with each theory and determined whether the theoretical frameworks consist of components that overlap or are isolated in the brain.

Table 1 shows the most important information for each of the three theoretical models that will be tested. The table presents the following information: theoretical model, authorship, domain (general or specific), system or subsystem/component, pure task, and brain region that is likely activated.

Table 1. Each theoretical model to explain working memory components, with related pure tasks and brain regions.

Model	Author	Domain	Subsystem	Task	Brain Regions
Multiple-component working memory	Baddeley, Allen, & Hitch (2011)	Specific	Working memory	Complex span tasks	Overlapping regions
		General	Central Executive	N-Back / Flanker task	Dorsolateral Prefrontal cortex
		Specific	Episodic Buffer	Delayed match-to-sample	Somatosensory Association cortex
		Specific	Visuospatial Sketchpad	Simple spatial span task	Associative visual cortex
		Specific	Phonological Loop	Simple word or letter span tasks	Premotor cortex, Pars opercularis-part of Broca's area, and Supramarginal gyrus-part of Wernicke's area
Embedded-processes model	Cowan (2010)	General	Embedded-processes	Complex span tasks	Overlapping regions
		General	Central Executive	N-Back	Prefrontal cortex
		General	Long-term memory	Recall and Feeling of knowing tasks	Somatosensory Association cortex
		Specific	Short-term memory	Delayed match-to-sample	Hippocampus
		Specific	Sensory memory	Delayed match-to-sample	Sensorial cortex
		Specific	Focus of attention	Orienting of attention / Flanker task	Locus Cerulean, Hippocampus and Anterior Cingulated cortex
Executive functions	Diamond (2013)	General	Executive functions	Maze tasks and tower tasks	Overlapping regions of the Prefrontal cortex
		Specific	Inhibitory Control	Simon task, Stroop task and Flanker task	Orbitofrontal cortex and Anterior Cingulated cortex
		Specific	Working memory	Complex span tasks	Dorsolateral Prefrontal cortex
		Specific	Short-term memory	Simple span tasks	Hippocampus
		Specific	Cognitive flexibility	Fluency tasks and Card sorting tasks	Overlapping regions of the Prefrontal cortex

3

Objective and Methods

3.1

General Objective

To study the brain circuitry that is involved in working memory tasks from different theoretical perspectives using functional magnetic resonance imaging (fMRI) meta-analysis.

3.2

Specific Objectives

- To test the theoretical models of Baddeley (2000), Cowan (2010), and Diamond (2013) using fMRI meta-analysis.
- To study phonological working memory in the brain using different stimuli that lead to encoding using fMRI meta-analysis.

3.3

Methods

The first step in the present study was to build a database of fMRI studies to perform the meta-analysis. We systematically searched theneurosynth.org (PubMed Automated Coordinate Extraction) database using the feature “working” to identify phonological working memory studies. We searched articles from the last 25 years that were published prior to August 2014. The search was limited to four languages: English, Portuguese, Spanish, and French (languages with which the author is familiar).

The second step was to identify missing articles from theneurosynth.org database by searching other databases. We used the keywords “working” + “fMRI” to identify working memory studies in the following databases: *PLoS One*, ScienceDirect (e.g., *NeuroImage*, *Neuropsychologia*, *Brain Research*, *Cortex*, etc.),Wiley & Sons (e.g., *Brain and Behavior*, *Human Brain Mapping*, etc.), Elsevier, *Journal of Neuroscience*, and Oxford University Press (e.g., *Brain*, *Cerebral Cortex*, etc.).

The third step involved applying inclusion and exclusion criteria to the search results and presenting the final findings for the systematic study. Article titles and abstracts were scanned to exclude articles based on the exclusion criteria. In case of doubts, the methods section of the articles was reviewed to determine whether it would be excluded. We then retrieved the full-text article to build a complete database, including authorship, year of publication, sample size, electromagnetic field of the fMRI machine (measured in Tesla), the task that was executed inside the machine, types of stimuli, a brief description of the task, and the contrast that was observed in the functional images. Coordinates were extracted from the results, and the meta-analysis was performed using the Activation Likelihood Estimation (ALE) method, which is explained below.

3.3.1
Inclusion and exclusion criteria

The inclusion criteria included the following: normal adult participants only, whole brain scans using fMRI only (positron emission tomography, magnetoencephalography, electroencephalography, and other imaging techniques were excluded), experiments in which English, Italian, French, German, Polish, Spanish, Russian, Dutch, Danish, and Portuguese languages were spoken by monolingual or first-language-only participants (Eastern languages that use other than the Latin or Cyrillic alphabet and its variations were excluded, such as Japanese, Chinese, Malayan, and Korean), and studies that provided brain coordinates in their results. Studies that compared groups (sex, normal control, and pathologies, etc.) were excluded. Duplicate articles that were indexed in multiple databases were excluded.

3.3.2
Meta-analysis: Activation Likelihood Estimation

Activation Likelihood Estimation meta-analysis is a method of conducting statistical analyses of human brain imaging studies using published coordinates in Talairach or Montreal Neurological Institute (MNI) space. Activation Likelihood Estimation was originally developed by Peter Turkeltaub (Turkeltaub, Eden, Jones, & Zeffiro, 2002). It has come to also mean “anatomic likelihood estimate” when used in conjunction with anatomic data, such as the voxel-based morphometry database. Activation Likelihood Estimation uses a null-hypothesis test for each voxel to be activated during a task. Much criticism has been given to the uncertainty in spatial coordinate determination in neuroimaging studies. Turkeltaub et al. (2002) suggested that each focus is best viewed not as a single point but rather as a probability distribution that is centered around a peak at the reported coordinates. By evaluating the union of these distributions for all brain locations, a map for the entire brain that represents the differential likelihood of activation at all locations can be generated.

To organize our database, we adapted the MNI coordinates to Talairach space using icbm2tal transformation (Lancaster et al., 2007). We then separated the database by type of stimuli and lastly conducted the ALE analysis to test significant differences between networks by considering the types of stimuli, with code types as the independent variable. We used three different software programs to conduct the analyses: GingerALE (Eickhoff et al., 2009; to test the null-hypothesis),icbm2tal transformation (Lancaster et al., 2007; to transform MNI data into Talairach space), and Mango 2.1 (to generate the images).

4

Results

4.1

Systematic Search

The systematic search in the neurosynth.org database retrieved 476 articles on working memory. Among these, 28 assessed phonological or auditory working memory. Table 2 depicts the neurosynth.org database results.

Table 2. Total of studies retrieved from theneurosynth.org database, divided by type of study based on the inclusion and exclusion criteria.

Variable	**Number of articles**
Visual working memory	39
Studies that usedregions of interest	16
Unclear behavioral methods	13
Studies that did not assessworking memory directly/clinical samples	380
Phonological, auditory, or verbal working memory	28
TOTAL	476

When other databases were considered, we found 233 articles, but 137 of them were already in the neurosynth.org database. Considering the other 96 articles, two assessed phonological working memory. The final result of the systematic search yielded 30 articles that studied phonological working memory. Table 3 shows the results of the other databases.

Table 3. Total of retrieved studies from other databases other than neurosynth.org divided by database.

Database	**Number of articles**
PLoS One	2
Oxford	9
SpringerLink	54
Elsevier	0
Cambridge	0
Wiley& Sons	31
Total	96

The total number of scans (i.e., number of participants) was 596. The minimum sample size was eight participants (Stoodley, Valera, & Schmahmann, 2012). The maximum sample size was 87 participants (Spielberg et al., 2011), with an average of 19.9 participants per study (standard deviation = 16.5). With regard to the fMRI machine that was used to collect the data, 11 used 1.5 T scanners, 17 used 3.0 T scanners, and two used 4.0 T scanners. With regard to the time of publication of the phonological working memory studies, the oldest study was published in 2000 (Martinkauppi, Rama, Aronen, Korvenoja, & Carlson, 2000), and the newest study was published in 2013 (Dima, Jogia, & Frangou, 2013). Table 4 presents the results of the articles retrieved based on the established criteria.

Table 4. Authorship, year of publication, sample size, machine used for neuroimaging, task description, and contrast observed in the experimental protocol.

Author	Year	Sample size	Machine	Task description	Contrast
Barry JG, Sabisch B, Friederici AD, Brauer J	2011	16	3.0 T	Participants were asked to engage in two tasks. The first was nonword repetition with 19 pseudowords that varied from one to five syllables. The second task was a complex delayed match-to-sample. The participant first both heard and saw a pair of words for 1 s, and then another pair of words was presented for 1 s(encoding phase). A rehearsal phase followed for 4, 6, or 8 s. The rehearsed stimuli could be the words that were heard(an ear appeared on the screen), the words that were read (an eye appeared on the screen), or neither (a hand appeared on the screen). Finally, the participant had to respond whether the targets were both correct (the same of the two stimuli), one correct and one wrong, or both wrong.	Main effect: correlation between nonword repetition and encoding, nonword repetition, and recognition Interaction: correlation between nonword repetition and encoding minus baseline, nonword repetition and recognition minus baseline, nonword repetition and encoding minus recognition

Author	Year	Sample	Machine	Task Description	Contrast
Bunge SA, Ochsner KN, Desmond JE, Glover GH, Gabrieli JD	2001	16	3.0 T	The Sternberg Item Recognition paradigm is a computerized protocol that consists of presenting a single stimulus or set of stimuli at one time. After a short period of maintenance, participants must respond whether a probe item was among the previously presented stimuli. Sets in this experiment have one, four, or six stimuli in each trial (Load 1, 4, or 6). Stimuli from the previous two trials were not presented as either stimuli or probes. However, in this experiment, one condition was established using probes from the immediately prior trial. This conditions was called Load 4 High Recency.	Main effect: Load 6 minus Load 4;Load 4 High Recency minus Load 4 Interaction: all load-related activation
Chein JM, Fiez JA	2001	12	1.5 T	The task consisted of a list of five words (for each type of stimulus) that was serially presented for 8 s(encoding phase). A 20 s maintenance phase followed. A retrieval task was then conducted, in which a probe word was presented, and the participant had to answer “yes” or “no” regarding whether the probe was presented previously during encoding. The number of syllables, distinction or similarity between phonetics, and word *vs.* nonword conditions were only treated in terms of difficulty rather than analyzed one at a time. The intertrial interval was 20 s(baseline).	Main effect: encoding minus baseline; maintenance minus baseline; retrieval minus baseline; encoding plus maintenance minus baseline; encoding plus retrieval minus baseline; maintenance plus retrieval minus baseline; encoding plus maintenance plus retrieval minus baseline Interaction: encoding minus maintenance; encoding minus retrieval; maintenance minus retrieval; maintenance in the four difficulty conditions
Dima D, Jogia J, Frangou S	2013	40	1.5 T	Participants were asked to respond to 0-, 1-, 2-, and 3-back procedures for letters in a total of 252 trials.	Main effect: 1-back minus 0-back; 2-back minus 0-back; 3-back minus 0-back
Fleck MS, Daselaar SM, Dobbins IG, Cabeza R	2006	14	4.0 T	Participants were asked to memorize a list of words before scanning. The word recognition task consisted of deciding whether a word was seen in the list. The visual perception task consisted of deciding whether one color or another was predominant. After each trial, the participants were asked to evaluate their confidence in the responses they gave.	Main effect: four confidence levels in both tasks Interaction: recognition minus visual perception in the four confidence levels

Table 4. Continued.

Author	Year	Sample	Machine	Task description	Contrast
Gluber	2001	11	3.0 T	Four letters were simultaneously presented as stimuli for 1 s. A 4 s maintenance phase followed. The participant then had to respond whether the probe letter was present in the previously presented stimuli. The intertrial interval was 1 s(baseline). Two conditions were implemented: in the first condition, the participants were asked to suppress any articulatory rehearsal during the maintenance phase; in the second condition, the participants were asked to articulate the string of letters during maintenance.	Main effect: articulatory suppression minus rest; non-articulatory suppression minus rest Interaction: articulatory suppression plus non-articulatory suppression minus rest
Hester R, D'Esposito M, Cole MW, Garavan H	2007	13	4.0 T	Participants were asked to pay attention to a list of five letters on a screen (encoding phase). After this phase, a maintenance phase (8-12s) occurred. A probe item (one letter among the ones that were presented in the list) was shown for 2 s (selection phase), and a 6-10 s preparation phase was followed by a stable recall or variable recall task. In the stable recall task, the participant had to retrieve the item that followed the probe in the list using a simple serial code for the response buttons. In the variable condition, the participants had to respond using randomly assigned buttons according to the order that was presented on the screen.	Main effect: encoding minus rest; preparation plus selection minus rest; maintenance minus rest Interaction: (variable minus stable) minus rest
Karlsgodt KH, Shirinyan D, van Erp TG, Cohen MS, Cannon TD	2005	13	3.0 T	Participants were asked to pay attention to a list of five words that were presented one-by-one on the screen for 1 s each (encoding phase). After an 8-sdelay (maintenance phase), the participants were asked to match 8-10 probe words to the list that was previously shown (retrieval) by pressing "yes" or "no" buttons.	Main effect: encoding minus rest; maintenance minus rest; retrieval minus rest Interaction: encodingminus maintenance minus retrieval
Leung AW, Alain C	2011	16	3.0 T	Sounds were presented in three location conditions (-90º, 0º, 90º). Four experimental conditions were extracted using a 2×2 design: (1) category *vs*. location and (2) n-back 1 *vs*. n-back 2.	Main effect: Category minus Location Interaction: Category2-back minus Category1-back > Location2-back minus Location1-back
Ma L, Steinberg JL, Hasan KM, Narayana PA, Kramer LA, Moeller FG	2012	18	3.0 T	An Immediate Memory Task (IMT) consisted of a matching-to-sample task in which a target was presented and matching stimuli were presented after the target. A Delayed Memory Task (DMT) consisted of the same procedure, but a distraction (string 000000) was presented three times between the target and stimuli.	Main effect: DMT minusIMT-calledDI Interaction: DI7minusDI5; DI3minusDI5

Table 4. Continued.

Author	Year	Sample	Machine	Task description	Contrast
Majerus S, Van der Linden M, Collette F, Laureys S, Poncelet M, Degueldre C, Delfiore G, Luxen A, Salmon E	2005	12	3.0 T	Participants were asked to repeat words and nonwords that were randomly presented in three different blocks, with one 20-trial block for each condition. After the first section of tasks, the participants were exposed to another 20 stimuli six times. This phase was called familiarization. Those stimuli were different from the first 20 stimuli. After familiarization, the participants performed the task again with the familiar stimuli.	Main effect: Familiarization minus Non-familiarization for words and nonwords; Non-familiarizationminus Familiarization for words and nonwords
Martinkauppi S, Rama P, Aronen HJ, Korvenoja A, Carlson S	2000	10	1.5 T	Sounds were presented in three location conditions (left, right, and middle).The participants had to perform n-back tasks for the location of the sounds. A control experiment consisted of a visual n-back of 2, in which a white square was presented in three possible locations on a black screen (left, top-middle, and right), and the participants had to respond 2-back for the locations.	Main effect: 3-back minus 1-back; 2-back minus 1-back Interaction: Auditory 2-back minus Visual 2-back
Marvel CL, Desmond JE	2010	16	3.0 T	In a simple matching-to-sample condition (called match condition), sets of two or six letters were presented to the participants for 2 s (encoding phase). A 4-6 s interstimulus interval then occurred (maintenance phase). One single letter was then presented as the target for 1 s, and the participants had to judge whether this letter belonged to the set of letters that was previously presented (retrieval phase). In the complex matching-to-sample condition (called executive condition), the same procedure was adopted with regard to the target being a letter that was two positions before in the alphabet(e.g., if the letter *f* was shown in a set, and the letter *d* appeared as the target, then the participant has to press the “yes” button because *d* is two positions before *f* in the alphabet).	Main effect: executive condition minus match condition Interaction: executive condition minus match condition during encoding phase; executive condition minus match condition during maintenance phase; executive condition minus match condition during retrieval phase
Marvel CL, Desmond JE	2012	16	3.0 T	Two conditions of a verbal version of the Sternberg working memory task were designed. In the first condition, one or two strings of three elements of the same letter (e.g., F-F-F and Q-Q-Q) were presented for 1 s(encoding phase). A maintenance phase then followed, varying from 4 to 6 s. A retrieval task was then conducted, asking the participants to judge whether a probe letter was presented in the previously shown string. The second condition was identical to the first condition, with the exception that the probe letter would have to be two positions ahead in the alphabet of the presented letter instead of the encoded letter (e.g., if the stimuli were F-F-F, then the correct probe letter should be H because it is two positions ahead in the alphabet).	Interaction: 2-target minus 1-target in the second condition (manipulation) minus 2-target minus 1-target in the first condition (storage)

Table 4. Continued.

Author	Year	Sample	Machine	Task description	Contrast
McNab F, Leroux G, Strand F, Thorell L, Bergman S, Klingberg T	2008	11	1.5 T	Verbal DMT. The participants were required to encode five letters that were sequentially presented for 500 ms each. A 1 s maintenance phase followed. A probe cue that consisted of a number and a letter was then shown, and the participant had to decide whether the serial position of the letter in the probe cue was the same compared with the serial position of the previously presented stimulus (e.g., for the sequential stimuli G, D, W, F, and M, the probe cue 3:W would be a correct match, as well as 2:D, 4:F, and so on). A control task consisted of always presenting the letter *a* in lower case, and the letter *A* in upper case was the cue probe.	Main effect: DMT minus control; Conjoint Visual and Verbal DMT plus Go/No-Go Task; Conjoint Visual and Verbal DMT plus Flanker Task; Conjoint Verbal and Visual DMT plus Go/No-Go Task plus Flanker Task
Nee DE, Jonides J	2011	25	3.0 T	The task consisted of a DMT using a list of six four-letter words for each trial. Words were serially presented (500 ms per word), followed by a 300 ms mask (%%%%) and a retrieval task with a probe word. The probe word was either in activated long-term memory (a LTM; first presented stimuli in the list) at the region of direct access (RDA; positions 5 to 2) or at the focus of attention (FA; the last presented word), according to Oberauer's (2002) 3-state model of memory. The intertrial interval was 4-7 s(baseline).	Main effect: aLTM minus baseline; RDA minus baseline; FA minus baseline Interaction: FA minus RDA; FA minus aLTM, RDA minus aLTM
Newton AT, Morgan VL, Rogers BP, Gore JC	2011	8	3.0 T	Participants were asked to respond to 0-, 1-, 2-, and 3-back procedures for letters in 20 trials in each condition.	Interaction: 3-back minus 2-back minus 1-back minus 0-back minus rest
Novais-Santos S, Gee J, Shah M, Troiani V, Work M, Grossman M	2007	19	3.0 T	Participants were asked to read Direct Object and SC sentences in a "moving window" paradigm. Phrases from the sentences were presented in the following order: initial-phrase; verb-phrase; noun-phrase (working memory[WM]-phrase/50% of the cases); concluding-phrase. In 20% of the trials, the participants were asked to answer simple comprehension questions to ensure they were paying attention. However, this part of the procedure was not entered into the analysis. Sentences with a WM phrase were considered "more WM" because they demanded higher loads to be comprehended.	Main effect: SC minus DO; More WM minus Less WM
Relander K, Rama P	2009	10	3.0 T	A matching-to-sample task was conducted using auditory input. The participants were asked to respond whether the target matched the stimuli in three different situations: only voices, only words, and control. A word that consisted of "Voice,""Word," or "Control" was shown on the screen 3 s before each trial, so participants could know whether they should answer based on the speaker's voice, the spoken word, or no response (control condition) in each particular trial. The stimuli then appeared for 0.9-1.2 s (encoding phase), followed by an interstimulus interval of 4.5 s(maintenance phase). The target was then presented, and the participants had 3.0 s to answer (retrieval phase).	Main effect: voice minus control; words minus control Interaction: voice minus word during encoding; voice minus word during maintenance; voice minusword during retrieval

Table 4. Continued.

Author	Year	Sample	Machine	Task description	Contrast
Rodriguez-Jimenez R, Avila C, Garcia-Navarro C, Bagney A, Aragon AM, Ventura-Campos N, Martinez-Gras I, Forn C, Ponce G, Rubio G, Jimenez-Arriero MA, Palomo T	2009	13	1.5 T	Participants were asked to respond to 2-back procedures for letters that were presented in two different conditions (visual and verbal)in 23 trials in each condition.	Main effect: Auditory plus Visual minus rest Interaction: Auditory minus Visual
Rose M, Schmid C, Winzen A, Sommer T, Buchel C	2005	14	1.5 T	All stimuli consisted of a scene that was superposed by a letter. Different levels of visibility (0%, 25%, 50%, 75%, 100%) of the scenes were covered by abstract patterns and with color reduced by RGB color palette were used during both n-back tasks. The participants were asked to ignore the background for task purposes and only respond to the n-back procedure.	Main effect: 2-back minus 1-back; random effects for the 5 levels of visibility Interaction: random effects for visibility during 2-back minus 1-back
Rudner M, Fransson P, Ingvar M, Nyberg L, Ronnberg J	2007	13	1.5 T	Participants performed a 2-back task for each condition: sign language, speech language, and both (binding).	Main effect: sign language minus rest; speech minus rest; binding minus rest Interaction: sign minus speech; binding minus (sign plus speech)
Sabb FW, Bilder RM, Chou M, Bookheimer SY	2007	17	3.0 T	In each trial, the participants saw a list of words with 3 (low load), 5 (medium load), or 7 (high load) items that were presented one at a time in the middle of the screen. The participants had to respond as quickly as possible if each list item was a living or nonliving object. After presenting the list, the participants were asked a probe question regarding whether a particular item in the set was a member of a particular category (e.g., “Was the second item a fruit?”). Some items were used as priming for others in a hierarchical level (e.g., “guitar” and “violin”).	Main effect: low load minus rest; medium load minus rest; high load minus rest; primed items minus unprimed items in low load; primed items minus unprimed items in medium load; primed items minus unprimed items in high load Interaction: primed minus unprimed in all loads
Schaefer A, Braver TS, Reynolds JR, Burgess GC, Yarkoni T, Gray JR	2006	53	1.5 T	The participants first watched a film to increase emotional arousal or maintain it (control condition). The participants were then asked to respond in 1- and 3-back procedures for words (concrete nouns) and faces in 21 trials in each condition.	Main effect: 3-back minus1-back Interaction: 3-back minus 1-back in either emotional or control condition

Table 4. Continued.

Author	Year	Sample	Machine	Task description	Contrast
Spielberg JM, Miller GA, Engels AS, Herrington JD, Sutton BP, Banich MT, Heller W	2011	87	3.0 T	Participants answered three questionnaires to determine whether they presented personality traits that were closer to an approach temperament or avoidance temperament. A color-word Stroop test with 256 trials was then conducted to determine how different levels of temperament traits would be reflected in task performance.	Main effect: congruent words minus incongruent words; congruent words minus incongruent words in approach temperament; congruent minus incongruent words in avoidance temperament Interaction: congruent words minus incongruent words in avoidance minus approach temperaments
Stoodley CJ, Valera EM, Schmahmann JD	2012	8	3.0 T	Participants were asked to respond in 0- and 2-back procedures for letters in 16 trials in each condition.	Main effect: 2-back minus 0-back
Suchan B, Linnewerth B, Koster O, Daum I, Schmid G	2006	13	1.5 T	Participants were asked to respond in 0- and 2-back procedures for concrete nouns or pictures of these nouns that were presented in four different conditions: visual-visual (VV; only pictures were presented), auditory-auditory (AA; only words were spoken), auditory-visual (AV; the noun was first spoken and the target was the picture associated with this noun), and visual-auditory (VA; the opposite of the AV condition). Each condition had 30 trials.	Main effect: VV minus AA Interaction: VA minus AA
Vandewalle G, Gais S, Schabus M, Balteau E, Carrier J, Darsaud A, Sterpenich V, Albouy G, Dijk DJ, Maquet P	2007	18	3.0 T	An auditory 2-back design was established using nine phonologically different monosyllabic consonants. The experimental condition was the exposure of one eye of the participant to a green or blue light for 18 min before starting the 2-back experiment on two different days and in three different sessions during each day. The participants were randomly assigned to green or blue light on the first day.	Main effect: blue light exposure minus green light exposure Interaction: blue light minus green light in session 1 minus session 2; blue light minus green light in session 2 minus session 3
Woodward TS, Cairo TA, Ruff CC, Takane Y, Hunter MA, Ngan ET	2006	18	1.5 T	Strings of 2, 4, 6, or 8 letters were presented to the participants for 4 s(encoding phase). A maintenance phase then followed, varying from 3 to 5 s. The retrieval task consisted of answering “yes” or “no” regarding whether a target probe was present in the string of letters. The intertrial interval was 3 s.	Main effect: encoding minus rest, maintenance minus rest Interaction: encoding minus maintenance

Table 4. Continued.

4.2

ALE meta-analysis results

The results of the ALE meta-analysis considered the average activation (and average errors) in 30 phonological working memory studies (*n* =596). For the analyses, we categorized three types of stimuli: (1) tones (nonhuman sounds), (2) syllables (letters or phonemes without meaning),and (3) words (meaningful morphemes, nonwords, and phrases). Figure 6 shows activation related to tones (blue is peripheral and green is the center of activation), words (orange is peripheral and white is the center of activation), and syllables (red is peripheral and white is the center of activation) as the types of stimuli. Overlapping regions are depicted in yellow-red colors. Figure 7 depicts only overlapping regions of words>syllables.

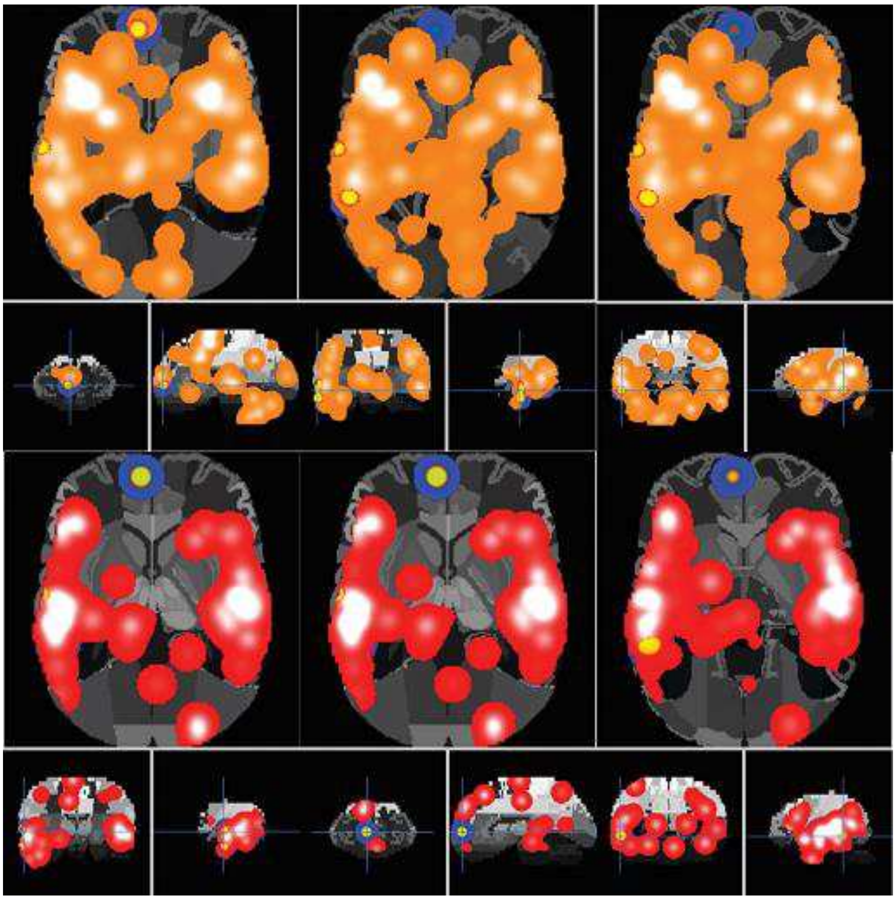

Fig. 6. Average activation of the participants (*n*=596) and standard deviation represented by types of stimuli.

The results in Figure6 show that important regions that are associated with working memory overlap while executing experimental tasks. With regard to tones and syllables, significant activation of the left prefrontal cortex is seen, going from the anterior to dorsolateral portions. Another notable aspect is the overlapping activation of both the auditory association cortex at the temporal lobe and supramarginal gyrus (part of Wernicke's area). Another interesting aspect is significant activation in parietal and premotor areas but only when the participants were executing tasks using syllables, which can explain why no overlap was observed in these regions between types of stimuli. The same phenomenon occurred when tones and words that overlapped but at a higher intensity. Almost the whole brain was activated in working memory tasks that used words or phrases as stimuli, but the overlapping regions were restricted to what was found with syllables>tones, with higher overlapping of the auditory association cortex. These results are discussed in more detail below.

Figure 7 shows only the overlapping activation of words>syllables. The results suggest double activation of the prefrontal cortex in both the anterior and dorsolateral portions of this region. They also appear to be separate, which likely is associated with the type of analyses that were conducted (i.e., using clusters to find centers of activation). Additionally, the bilateral medial frontal cortex was activated during tasks with words and syllables. Other regions of activation included the supramarginal gyrus (part of Wernicke's area), a small portion of the anterior intraparietal sulcus, and bilateral activation of the cingulate cortex (anterior insula). The pars opecularis (part of Broca's area) was also activated in working memory tasks using both types of stimuli.

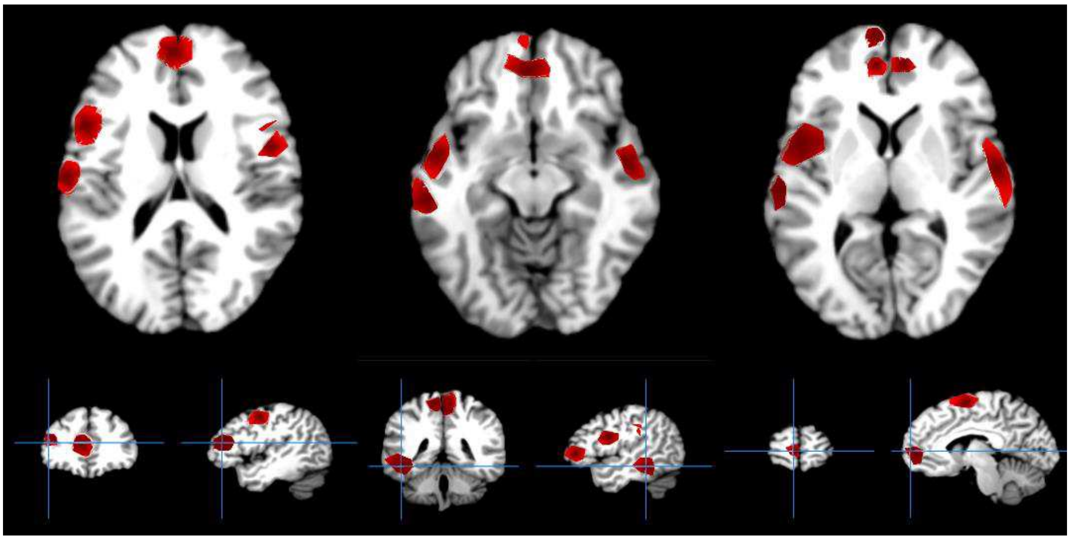

Fig. 7. Significantly overlapping regions using the contrastwords>syllables,excluding tones. The centers of activation were situated in Brodmann areas 6, 10, 40, 42, 44, and 46.

Using the ALE cluster method of contrast, we subtracted from the most widespread activation (involving words); the other activation likelihoods were used to generate the final results that are depicted in Figure 8. Contrast is represented by words>syllables>tones (*p*<0.001). The centers of activation were the left anterior prefrontal cortex (Brodmann area 10), left fusiform gyrus at the surface of the temporal lobe (Brodmann area 37), and left anterior transverse temporal gyrus at the surface of the temporal lobe (Brodmann area 42). These results are discussed in more detail below with regard to the function of these regions and the theoretical model they may support.

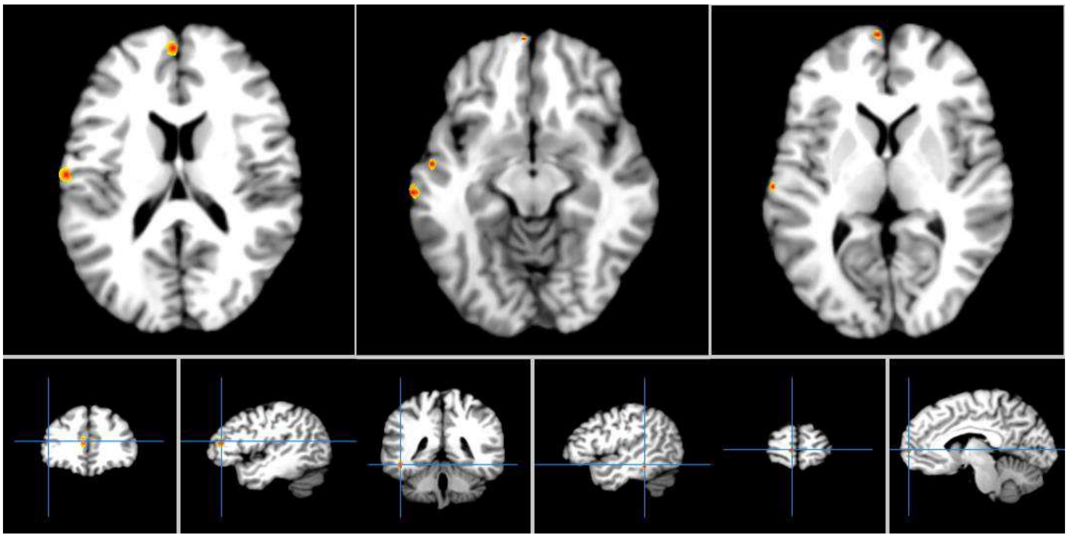

Fig. 8. Significantly overlapping regions using the contrast words>syllables>tones. The centers of activation were situated in Brodmann areas 10, 37, and 42.

5

Discussion

The results showed several important findings. The present discussion attempts to pinpoint the most important findings based on the data that were gathered. The major result of this entire work was confirmation that the prefrontal cortex is a center of neural activity during working memory tasks. Although this result was expected, the most important region of the prefrontal cortex was its left anterior portion. Brodmann area 10, more specifically the fronto-polar prefrontal cortex, is responsible for controlled attention and task switching. The prefrontal cortex has been suggested to account for the central executive (D'Esposito & Postle, 2015). The results of the present study also suggest core activation of the anterior portion of the PFC. Thus, attentional control and task switching appear to be dimensions of the central executive as suggested by Baddeley (2012).

Dove, Pollman, Shubert, Wiggins, and von Caron (2000) performed a task switching experiment and found that the fronto-polar prefrontal cortex, combined with the anterior insula and left intraparietal sulcus, was activated when the participants tried to keep in mind one task and execute another. In another experiment, Braver and Bongiolatti (2002) tested the involvement of the entire prefrontal cortex in working memory tasks. They found a triple dissociation of function within prefrontal cortex regions, including the anterior, dorsolateral, and orbitofrontal portions, and further indicated that the anterior prefrontal cortex is selectively engaged by the requirement to monitor and integrate subgoals during working memory tasks. Koechlin, Basso, Pietrini, Panzer, and Grafman (1999) assigned secondary tasks to participants at the same time they executed a working memory task. They found that the fronto-polar prefrontal cortex selectively mediated the ability to hold subgoals in mind while exploring and processing secondary goals, a process that is generally required in planning and reasoning. Simple working memory tasks are believed to not require planning or any kind of thinking. In fact, Collette and Linden (2002) reviewed neuroimaging studies in an attempt to find a center for the central executive. They found that controlled attention and supervisory systems are actually very widespread in different neural networks, mainly in frontal and parietal regions. Thus, our results that showed activation of the anterior prefrontal cortex may be unrelated to the central executive because the participants were trying to think of strategies and alternatives to perform well on the diverse tasks.

We compared the results of overlapping activation between words>syllables and the three types of stimuli together. When the participants had to use an abstract phonological code, such as syllable phonemes and word semantics, they tended to use similar regions. Rottschy et al. (2012) reported similar results of an ALE meta-analysis using verbal, non-verbal, and visual working memory tasks. The only difference between the present results and the results of Rottschy et al. (2012) was significant activation of the anterior prefrontal cortex.

Another major aspect of the present results is the unexpected activation of the left fusiform nucleus. Lesions of this region can lead to color-phoneme synesthesia and visual hallucinations. However, the activated portion of the fusiform nucleus in the present study also corresponds to the visual word form area. The visual word form area is an hypothesized functional region of the fusiform gyrus, and there is concrete evidence of a separation within this region. It seems to be related to identifying words from lower-level shape images prior to associations with phonology or semantics (i.e., shape-related identification; Dehaene & Cohen, 2011). According to these authors, the written language is relatively new in human evolution. Thus, this region unlikely developed as a result of natural selection related to word recognition. Nonetheless, the visual word form area of the fusiform gyrus may be specialized for certain types of shapes that occur naturally in the environment and are likely to resemble human handwriting. fMRI studies usually use written instructions and written stimuli during the tasks which can explain this area activation. Another possibility is participants may attempt to imagine a shape for the tones and sounds that reminded them of a letter to facilitate the execution of tonal working memory tasks (Baddeley, 2003a). Further studies are needed to test these possibilities.

Another overlapping region was Brodmann area 42 (the left anterior transverse temporal gyrus at the surface of the temporal lobe). This region functionally corresponds to the primary auditory association cortex, which executes two main functions in the brain: processing sensorial auditory information and creating associations between sounds and auditory memory (Petkov et al., 2004; Weinberger, 2007). One could argue that memory is spread throughout the entire brain, but evidence indicates a role for the auditory cortex as the first storage site for sound information. Primate studies showed that the representation of known sounds, such as a bird singing or a known song, is associated with activation of the primary auditory cortex together with the hippocampus, medial geniculate complex, and other parts of the thalamus (Kaas, Hacket, & Tramo, 1999). In humans, the anterior transverse temporal gyrus is linked to the recognition of familiar sounds (Petkov et al., 2004) and identification of the human voice when voice-like sounds arrive in the cortex (Weinberger, 2007). Interestingly, primary visual areas are also responsible for storing visuospatial information (Mance & Vogel, 2013). The activation of this region is consistent with the models of both Baddeley, Allen, and Hitch (2011) and Cowan (1999, 2010). The results suggest the existence of sensory memory that is located within the neural circuit that is formed by the primary auditory cortex, which is responsible for storing this information until it is encoded. After encoding, this region stores represented information in the the same way the activated portion of memory allows information to be manipulated. Petkov et al. (2004) suggested that the primary auditory association cortex plays an important role in auditory attention. He argued that automatic attention should be activated in the same region where it is stored for faster responses to the environment. Evidence suggests that individuals with any kind of lesion of the primary auditory cortex exhibit impairments in automatic auditory attention, whereas voluntary auditory attention and visual attention, regardless of modality, remain intact. Therefore, auditory inhibition could be the opposite of automatic attention, which would go against Diamond’s (2013) claim of an independent special feature of executive functions called inhibitory control.

Our main results raise two different hypothesis: (1) Cowan’s (1999) theoretical model makes more sense than the others due to significant differences between types of stimulus and (2) the complexity of tone tasks requires planning and reasoning for execution, whereas syllable and word tasks require the further integration of information.

Both hypotheses may likely be true. Cowan suggested that encoding is the ability of the human mind to create a code to mentally represent environmental information (Cowan, 2010), and codes can be divided into two categories: abstract and sensorial. If we categorize our results based on this classification, then tones would probably require sensorial codes to be represented, whereas syllables and words would require abstract codes, such as phonological codes or semantic codes, to be mentally represented. Our results suggest minor overlap between tones and other types of stimuli, whereas syllables and words show significantly more regions of overlap. Becauseof the different types of encoding, the neural network of phonological working memory can be divided into abstract and sensorial codes.

Humans tend to use such strategies as naming and chunking to perform better in working memory tasks (Cowan, 1999; Engle, Kane, & Tuholski, 1999). In olfactory tasks, the performance of participants in a 2-back span task was 20% higher when participants were able to name the odor when compared to unnamed odors (Jönsson, Moller, & Olsson, 2011). Whenever we deal with a new task, we tend to constantly plan and try to execute the task accordingly. The familiarity of sounds may lead participants to try to name or chunk similar sounds to facilitate encoding. We did not see activation in Broca's or Wernicke's areas. These areas are associated with language, and sounds do not seem to require any kind of spoken language to be stored. While the participants were executing auditory tasks with merely sensorial stimuli, they may have attempted to plan and actively execute the task in such a way that they could perform better than chance while not consciously being aware that they were doing this. If so, then Diamond's (2013) proposition of the inseparability of higher cognitive functions even during simpler tasks appears to be true. Diamond suggested that executive functions indeed have pure measures, but they tend to work simultaneously. Activation of the fronto-polar prefrontal cortex may be evidence that participants attempt to use higher cognitive functions to deal with simpler working memory tasks.

The main results of the present study appear to support Cowan's (1999, 2010) theoretical model, with evidence of the existence of sensory memory and significant differences between the neural bases of different types of encoding within the same modality (i.e., phonological working memory). Nonetheless, we did not find any evidence of separation between voluntary and automatic attention, despite some suggestions of such in the literature (e.g., Petkov et al., 2004;Weinberger, 2007). We cannot assume that mere activation of the primary auditory cortex is attributable to both attention and memory. Additionally, no activation of regions that are responsible for voluntary attention was seen, which does not corroborate Cowan's model. The strongest claim in favor of Cowan's model is the difference between types of stimuli and thus the difference between encoding processes.

Evidence of the model of Baddeley, Allen, and Hitch (2011) was almost nonexistent. First, the overlapping regions were minor, suggesting significant differences between core phonological working memory neural networks. Second, no evidence was found in the literature regarding the role of the anterior prefrontal cortex as the central executive. We cannot say that fronto-polar prefrontal cortex activation is caused by attentional control. The only support for this model is activation of the primary auditory association cortex, which is likely attributable to auditory storage. However, if we look at words>syllables contrast (while excluding tones from the analysis), then we can see the core network of working memory as Baddeley (2000) suggested. One possibility is that other neuroimaging meta-analyses neglected tone-and sound-related working memory tasks because they do not corroborate the model of Baddeley, Allen, and Hitch (2011). For example, Rottcshy et al. (2012) reported results from both visual and auditory working memory imaging studies. They presented 113 articles, but only two of these used tones. They also did not utilize any algorithm to correct possible bias. Our results of the words>syllables analysis were very similar to those reported by Rottcshy et al. (2012). However, when we include tonal working memory using the new ALE algorithm (Eickhoff et al., 2009), which attempts to reduce bias, we found completely different results. Despite the results of the present study, Baddeley's model appears to be the most adequate for explaining behavioral data (Allen, Baddeley, &Hitch, 2014).

Working memory is argued to be one of the most important cognitive functions of humans. It serves as a foundation for cognitive flexibility, language, writing, logical thinking, abstract thinking, planning, and learning (Diamond, 2013). The present results suggest that working memory is indeed a complex cognitive function that is based on the architecture of our contemporary brain. The most important conclusion that we can make is that the prefrontal cortex is responsible for the central executive as suggested in the literature, but there are significant differences between semantic, phonological, and auditory encoding in the brain that can be explained by different storage sites, depending on the code type. These storage sites appear to be both sensory- and code-dependent. One interesting hypothesis is that primary cortices can also account for long-term memory, as suggested by Cowan (2010) and D'Esposito and Postle (2015).

5.1

Limitations and future directions

The present study has limitations but also leads to future directions in the study of working memory. Two main limitations should be highlighted. First, although Cowan's framework explains a little better the found results, working memory is still a psychological construct and theoretical model that aims to explain behavioral performance. No evidence suggests that working memory is a scientific law, such as gravity or relativity. Different tasks tap into different neural networks during working memory tasks. All fMRI meta-analyses seek to discover intersections between regions of activation in working memory tasks, but the neural networks are clearly distinct and strongly rely on the type of task. Thus, it is possible that none of these theoretical models can fully explain or prove the existence of working memory.

Second, the methodology of the present study has limitations. The ALE method of meta-analysis utilizes only significant activation results from other studies. This means that possible differences in voxels that are not significantly activated are ignored. For example, if a voxel does not present a significant difference in particular studies, but instead only presents marginal significance, an author who performs a meta-analysis may reanalyze those nonsignificant results such that statistical significance becomes evident. In ALE meta-analyses, nonsignificant results are not considered because the database consists only of articles that present significant differences in contrast. Thus, the present study was limited by relying solely on significant results.

Future studies can fill the gaps that remain. One interesting line of investigation would be to perform meta-analyses that include other sensorial inputs, such as visual, olfactory, and tactile. fMRI meta-analyses can also utilize raw data by asking the authors of previous studies to share their data. This would allow previously nonsignificant results to be further analyzed. Another frontier of working memory studies would be to develop theoretical and computational models to explain neuroscientific results rather than solely behavioral results.

6

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ANNEX I
Filgueiras, Charchat-Fichman, & Landeira-Fernandez (2013)

CONEXÕES PSI

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WORKING MEMORY IN ALZHEIMER DISEASE: A 5-YEAR SYSTEMATIC REVIEW OF EMPIRICAL EVIDENCES FROM BADDELEY'S WORKING MEMORY MODEL

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ABSTRACT

The Alzheimer's disease is the most common of the neurogenerative conditions associated with dementia. It is known as a pathological frame that comes with several impairments in cognitive and psychological processes. This study aimed to understand the relationship between Alzheimer's disease and Working Memory impairments. We adopted Baddeley's Working Memory Model to systematically review if impairments in the subcomponents of this theoretical model – phonological loop, visual sketchpad, episodic buffer and central executive – follow distinct or similar paths. The systematic review consulted Medline, Psycinfo and Scielo databases. From 329 articles, only 11 were accepted by the established criteria. Results suggested that episodic buffer and central executive, respectively, decline with AD severity. Phonological loop and visual sketchpad are the last of the Baddeley's Working Memory Model subcomponents impaired.

Kewords: Alzheimer Disease. Working Memory. Dementia. Systematic Review.

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1 INTRODUCTION

The Alzheimer's disease (AD) is a neurodegenerative condition related to abnormal aging from the dementia family. The main characteristic of the AD is the appearance of neurofibrillary tangles and plaques interfering normal neuronal action potential in the brain (LAMBERT; KINSLEY, 2006). Several researchers dedicate their careers to understand this pathology since its impacts are relevant in all aging people worldwide. The prevalence of this disease presents world rates of 0.9%, 4.2%, and 14.7% at ages 65, 75, and 85 years, respectively. In the future, giving the increase rating of AD prevalence, it is expected to have almost 106.2 million people with AD in the year 2050 (BROOKMEYER *et al.*, 2007).

Clinical evidence of memory loss of recent events in early stages of AD is the most common symptom and brings consequences to daily activities. In advanced stages, the AD patient can show impairments in other cognitive functions such as language, executive functioning, visuospatial tasks and other long-term memory losses (TEIXEIRA; CARAMELLI, 2008).

Regarding the working memory, it presents a decrease of functioning in normal aging people (YOKOTA *et al.*, 2001). Nonetheless, several evidences also point out impairments in working memory in AD when compared to normal aging controls (BADDELEY *et al.*, 2001). Despite of those findings, if this working memory impairment in AD is general or if there is a specific decrease in one of the WM subcomponent's functioning, the scientific literature still to discover. In this study, our goal is to review the last 5 years of experimental researches using AD and normal control to compare groups in working memory tasks. We will try to have a glimpse in which of Baddeley's working memory model subcomponents resides the impairment or if the loss is on overall WM.

2 THE WORKING MEMORY

The working memory (WM) is one of the most studied psychological constructs for the past five years. For example, in PubMed, the term "working memory" was used as keyword in 1,140 studies produced in 2008 against 1,843 studies published until December 2012 – an increment in academic production of 61,7%. More and more attention have been given by the scientific literature to WM since 1974 when A. Baddeley and G. Hicth proposed a model to explain the ability of retain information for a short period of time and process this novel information giving a satisfactory answer. This system design allowed researchers to explain several phenomenons associated to tasks such as learning, understanding and reasoning (BADDELEY; HITCH, 1974; BADDELEY, 1998). From this framework is possible to understand the empirical data using different methodological approaches – confirmatory factor analysis (CONTI-RAMSDEN; CRUTCHLEY; BOTTING, 1997; CONWAY *et al.*, 2002; ALLOWAY *et al.*, 2004), clinical evidences (BISHOP; ROSENBLOOM, 1987; ARCHIBALD, 2006), and neuroimaging (SMITH; JONIDES, 1997; JONIDES *et al.*, 1993).

The concept of a system of limited attentional capacity that supervises the processing of information by few short-term storage systems is well accepted in the literature (BADDELEY, 2003). However, there are several discrepancies between the concepts of WM. From one perspective, Baddeley (1998, 2000, 2003) assumed that the WM is an independent system associated to the long-term memory (LTM) by one of its subcomponents. In the other hand, Cowan (1995) described the WM under an integrative framework proposing that it is one of several systems serving the LTM. Baddeley's WM model appears to have more solid evidence due to separation of LTM and short-term storage in different dimensions from factor analysis studies (STOPFORD *et al.*, 2007; MORRA; CAMBA, 2009). Nonetheless, there are no evidence to support that there is no relation between WM and LTM. Baddeley (2003) reminds that WM has an intimate relation to long-term memory since it organizes information in a shape that the human brain can understand.The episodic buffer, one of WM's subcomponents,links the WM to long-term memory to bind together information and build integrated episodes – allowing the interface between WM and LTM (BADDELEY, 2003).

Baddeley's WM model is divided by 4 subcomponents in a hierarchical organization: the central executive, phonological loop, visual sketchpad and the episodic buffer. According to Archibald (2006), the phonological loop and the visual sketchpad are short-term storage systems more related to the historical notion of short-term memory as conceptualized by Miller (1956, 2003).

The central executive is a supervisory system divided in two attentional processes: the control of the behavior by schemas previously learned and an attentional voluntary control when the schema does not suffice (NORMAN; SHALLICE, 1986; BADDELEY, 2003). This supervisory attentional system permits the WM to have access to the LTM by using three aspects of attention: dividing, switching and sustaining the attentional control (BADDELEY, 1996).

Finally, the episodic buffer was a recent proposition by Baddeley (2000, 2003) to solve several problems of his WM model. It is a limited-capacity storage and retrieval system linked to the LTM used to hold episodes whereby information is integratedacross space and potentially extended across time. However, the episodic buffer is assumed to be temporary and not a part of the LTM since patients with severely impaired LTM still have the ability to retain and rehearse responses for novel demands (BADDELEY, 2000).

3 ALZHEIMER'S DISEASE AND MEMORY IMPAIRMENT

Memory impairment of recent events happens in early stages of AD. It is followed by impairments in language, executive functions, visuospatial tasks and other long-term memory losses (TEIXEIRA; CARAMELLI, 2008). Daily activities such as remembering where the patient left the keys or remembering to throw away the kitchen's garbage are impaired in AD and it brings consequences in the care and well being of the patient and his familiars. The advanced stages of AD, however, are worse since independence of the patient is severely compromised.These deficits are clearly associated to the WM and can be articulated with the notion of central executive as proposed by Baddeley (2003). The central executive's first responsibility is to organize the information in schemas stored in the LTM. Once a daily activity is structured by a schema, such as throw away the garbage, if the central executive presents impairment, consequently, the activity will suffer. There is several evidence of this hypothesis.

Studies with AD patients were conductedby Baddeleyto understand the central executive and its associations with LTM (BADDELEY *et al.*, 1991; BADDELEY *et al.*, 2001, BADDELEY, 2003). The impairment of the WM, according to these studies, is strict to dividing and switching attention. Yokota *et al.* (2001) also find evidence of hierarchical and gradual decline of memory loss. According to their results, normal aging people memory functioning pertaining to verbal WM performance declined first. Visual span – WM's visual sketchpad – declined next; overall knowledge – related to LTM – declined after and was followed bymemoryof ordinary objects – LTM. This resultsuggests that the deterioration of memoryfunctions is probably affected differently by progressive risk of AD.

Nonetheless, impairments in global WM should not be discarded. Cairn *et al.* (2009) pointed out that episodic LTM declined before WM in an AD patientfrom a case study. In this study we will adopt the perspective of Alan Baddeley (2003) to understand the relationship between AD and possible decline on the WM activity. The main goal of this paper is to understand if, in the last five years, there is novel empirical evidence that points to impairments in one specific subcomponent of Baddeley's WM model or if it is a global decrement.

4 METHOD

The method used in this study was a systematic review conducted to gather information about empirical data regarding working memory in Alzheimer disease.

4.1 Literature Search

In order to identify publications on working memory in Alzheimer Disease (AD) patients, a systematic search was performed in Medline, Psycinfo and Scielo databases. We searched articles from the last 5 years published prior November 2012. The search was limited to four languages: English, Portuguese, Spanish and French – languages of authors' acquaintance. Four key terms were used in the various databases: Working Memory, Phonological Loop, Visual Sketchpad, Episodic Buffer and Alzheimer. For all databases, a specific combination of the key features was made to select relevant records:

a) working memory;
b) phonological loop;
c) visual sketchpad;
d) episodic buffer; e
e) alzheimer.

They were combined as follow: (a or b or c or d) and e.

4.2 Inclusion and exclusion criteria

The search yielder a large set of publications which were further limited using the article title, abstract and a number of in- and exclusion criteria which are below detailed. We only included participants with age ranging from 65-or more years old. Studies using animal models of AD were excluded. Case studies and reviews of any kind were also excluded. Studies containing both AD and normal aging control groups were included. Eventually, some study included groups other than the control group, however the conclusions regarding these other groups were also considered in this study – for example, Franceschi *et al.* (2011) reported the results of AD and fronto-temporal dementia (FTD) groups for differential diagnose criteria.

In the regards of Working Memory, we only included studies using the model proposed in Alan Baddeley's (1998, 2000, 2003) studies. This decision is justified by the objective of this study. We intended to understand if there are novel contribution regarding impairments in the different subcomponents of Baddeley's working memory model – central executive, phonological loop, visual sketchpad and episodic buffer – and if these impairments follow distinct paths between AD and normal aging.

5 RESULTS AND DISCUSSION

Initial search – already applying the 5-years filter – found 175 articles in Medline database, 149 papers in Psycinfo and 5 studies in Scielo, a total of 329 articles. There was no article published in Portuguese, Spanish or French within the established criteria. After reading the abstracts, we excluded non-controlled trial studies, reviews of any kind, and experimental studies with participants younger than 65 years of age in the AD group and without AD *plus* a control group with healthy older adults. These limitations reduced the numbers of articles to: 9 in Medline, 5 in Psycinfo – 3 of them already found in Medline – and 3 in Scielo. Finally, we read the articles looking for the WM adopted model. Only 7 articles from Medline, 1 article from Psycinfo and 3 articles from Scielo – totalizing 11 studies – referred to Baddeley's WM model as theirs perspective. Table 1 depicts authors, year of the publication, the tasks involved in WM measurement, the experimental and control groups with the sample size, a brief description of the results and the possible conclusions based on the authors discussions.

According to ours study aim, we analyzed separately evidence for each Baddeley's WM model subcomponents (BADDELEY, 1996, 1998, 2000, 2003). We began with the short-term memory components associated with temporary storage – phonological loop and visual sketchpad. Then, we studied the effects of the central executive and finally the episodic buffer.

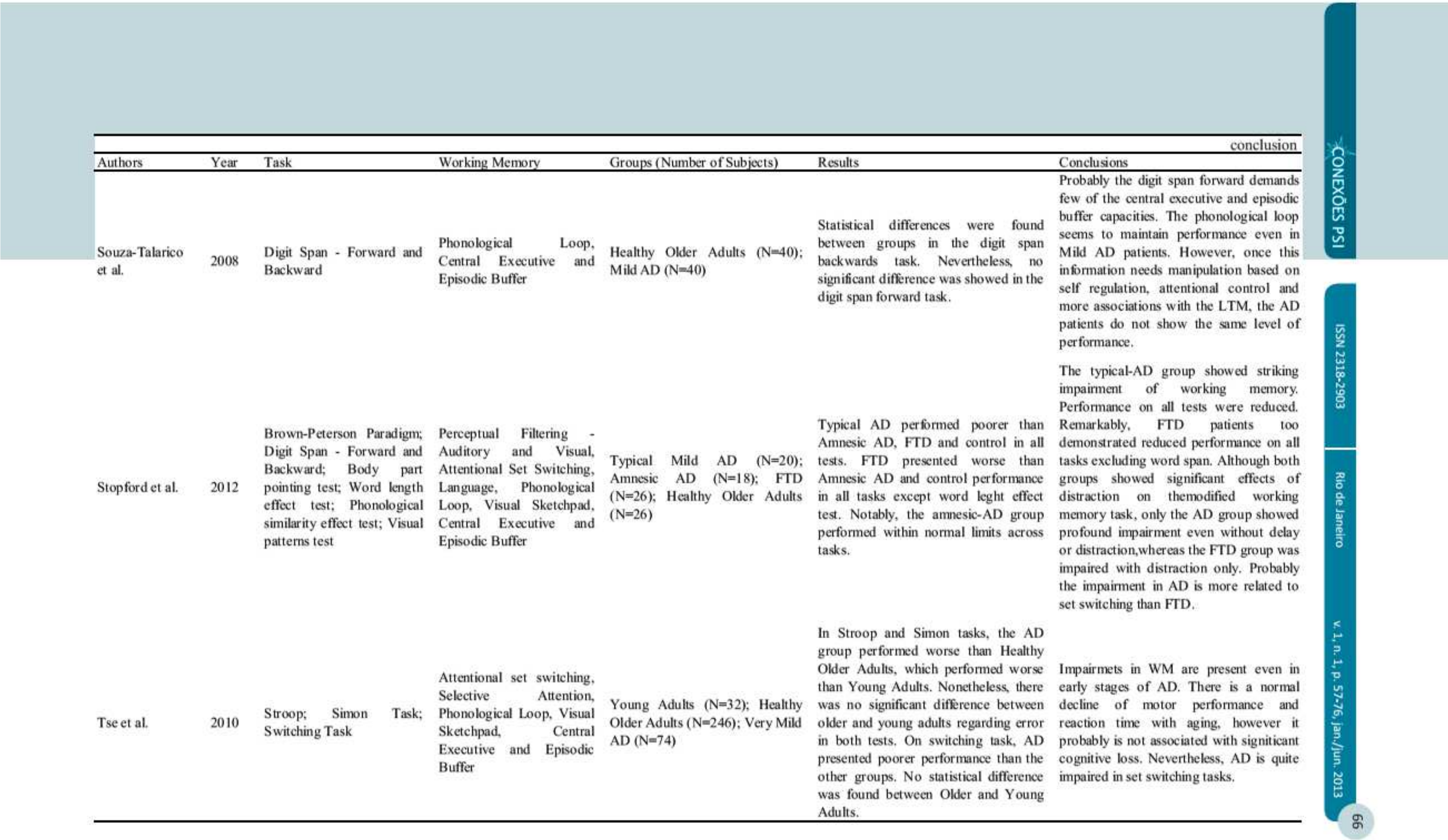
Table 1 - Authos in alphabetical order, year of publication, WM-related task, subcomponents assessed, groups division, brief results and conclusions.

continues

Authors	Year	Task	Working Memory	Groups (Number of Subjects)	Results	Conclusions
Castel, Balota & McCabe	2009	Computation and Reading Complex Span	Phonological Loop, Central Executive and Episodic Buffer	Younger Adults (N=35); Healthy Older Adults (N=109); Very Mild AD (N=41); Mild AD (N=13)	All groups differ from each other in recall performance - phonological loop, however the selective index that measures the central executive and episodic buffer capacities showed no significant differences between younger and older healthy adults, and differences among all other groups.	AD leads to impairments in strategic control at encoding and directed remembering.
de Paula et al.	2012	Token Test; Semantic Verbal Fluency; Forward Digit Span; Corsi Blocks	Phonological Loop, Visual Sketchpad, Central Executive and Episodic Buffer, Language	Healthy Older Adults (N=80); Mild AD (N=80)	Both groups presented significant differences among all tasks.	Probably the language impairment in AD patients detected by the Token Test is associated with both verbal and non-verbal WM impairments.
Fernandez-Duque & Black	2008	Reaction Time Task; Trail Making; Digit Span; Rey-Osterrieth; Semantic and Verbal Fluency; Raven's Progressive Matrices (RPM)	Selective Attention, Perceptual Filtering, Attentional Set Switching, Language, Phonological Loop, Visual Sketchpad, Central Executive and Episodic Buffer	Younger Adults (N=32); Healthy Older Adults (N=31); Probable AD (N=31)	No evidence of impaired perceptual filtering probable AD. Early DAT patients did presented significant differences on tasks involved in attentional set switching consistent with an inability to maintain the goals of the task (mental set).	The impairment of WM in AD aperantly is associated with the central executive. Impairment is shown in the supervisory system previously than other neuropsychological aspects.
Gyurak et al.	2009	Stroop; Trail Making; Verbal Fluency; Digit and Spatial Span	Phonological Loop, Visual Sketchpad, Central Executive, Episodic Buffer, Executive Functions - Language, Attentional Set Switching, Inhibitory Control	Frontotemporal Lobar Degeneration - FTLD (N=24); Probable AD (N=7); Healthy Older Adults (N=17)	No statistical difference was found between the three groups in both WM and Attentional Set Switching tasks. In the Inhibitory Control task - Stroop - AD groups reults were statistically worse than the other groups. On Verbal Fluency, Control had significant higher mean scores than the other two groups.	Inhibitory Control and Verbal Fluency are probably a key features associated with monitoring, controling and regulating own emotions when proceeding cognitive tasks.
Pereira et al.	2012	Philadelphia Brief Assessment of Cognition	Phonological Loop, Visual Sketchpad, Central Executive, Episodic Buffer, Language, Episodic LTM and Behavior	Younger Adults (N=100); Healthy Older Adults (N=100); Probable AD (N=30)	No statistical difference was found between the three groups in Language and Behavior tasks. However, AD showed significant lower mean scores in WM and Episodic LTM .	Patients with diagnosed AD from clinical assessment present poor performances in WM and Episodic LTM. Specifically the visuospatial tasks provided evidence that WM in AD is compromised as a whole.

continuation

Authors	Year	Task	Working Memory	Groups (Number of Subjects)	Results	Conclusions
Pietrzak, Maruff & Snyder	2009	Groton Maze Learning Test - GMLT	Phonological Loop, Visual Sketchpad, Central Executive and Episodic Buffer	Healthy Older Adults (N=15); Mild AD (N=14)	The performance of the healthy older adults groups showed better performance than the Mild AD group. Also, the drug donepezil provided improvement on the performance of both groups when compared to baseline and placebo.	Donepezil is a good assett to AD treatment improving performance on cognitive tasks. Global WM in AD is impaired when compared to healthy older adults on maze tasks.
Sebastián & Hernández-Gil	2012	Direct Digit Span	Phonological Loop	Healthy Older Adults (N=25); Frontotemporal Dementia - FTD (N=9); Mild AD (N=25)	No significant differences was found between groups.	The direct digit span is a task associated with short-term memory and uses the phonological loop as a temporary storage of the information. This type of task relies little on the central executive and the episodic buffer allowing the AD patients to perform as good as any healthy older adult. Direct spans do not require full access to LTM or a constant attentional control, what can explain this data.
Sebastián & Hernández-Gil	2010	Digit Span; B-P task; Tracking task; Dual task (Tracking + Digit Span)	Divided Attention, Attentional Set Switching, Phonological Loop, Visual Sketchpad, Central Executive and Episodic Buffer	Healthy Older Adults (N=25); Frontotemporal Dementia - FTD (N=9); Mild AD (N=25)	In digit span forward task, no significant difference was found. Errors in B-P task was statistically similar between FTD and AD groups, however the control group presented better performance. Nonetheless, regarding perseveration in the B-P task, AD performed significantly poorer than FTD and control where FTD group also had worse results than healthy older adults. Finally, on Tracking Task (single task) and the Dual task, AD and FTD presented worse results than the control group, but no difference between them.	There are several alterations on executive functioning in both AD and FTD due to neurodegeneration. However, AD cognitive impariment is probably more associated with attentional set switching as AD peerseverated more than FTD. The neural circuitry involved in both pathologies are probably similar with just few differences.



conclusion

Authors	Year	Task	Working Memory	Groups (Number of Subjects)	Results	Conclusions
Souza-Talarico et al.	2008	Digit Span - Forward and Backward	Phonological Loop, Central Executive and Episodic Buffer	Healthy Older Adults (N=40); Mild AD (N=40)	Statistical differences were found between groups in the digit span backwards task. Nevertheless, no significant difference was showed in the digit span forward task.	Probably the digit span forward demands few of the central executive and episodic buffer capacities. The phonological loop seems to maintain performance even in Mild AD patients. However, once this information needs manipulation based on self regulation, attentional control and more associations with the LTM, the AD patients do not show the same level of performance.
Stopford et al.	2012	Brown-Peterson Paradigm; Digit Span - Forward and Backward; Body part pointing test; Word length effect test; Phonological similarity effect test; Visual patterns test	Perceptual Filtering - Auditory and Visual, Attentional Set Switching, Language, Phonological Loop, Visual Sketchpad, Central Executive and Episodic Buffer	Typical Mild AD (N=20); Amnesic AD (N=18); FTD (N=26); Healthy Older Adults (N=26)	Typical AD performed poorer than Amnesic AD, FTD and control in all tests. FTD presented worse than Amnesic AD and control performance in all tasks except word leght effect test. Notably, the amnesic-AD group performed within normal limits across tasks.	The typical-AD group showed striking impairment of working memory. Performance on all tests were reduced. Remarkably, FTD patients too demonstrated reduced performance on all tasks excluding word span. Although both groups showed significant effects of distraction on themodified working memory task, only the AD group showed profound impairment even without delay or distraction,whereas the FTD group was impaired with distraction only. Probably the impairment in AD is more related to set switching than FTD.
Tse et al.	2010	Stroop; Simon Task; Switching Task	Attentional set switching, Selective Attention, Phonological Loop, Visual Sketchpad, Central Executive and Episodic Buffer	Young Adults (N=32); Healthy Older Adults (N=246); Very Mild AD (N=74)	In Stroop and Simon tasks, the AD group performed worse than Healthy Older Adults, which performed worse than Young Adults. Nonetheless, there was no significant difference between older and young adults regarding error in both tests. On switching task, AD presented poorer performance than the other groups. No statistical difference was found between Older and Young Adults.	Impairmets in WM are present even in early stages of AD. There is a normal decline of motor performance and reaction time with aging, however it probably is not associated with signiticant cognitive loss. Nevertheless, AD is quite impaired in set switching tasks.

5.1 The Phonological Loop

Almost all studies used the phonological loop somehow. Archibald (2006) depicts that even visual tasks can be transformed in verbal tasks if the subject gives names to the stimuli. For example, a color span can easily switch to an oral span since the person recalls the nameof the color combined with the temporary memory of the colors tone.

Verbal span tasks in the forward form are considered a good index for the phonological loop since it does not require much of the episodic buffer and central executive's capacity (ARCHIBALD, 2006). Overall, there is little evidence that early stages of AD compromise short-term storages – specifically the phonological loop. In very mild and mild groups of AD, when compared to healthy older adults, there were no significant differences in quantity of spans on the studies of Fernandez-Duque & Black (2008), Gyurak *et al.* (2009), Sebástian & Henándes-Gil (2010, 2012) and Souza-Talarico *et al.* (2008).

However, the evidence presented by De Paula *et al.* (2012) and Stopford *et al.* (2012) demonstrated significant differences between AD and control group in similar tasks. Regarding this contradiction in the literature, we can hypnotize two aspects: the severity of AD and the assessment instrument. Huntley and Howard (2009) depicted the relevance of AD severity in the phonological loop impairment. There are several discrepancies about the classification of Mild AD. Nevertheless, the use of the Mini-Mental State Exam (MMSE) is a reference to consider severityof AD. De Paula *et al.* (2012) used the NINCDS-ADRDA criteria. Duboiset *et al.* (2007) discussed this criteria based on novel empirical evidence using PET and *f*MRI techniques. The revision of this criterion would probably interfere in De Paula's study regarding AD severity what may influence in the results.

Stopford *et al.* (2012) divided AD in two distinct groups, what is not usual on the selected studies. Separating the participants allowed overlooking that Mild AD with worse performance in phonological loop tasks than Amnesic AD. This result is probably due to little impairment in storage and more demand of the central executive. This hyphotesis works with Huntley and Howard's perspective in which AD starts to present impairment initially in divide attention and in attentional set switching – processes of the central executive (HUNTLEY; HOWARD, 2009).

5.2 Visual Sketchpad

As Baddeley (2003) depicted, there are rare tasks involved in pure assessment of the visual sketchpad. The most used measure is the Corsi Blocks task. Only De Paula (2012) used this test in our review. We already saw that this study's results vary from the others regarding short-term storage systems and in this particular case it is not different. We can believe that visual sketchpad follow similar path than the phonological loop, however within the last 5-year period, it is not possible to affirm any evidence either way.

5.3 The Central Executive

All studies presented differences between performances of tasks involving the central executive. Baddeley (2003) and Baddeley *et al.* (1991, 2001) already showed that dividing attention and retrieving learned schemas are difficult processes in very mild and mild AD. Huntley and Howard (2009), Lambert and Kinsley (2006) and Teixeira and Caramelli (2008) remembers that AD is associated with impairments of the brain in metabolizing acetylcholine in frontal lobe regions. Desimore and Duncan (1995) suggested the importance of cholinergic neurotransmission on attentional processes – mainly selective and sustaining attention.

Self monitoring and self regulation, aspects of pivotal importance in the central executive system are clearly impaired in all evidence that we collected in this review. On attentional set switching tasks, the AD patients presented worse performance than controls (SEBÁSTIAN; HERNÁNDES-GIL, 2012; STOPFORD *et al.*, 2012; TSE *et al.*, 2010,). Pietrzak, Maruff and Snyder (2009) showed that donezepil, an inhibitor of cholinesterase, facilitate the acetylcholine concentration extracellular and improved performance of AD patients in complex WM tasks. This increase is probably due to better attentional system.

5.4 The Episodic Buffer

Finally, the episodic buffer is a temporary storage responsible for the manipulation of the information. It is the main filter of novel memories (BADDELEY, 2000, 2003). The episodic buffer impairment is associated with what probably is considered the first symptom of AD: loss of memory of recent events. To consolidate a schema or to organize information to be accessed in the LTM, the episodic buffer constitutes the more important asset to Baddeley's WM model (ARCHIBALD, 2006).

All articles demonstrated that the episodic buffer is impaired (DE PAULA *et al.*, 2012; FERNANDEZ-DUQUE; BLACK, 2008; GYURAK *et al.*, 2009; Pereira *et al.*, 2012; PIETRZAK; MARUFF; SNYDER, 2009; SEBÁSTIAN; HERNÁNDES-GIL, 2010, 2012; SOUZA-TALARICO *et al.*, 2008, STOPFORD *et al.*, 2012), even in early stages of AD (TSE *et al.*, 2010).

Despite of also being impaired, factor analysis studies show that episodic buffer relies more in manipulation of the information and less in dividing attention or set switching (STOPFORD *et al.*, 2007; MORRA; CAMBA, 2009). Our hypothesis is that the episodic buffer is more associated with LTM and the central executive refers to the supervisory system responsible to allow cognitive processes not particularly with the episodic buffer itself, but also with the other subcomponents. In this case, if this hypothesis is correct, probably the first impairment of the Baddeley's WM model subcomponents is the episodic buffer, even before the central executive.

6 CONCLUSION

The WM present impairments in early stages of AD, however, due to the empirical findings in this review, the decline of the WM is first associated with decrement of the episodic buffer linking capacity with the LTM. The Central Executive appears to suffer in parallel since its functions decline regarding attentional set switching. Nevertheless, it decreases a little after the episodic buffer, since the short-term storages rely few, but significantly in the central executive and its impairments come last. Visual sketchpad and phonological loop decline after the other processes. This evidence suggests that subcomponents of Baddeley's WM model follow distinct paths in the progression of its decrements, nonetheless all are impaired in advanced stages of AD as well as other cognitive processes such as language and perception.

CONEXÕES PSI
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MEMÓRIA DE TRABALHO NA DOENÇA DE ALZHEIMER: UMA REVISÃO SISTEMÁTICA DOS ÚLTIMOS 5 ANOS DE EVIDÊNCIAS EMPÍRICAS SOBRE O MODELO DE MEMÓRIA DE TRABALHO DE BADDELEY

RESUMO

A doença de Alzheimer é a mais comum das condições neurodegenerativas associadas à demência. É conhecida como um quadro patológico que vem acompanhado de diversos comprometimentos nos processos cognitivos e psicológicos. O presente estudo objetiva compreender as relações entre a doença de Alzheimer e comprometimentos da memória de trabalho. Foi adotado o modelo de Baddeley para memória de trabalho a fim de revisar sistematicamente se o comprometimento dos subcomponentes desse modelo teórico – alça fonológica, esboço visuoespacial, retentor episódico e executivo central – trilham caminhos distintos ou similares. A revisão sistemática consultou as bases de dados da Medline, Psycinfo e Scielo. Dos 329 artigos encontrados, somente 11 foram aceitos dentro dos critérios estabelecidos. Os resultados sugerem que o retentor episódico e o executivo central declinam na proporção em que a severidade da doença de Alzheimer aumenta. A alça fonológica e o esboço visuoespacial são os últimos subcomponentes comprometidos dentro do modelo de memória de trabalho de Baddeley.

Palavras-chave: Doença de Alzheimer. Memória de Trabalho. Demência. Revisão Sistemática.

CONEXÕES PSI

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LA MEMORIA DE TRABAJO EN LA ENFERMEDAD DE ALZHEIMER: UNA REVISIÓN SISTEMÁTICA DE LOS ÚLTIMOS CINCO AÑOS DE EVIDENCIA EMPÍRICA SOBRE EL MODELO DE MEMORIA DE TRABAJO DE BADDELEY

ABSTRACT

La enfermedad de Alzheimer es una de las condiciones neurodegenerativas más comunes asociadas con la demencia. Se le conoce como una condición patológica que viene con diversas alteraciones en los procesos cognitivos y psicológicos. Este estudio tiene como objetivo comprender la relación entre la enfermedad y el deterioro de la memoria de trabajo en la enfermedad de Alzheimer. Adoptamos el modelo de Baddeley de memoria de trabajo con el fin de revisar sistemáticamente el déficit de los subcomponentes de este modelo teórico – el bucle fonológico, el esquema visuoespacial, el ejecutivo central y la retención episódica – pisando en caminos separados o similares. Una revisión sistemática examinó las bases de datos Medline, SciELO y PsycINFO. De los 329 artículos encontrados, sólo 11 fueron aceptadas dentro de los criterios establecidos. Los resultados sugieren que el retenedor episódico y el ejecutivo central tienen disminuciones en proporción a la severidad de la enfermedad de Alzheimer. El bucle fonológico y el esquema visuoespacial son los últimos subcomponentes acometidos en el modelo de memoria de trabajo de Baddeley.

Palavras clave: Enfermedad de Alzheimer. Memoria de Trabajo. Demencia. Revisión Sistemática.

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