Executive *n*-back tasks for the neuropsychological assessment of working memory

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HIGHLIGHTS

- A new modified *n*-back task for the assessment of executive working memory.
- Modified and classic *n*-back tasks activate the same regions in the prefrontal cortex.
- Executive working memory increases oxyHb levels in the prefrontal cortex.
- Modified n-back is suitable for the neuropsychological assessment of working memory.

ABSTRACT

Keywords:
Working memory
Prefrontal cortex
Dorsolateral cortex
Near-infrared spectroscopy (fnirs)
Executive memory
***N*-back**

Working memory (WM) has been defined as a cerebral function which allows us to maintain and manipulate information "online". One of the most widely used paradigms to assess WM is the *n*-back test. Despite its extensive application, some authors have questioned its capacity to assess the manipulation of WM load. The present study introduces a new version of the *n*-back test to carry out this assessment. We use functional near-infrared spectroscopy (fNIRS) to evaluate prefrontal cortex (PFC) activation. The modified n-back requires monitoring of sequentially presented stimuli (in this case the days of the week). The target response relates to a stimulus which appears previously, from 0 to 2 items back, on the computer screen. Our data reveals that while modified and unmodified n-back activate the same regions of the left PFC, our modified 2-back version shows significantly higher activation in the left dorsolateral PFC (DLPFC) and the left frontal opercula. These results suggest that increased complexity in verbal WM tasks entail greater executive control, which would lead to an increase in cerebral blood flow to the areas associated with verbal WM. Therefore, an increase in the manipulation of WM load in verbal tasks reflects greater physiological activity in the left DLPFC and the left frontal opercula. The modified *n*-back test may also be incorporated into the armamentarium of valid instruments for the neuropsychological assessment of the maintenance and manipulation of verbal information in tasks requiring working memory.

1. Introduction

Working memory (WM) has been a central theme in cognitive physiology research and in cognitive neuroscience in general. WM is the brain function which provides access to representations which are necessary to carry out higher-order cognitive tasks as well as daily living activities. Theoretically, WM has been defined as a cognitive system for the temporary storage and manipulation of remembered information . It has also been viewed as a type of memory which is active and relevant for only short periods of time and more specifically, as a process by which a remem- bered stimulus is kept "online" to guide behavior in the absence of external clues.

Different authors have pointed out that prefrontal cortex (PFC) intervention in WK involves two main components: short-term memory and executive processes. While short-term memory is a process that involves keeping a limited amount of information active, executive processes are linked to the management and content of this stored information. Neurophysiological studies have shown that neurons in the dorsolateral prefrontal cortex (DLPFC) play a role in the coding and monitoring of the information temporarily kept "online".

A meta-analysis performed by Owen et al. illustrated which brain regions were activated by *n*-back tasks, regardless of the

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input modality (verbal vs. nonverbal) . Six cortical regions were identified: medial and lateral posterior parietal cortex, including the precuneus and inferior parietal lobes (BA7, 40); bilateral premotor cortex (BA6, 8); anterior medial/cingulate premotor cortex, including supplementary motor areas (AB32, 6), bilateral rostral PFC (BA10), bilateral dorsolateral PFC (BA9, 46), and medial ventrolateral PFC (BA45, 47). These results show that 5/6 of these cortical regions are associated with frontal lobes, and half (3/6) with the PFC.

The classic *n*-back test has traditionally been used to assess working memory. However, this test evaluates storage processes without considering the manipulation component of WM information included by Baddeley. In this study, we employ a modified verbal *n*-back test which adds the manipulation of WM to the classic *n*-back task. Our main objective is to demonstrate that by adding the manipulation of information as a condition, task complexity increases, which triggers increased activation in brain regions associated with WM. Another goal is to validate the modified *n*-back test by comparing its implementation and physiological activation with previous neuroimaging studies.

To assess the manipulation component of WM, we added a cognitive task to the classic *n*-back test which requires the manipulation of stored information. The modified *n*-back tasks make increasing demands on WM load, given that the individual must manipulate information as well as store it. This manipulation requires the use of executive components which can control information stored online. This, in turn, requires greater cognitive effort, which leads to an increase in PFC activation. To facilitate the assessment of this component, we designed a task based on the manipulation of the days of the week, which is an overlearned and routine cyclic wordlist.

Our study uses functional near-infrared spectroscopy (fNIRS) and concentrations of oxygenated hemoglobin (oxyHb) to investigate activation in the PFC. The study presupposes that PFC activation increases as memory load increases ($n > 1$) . We also hypothesize that the modified *n*-back reveals higher levels of DLPFC activation than the classic *n*-back test.

2. Methods

2.1. Subjects

This study included 20 healthy right-handed volunteers (14 female, 6 male), aged 22–39 (mean age = 26.6; SD = 4.15), and with a mean of 16.5 years of formal education. The subjects were recruited from the faculty and student body of the University of Seville, Spain. Inclusion criteria included fluency in Spanish, good eye sight, no medical record of psychiatric or neurological illness, and no prescribed medication at the time of the study. The study protocol was in accordance with the Declaration of Helsinki (http://www.wma.net/e/policy/b3.htm), and approved by the University of Seville Ethics Committee. Written informed consent was obtained from all subjects prior to participation in the experimental procedure.

2.2. Functional near-infrared spectroscopy (fNIRS) imaging

fNIRS is an optical functional neuroimaging technique, developed according to the method designed by Chance and Leigh . Both human and animal studies have tested the validity of this method. Research has provided evidence of a functional correspondence between fNIRS and neuroimaging tech- niques. These studies have reported a high positive correlation between PET measurements and fNIRS oxyHb, while a good spatial agreement has been found in studies that employed simultaneous fMRI and fNIRS.

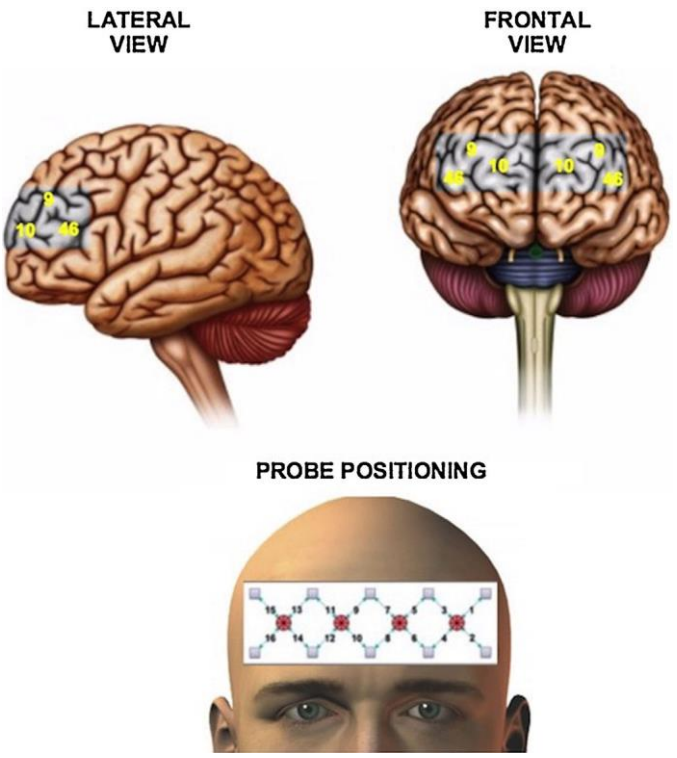

Fig. 1. The probe consists of 10 photo-detectors and 4 light sources that divide the prefrontal cortex (PFC) into 16 functional channels. Channels –1##8 gather information on the left PFC; channels #9–#16 provide information on the right PFC. The top image displays the 16 channels and their neuroanatomical location relative to Brodmann areas (BA). The probe channels on each side (–1##6, #11–#16) correspond to the DLPFC (BA 9 and 46), while the middle channels (#7–#10) correspond to the medial PFC (BA10).

Our NIRS system (NIM, Inc., Philadelphia, PA) applies light to tissue at constant amplitude and can provide measurements of oxy- and deoxy-Hb relative to baseline concentrations. The fNIRS probe is 17.5 cm long and 6.5 cm wide. It contains four light sources surrounded by ten detectors, for a total of 16 channels of data acquisition, covering an area of 14×3.5 cm on the forehead. A source-detector distance of 2.5 cm provides a penetration depth of 1.25 cm. The probe positioning is such that the line of sources is set at the line of fronto-polar electrodes [FP1–FP2] (in the International 10–20 system). This is designed to image cortical areas that correspond to DLPFC . The DLPFC generally occupies the upper and side regions of the frontal lobes. It is comprised of BA 9 and 46. Area 9 occupies the dorsal region of lateral PFC and extends medially to the paracingulate in humans. Area 46 is generally located at the anterior end of the middle frontal sulcus. The frontal polar PFC, BA 10, is a region positioned above the Orbito Frontal Cortex (OFC), inferior to Area 9, and anterior to Area 46, serving as a junction point between the OFC and DLPFC (See Fig. 1). A complete data acquisition cycle lasts approximately 330 ms, making the temporal resolution approximately 3 Hz.

2.3. Working memory paradigm: unmodified n-*back and modified* n-*back*

To assess WM and DLPFC involvement in its functional processes, a visual *n*-back paradigm with verbal stimuli was used. This *n*-back test consisted of presenting sequential stimuli in different conditions with a variable mnesic load. The verbal stimuli comprised the Spanish words for the seven days of the week. The n-back paradigm used three conditions with a gradual increase in memory load (0-, 1-, and 2-back). In the 0-back condition, the subject was

required to respond (by pressing the left side of the mouse) whenever the word "Domingo" appeared on the computer screen. This condition, with a null memory load, serves as the control condition for the experimental design. In the 1-back condition, the subject must respond when the current stimulus is identical to the one shown previously, depending on the instructions given in each case (see Section 2.4). In the 2-back condition, the subject is required to respond when the stimulus is the same as the one shown two trials earlier.

Two types of tasks, each with different target stimuli, were designed for the unmodified 1-back and 2-back conditions (the 0-back remains the same). In these tasks, the subject was required to respond if the present stimulus coincided with the previously shown stimulus (1-back) or with the stimulus shown two trials earlier (2-back). Modified *n*-back, however, requires the subject to monitor the order of the stimuli, in this case the days of the week, therefore demanding the manipulation of information stored in short-term memory. In the modified *n*-back, memory storage load increased from $n = 0$ to 2, but the manipulation component was constant between *n*-back tasks. A prior pilot study verified that this variation of the classic n-back guarantees over 75% target detection in most subjects (data not shown). In the modified 1-back condition, the subject had to respond when the current stimulus coincided with the day of the week following the one shown previously. In the modified 2-back condition, the response was required when the current stimulus coincided with the day of the week following the one shown two trials earlier (see Fig. 2).

2.4. Procedure

After providing the subject with a general explanation of the procedure, he/she was seated in a dimly-lit room where *n*-back tasks and fNIRS recordings were carried out. The stimuli were presented using E-Prime 1.1. software (Psychology Software Tools, 1999), installed in a PC Pentium IV, and connected via serial port to the computer. Data was obtained using the PCMCIA data acquisition card (NI DAQCard-6024E; 20 kS/s, 12-Bit, 16 Analog Input Multifunction DAQ; National Instruments).

Once the fNIRS probe was in place, the subject was asked to relax while a 15-sec baseline was recorded. Prior to test administration, 20 test trials were performed to ensure that the subject understood the experimental procedure. In the 0-back condition, the criteria for understanding was the identification of 95% of the targets; for 1-back, 85% of the targets, and for 2-back, 75% of the targets. The test trials were repeated until the subject met the criteria.

The testing commenced with one of the two experimental tasks, unmodified *n*-back or modified *n*-back. Task order was counterbalanced between subjects. Each task consisted of nine trials, with two blocks of stimuli for each *n*-back condition. Block order was randomly selected to avoid repetition of two blocks from the same condition. During each trial, the instructions for the condition (7500 ms) appeared on the computer screen, followed by 20 stimuli, 20% of which were targets. Once the first task was completed, the subject was administered the corresponding second task.

The stimuli for each block lasted 500 ms, with a 2.5 s fixation point between each stimulus. The duration of each block was 67.5 s; each session lasted a total of 10 min and 30 s.

2.5. Statistical analysis

For behavioral results analysis, we analyzed sensitivity (number of identified targets/ number of identified targets + false negatives) and reaction time for each condition. We performed 2-way ANOVAs (3 conditions [0,1 and 2-back] $\times$ 2 tasks [unmodified vs. modified]) for repeated measures. Post-hoc tests included planned *t*-tests with Bonferroni correction when carrying out multiple comparisons.

For fNIRS data analysis, we recorded three different wavelengths (850, 805, 730). To obtain oxyHb, we applied the Beer–Lambert Law, which calculates relative changes to baseline values. Heart pulsation and respiration signals were removed from raw fNIRS data by using a 0.14–0.17 Hz finite impulse response low-pass filter. A 3-way ANOVA for repeated measures (3 conditions $\times$ 2 tasks $\times$ 16 channels) was performed, and post-hoc comparisons were done using *t*-tests, with Bonferroni correction for multiple comparisons.

3. Results

3.1. Behavioral results

Sensitivity measures are displayed in Fig. 3. Sensitivity decreased as memory load increased, indicated by a significant main effect for condition ($P < 0.001$). A significant main effect for task was also found in subjects who performed worse in the modified tasks ($P = 0.002$). Post-hoc analysis showed lower sensibility in the modified tasks (mean = 0.86; SD = 0.023), as compared to the unmodified tasks (mean = 0.96, SD = 0.013). In addition to this, a significant interaction for condition $\times$ task was detected ($P < 0.001$). Post-hoc analysis showed that subjects performed significantly poorer in the modified 1- and 2-back tasks as compared to their respective unmodified conditions (1-back condition, $P = 0.045$; 2-back condition, $P < 0.001$).

Analysis of reaction times showed a significant main effect for condition ($P < 0.001$). The post-hoc analysis indicated that reaction time was significantly higher for the 2-back condition as compared to 0-back and 1-back (Ps < 0.001). Moreover, reaction times in the 1-back condition were significantly higher than those of 0-back ($P = 0.004$). However, differences in task main effects and interaction in reaction time did not reach significance (Fig. 4).

3.2. fNIRS results

The 3-way ANOVA yielded a significant main effect for channel ($P < 0.001$), indicative of higher oxyHb levels in certain channels regardless of condition or task ($P < 0.001$). Post-hoc analysis showed higher oxyHb levels in channels 1 and 2, both located in the left DLPFC (channel 1 vs. channel 15, $p = 0.02$; channel 2 vs. channel 16, $p = 0.004$). This analysis also showed a significant interaction between condition and channel ($p < 0.001$), indicating that oxyHb levels changed as memory load increased. In the 2-back condition, channel 1 showed higher oxyHb concentration as compared to 0-back ($p = 0.01$) and 1-back ($p = 0.02$). The same occurred with channel 2 (vs. 0-back, $p = 0.006$; vs. 1-back, $p = 0.03$).

Finally, the ANOVA analysis showed significant second-order interaction between the 3 variables ($p < 0.05$). The post-hoc tests revealed an increase in oxyHb levels in channels 2, 3, 4 and 6 only during the modified 2-back task (for other conditions, all p's<0.05) (see Fig. 5).

4. Discussion

Our aim was to design a new paradigm for the study of working memory as defined by Baddeley [1–3], as short-term storage provider for information during its manipulation. WM assessment is often done using the original *n*-back test, but it has been criticized for its incapacity to assess the manipulation of information [27,28]. We propose a modified version of the *n*-back paradigm, based on an automatism (days of the week), where maintenance and manipulation of information are assessed simultaneously.

Our behavioral results reveal that subjects had greater difficulty with modified *n*-back tasks as compared to unmodified tasks. This was reflected in the precision needed to detect the target stimulus,

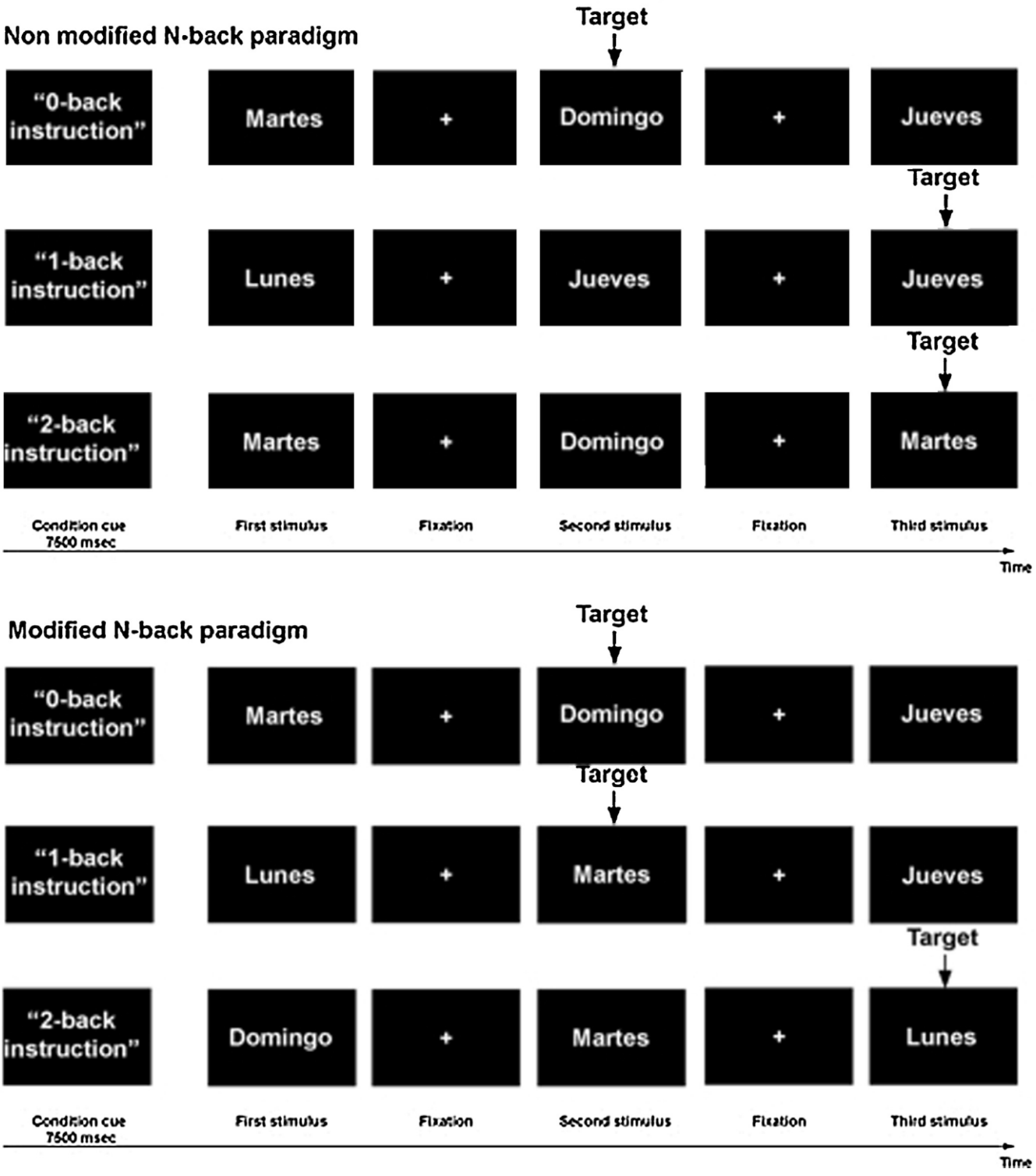

Fig. 2. Paradigm for the unmodified n-back (above) and modified *n*-back (below) tasks. The 0-back condition for both tasks required a response when the stimulus "Domingo" appeared on the screen. A fixation point was selected (+) between stimuli. In the unmodified 1-back condition, the subject must respond when a stimulus was repeated, while the unmodified 2-back condition required the subject to respond when the current stimulus coincided with the stimulus shown two trials earlier. In the modified 1-back condition, the subject was to respond when the current stimulus coincided with the day after the stimulus shown previously, while in the modified 2-back condition, the subject was instructed to respond when the current stimulus coincided with the day of the week following the one shown two trials earlier.

particularly in the modified 2-back task. One possible explanation for this drop in modified task performance could be attributed to the subject's strategic approach to solving the task. One strategy involves maintaining a larger memory load than needed in the unmodified version. The subject stores pre-target stimuli (1 or 2), in addition to the new stimulus, which must be manipulated. Another strategy involves direct manipulation of the content of WM. Here, the subject substitutes pre-target stimuli with their potentially correct responses, or targets, rather than add them to their memory load. In our modified *n*-back, the procedure would be to add a day to

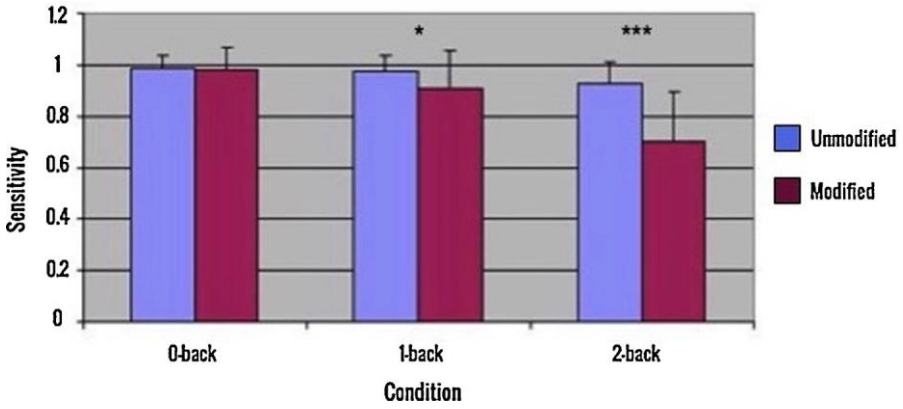

Fig. 3. Sensitivity measures for different *n*-back conditions across tasks. Means and standard deviations are displayed. Significant differences between modified and unmodified tasks were found in the 1- and 2-back conditions. *, $P < 0.05$; ***, $P < 0.001$.

the present stimulus and maintain the manipulated result in memory. According to Baddeley and Hitch's classic working memory model , later expanded upon by Baddeley in 2000 , performance in the first strategy is associated with greater saturation of short term memory store in WM. If the second strategy is applied, performance would be the product of increased involvement from central executive attentional components. Baddeley proposed that the central executive could influence the verbal content of memorized items in short term storage, in responding to different information sources, which include other WM components, as well as information stored in long term memory.

Our behavioral results showed that reaction times increased as memory load increased. However, this measure was not sensitive to the addition of the manipulation component in WM. These results suggest that the storage of verbal information in WM, and not its manipulation, is what increases reaction times. One explanation could be that the difficulty of the stimulus being manipulated does not increase the central executive's processing time, or that it does not affect decision making times. Further studies are needed to elucidate this result. Another explanation could be that task difficulty (based on an overlearned and highly automated list of daily stimuli) is not sufficiently sensitive to observe affects in reaction time.

Our hemodynamic results showed an increase in oxyHb concentration in the DLPFC between the different *n*-back conditions. These findings coincided with that of other research . Some studies attribute the left PFC with a specialty in verbal tasks requir- ing WM . Conversely, spatial tasks requiring the use of WM produce bilateral activation in the PFC . These findings support other studies employing fMRI . In our study, both the modified and unmodified 2-back task activated the same fNIRS channels as the 1-back task conditions, but with greater intensity. This could be due to the increased difficulty if the 2- back task, which contains the same stimulus but requires a larger memory load [15]. Yet, the modified 2-back task resulted in sig- nificantly higher channel activation intensity than the unmodified task. One explanation for this difference could be that the modi- fied 2-back task requires more elaborate information processing, as subjects must integrate semantic category and chronological order (days of the week) into their information processing. This involves greater executive control, and would lead to an increase in cerebral blood flow to the areas associated with verbal WM. Our study, as well as other research on WM [38,39], found significant differences in activation in these same areas, which correspond to the DLPFC and the left frontal opercula (Brodmann areas 9,10, 45 and 46). Other authors found that neuroanatomical disassociations in the PFC maintain (ventrolateral PFC) and manipulate (DLPFC) neural information [40,41,42]. Our results reveal activation in both the ventrolateral PFC and left DLPFC, suggesting that modified and unmodified *n*-back tasks entail both processes.

One of the advantages of the WM task we propose is that subjects only manipulate information that is kept *online* in memory. This allows us to assess the effect of increased memory volume as the single determining factor in subject performance. For example, dual tasks have been used to assess the central executive, employing executive processes to control subordinate systems (short term memory stores) that manipulate its parameters [43]. Some authors

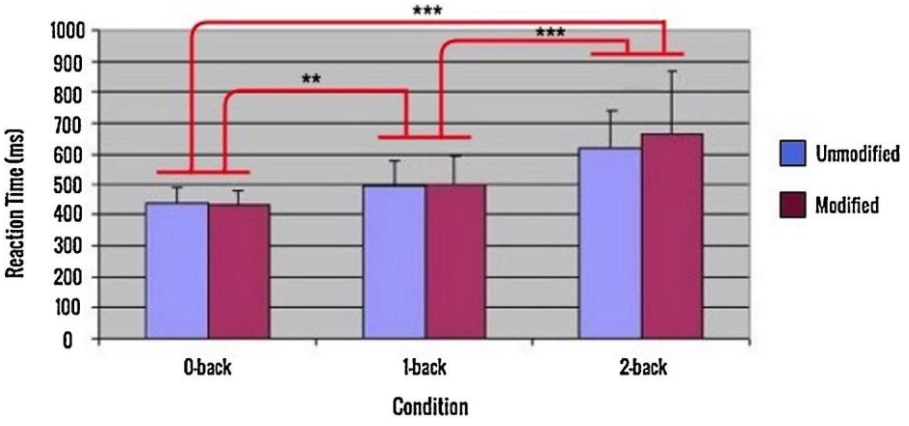

Fig. 4. Mean reaction times for the different *n*-back conditions across tasks. Higher reaction times were detected as memory load increases. Reaction times for correct answers in the modified 2-back were significantly higher than in the unmodified 2-back task. **, $P < 0.01$; ***, $P < 0.001$.

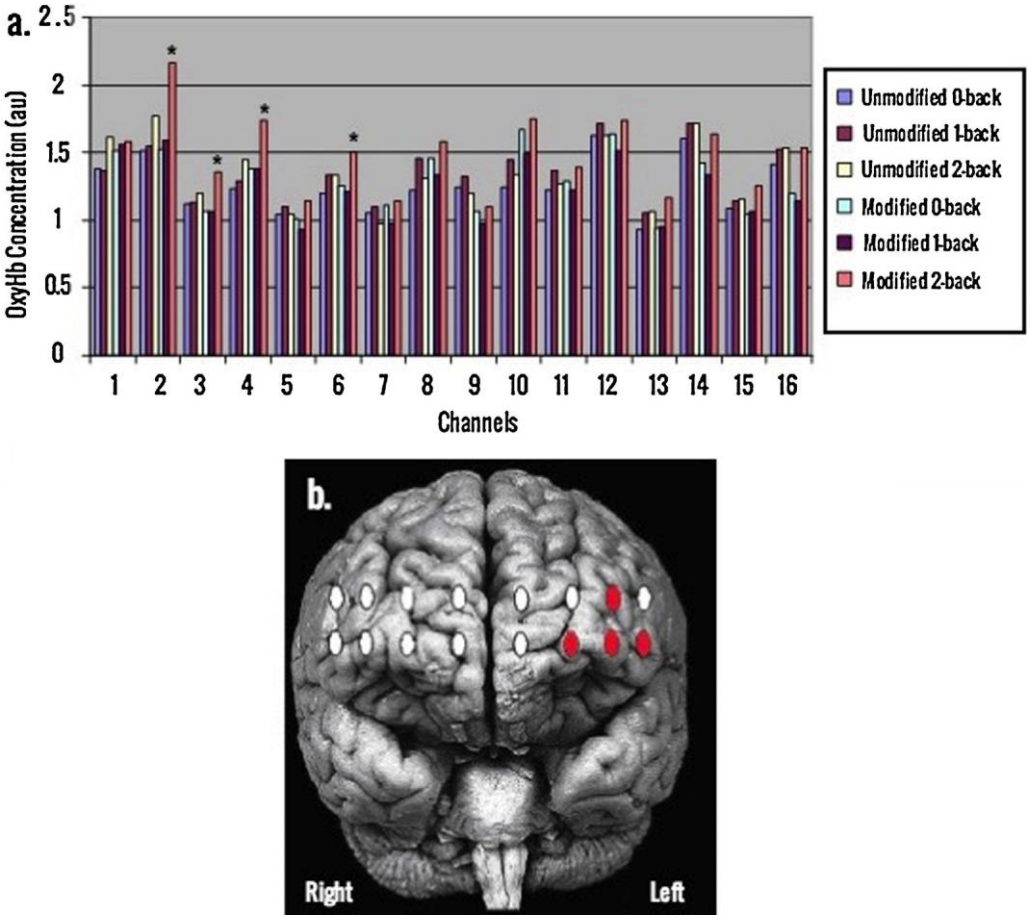

Fig. 5. (a) Mean oxyHb levels in the six experimental conditions. Higher oxyHb levels were detected in channels 2, 3, 4 and 6 in the modified 2-back task as compared with the unmodified 2-back task. *, $P < 0.05$. (b) Image of the spatial positioning of the significant channels 2, 3, 4 and 6 activated in the modified 2-back task. These channels are situated in the left frontal opercula and the left DLPFC (Brodmann areas 9, 10, 45 and 46).

recommend training with dual *n*-back tasks to improve fluid intelligence [28]. However, dual task execution usually reflects the effect of one task over the other, particularly when the demand on memory volume high.

Another neuropsychological test for WM is the digit test. The WAIS version has two tests, the direct test, where the subject must remember numbers in the order they are presented, or in the inverse order. The inverse test often shows poorer performance in item recall, presumably due to the cognitive load of manipulating items in WM. Owen [42] found that while both tasks share regions in the PFC, including the medial ventrolateral PFC, the inverse digit task involves other PFC regions, such as the medial DLPFC, which are closely linked to active areas in our study. Like ours, Owen's work includes tasks which can assess the manipulation of WM. How- ever, performance variation between inverse and direct digit tasks depends greatly on the spam present in short term memory, which varies widely among individuals. In our modified and unmodified *n*-back tasks, mnesic spam does not exceed 2 items, increasing the reliability of our assessment tool. We believe this modified paradigm provides a valid tool for measuring the manipulation of information kept online in working memory, while shedding light on the workings of the PFC in this process.

5. Conclusions

The modified *n*-back test, like the classic version, activates the same PFC regions, but with greater intensity. In our study, the left DLPFC and the left frontal opercula show significantly higher activation in the modified *n*-back tasks as compared to the unmodified version. This higher level of activation in areas associated with verbal WM is due to the increased participation of WM executive components. Our results suggest that the modified *n*-back assessment of WM involves greater involvement by the central executive, and consequently an increase in oxyHb in the left DLPFC and left frontal opercula. Our work may resolve questions as to whether or not the unmodified *n*-back is a viable test for assessing WM [27,28].

A future line of research could be the study of differential physiological activation and behavioral responses to memory storage and WM manipulation, in order to discern if both are intrinsically related or if they are two separate, but functionally dependent components. This paper opens the door to new research exploring the relationship between the modified *n*-back and nonverbal and spatial working memory, ultimately providing clinical settings with a means to assess pathologies associated with working memory.

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