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1. General Introduction

Selective attention focused on relevant stimuli is necessary for central cognitive functions and performance. However, attention can be disrupted by certain types of distracting events, like sound change or novelty, which break temporarily the current focus of activity. Such involuntary or exogenous attention plays an important biological role for survival in natural circumstances, because it brings, through the orienting response, new potentially significant stimuli into the focus of conscious evaluation.

Through a simple behavioral “distraction” task we are able to investigate the cerebral mechanisms underlying the exogenous control of attention. Subjects are instructed to concentrate on a simple visual task while ignoring an irrelevant sound presented 300 ms leading the visual stimulus. These irrelevant sounds are manipulated so that the “standard”, repeating stimulus (occurring in 80% of the cases) is replaced occasionally by a slightly different “deviant” or an environmental (novel) sound (i.e, a telephone ring, a glass breaking, etc.). We have shown that distracting sounds increase the response time and the number of incorrect choices in the visual classification task, revealing behavioural distraction during visual task performance (see review in Escera et al. 2000).

The concomitant recording of event-related potentials (ERPs) during performance of the distraction reveals a characteristic neuroelectric pattern, the so-called distraction potential (DP; Escera & Corral, 2003), characterized by tri-phasic waveform. Each of its phases provides an index for one of the three main processes involved in involuntary attention control (see Escera et al. 2000, Escera & Corral, 2003): a) the mechanism of attention capture, associated with the mismatch negativity (MMN) and/or with the N1 ERP components, b) the orienting of attention, associated with the novelty-P3, and c) the reorienting of attention towards the main task after a momentary distraction, associated with the so-called reorienting negativity (RON).

Whereas the cerebral networks involved in the generation of the MMN, and therefore in attention capture, are relatively well established, little is known about the underlying networks leading to the orienting response and the novelty-P3. Studies of patients with cerebral lesions (Knight, 1984, 1996, Yamaguchi & Knight, 1991), as well as intracraneal recordings in epileptic patients (Baudena et al., 1995, Halgren et al., 1995), and modeling of ERP (Mecklinger & Ullsperger, 1995, Yago et al., 2003) and MEG (Alho et al., 1998) responses elicited to novel stimuli have suggested that a largely distributed cerebral network, underlies the generation of the novelty-P3 (see review in Friedman et al., 2001). Recent fMRI studies using block designs have confirmed the involvement of part of this network, in auditory novelty processing (Opitz et al., 1999), but failed to show any activity in other related brain regions.

The studies reviewed above, have used the ERP/MEG methodologies, which have a powerful temporal resolution, capable to disentangle the sequence of brain events leading to the involuntary orienting and reorienting of attention. However, their spatial accuracy is considerably poor, compared to other brain imaging methods, so that the precise spatial distribution of the underlying cerebral regions involved remains less understood.

Recently, we were able to implement our distraction task for its use during functional magnetic resonance imaging, so that similar behavioral effects as those reported in previous studies were obtained (Escera et al., *in prep*). Moreover, we showed that distracting “deviant” tones activated the bilateral superior and middle temporal gyri, and distracting “novel” sounds engaged both the bilateral auditory cortex and the left inferior frontal cortex, both sets of results in parallel with the neuroelectric activity seen in EEG recordings (Escera et al., *in prep*).

A line of evidence which is gaining relevance in the field of involuntary attention is up to what extent exogenous attention elicited by bottom-up mechanisms interacts with top-down control processes to elicit the orienting response (Escera & Corral, 2003; see review in Lavie et al., 2005). For instance, Berti & Schröger (2003) have shown that under high working memory load conditions, the distracting effects of deviant tones are mitigated, and moreover, that this interaction takes place between the processes associated to MMN generation, which are insensitive to working memory load, and those generating the novelty-P3. In a similar vain, we have recently shown that increasing working memory load decreases the distracting effects of novel sounds (SanMiguel et al., *submitted.*) and modulates late (circa 230 ms), but not early (circa 100 ms) novelty processing in the auditory cortex, as indicated by magnetoencephalography (MEG) (Nowak et al., *in prep*). However, these results contrast with many other studies showing that increasing the cognitive demands of the primary task increase the distracting effects of task-irrelevant stimuli presented concomitantly (Lavie, 2005).

2. Objectives and work plan

To investigate under which conditions working memory load can exert a modulatory effect on the behavioral and brain responses to auditory novel, distracter stimuli, and to establish the spatio-temporal dynamics of such a modulation. Specifically, to establish whether the particular form of manipulating the cognitive set by increasing working memory load, will affect behavioral measures of distraction and the P3a and RON ERP components, whereas the MMN will remain unaffected, and which are the specific neural regions involved in P3a/RON, and with which specific temporal dynamics, that will be affected by such a form of top-down control.

According to the study hypothesis, we expect to find increased response time in novel trials, indicating behavioural distraction, but of a smaller magnitude under high working memory load conditions. As for brain activation, we expect to replicate previous findings indicating bilateral temporal cortex and left inferior frontal activity for novel trials, and an attenuation in the activation of the auditory cortex under the high working memory load condition.

As a practical objective, we aim at gaining theoretical and practical knowledge on the use of the few analysis methods available to integrate ERP and fMRI data, in one of the leader groups in the application of these methods.

In order to achieve these goals, first, a suitable task will be explored by means of behavioural testing, and based on the results of these piloting, the combined ERP and fMRI experiment will be planned and executed.

3. Behavioral testing

a. Introduction

Involuntary orienting due to a distracting stimulus has been thought to be largely automatic and not under the influence of top-down factors as task set. However, recent evidence proves that the effect of these distracting stimuli is indeed dependent on top-down factors (Pashler et al. 2001). Attentional capture by distractors is dependent upon the relationship between the distractor and the task stimuli (Folk et al. 1992, 1999, 1998). Distraction is either enhanced (Yi, Woodman, Widders, Marois, Chun, 2004; De Fockert, Rees, Frith, Lavie, 2001; Lavie & De Fockert, 2005; Lavie, 2005; for a review see Lavie et al. 2004) or reduced (Berti&Schröger, 2003; SanMiguel et al., *submitted*, Spinks et al. 2004) when working memory (WM) load is imposed, depending on the characteristics of the different task settings, or on the type of information used to load WM (Kim et al., 2005). ERP studies have shown that electrophysiological traces of distraction are modulated by top-down factors, being enhanced when the distracting novel sounds were identifiable to the listener (Escera et al., 2003) and also when they were contingent to the visual task stimuli as compared to when they appeared in isolation (Escera et al., 1998), both results demonstrating a bias of the orienting response towards behaviourally relevant stimuli. Moreover, several other studies have also shown that the novelty-P3 elicited by deviant stimuli is reduced when higher demands are imposed on the concurrent task (Harmony et al., 2000; Berti & Schröger, 2003; Restuccia et al., 2005). It is thus clear that top-down factors associated to the experimental setup have a great deal of influence on the effects that distracting stimuli may have on the task.

The following studies build upon previous knowledge of the distracting effect that novel, environmental sounds have on visual task performance when presented shortly before the visual task stimuli. Generally, these distracting sounds capture the attention of the subject, resulting in increased reaction times (RT) to the following visual stimuli

(Escera, Alho, Winkler, Näätänen 1998; Escera, Alho, Schröger, Winkler, 2000; Escera, Yago, Alho, 2001; Escera, Corral, Yago 2002; Escera, Yago, Corral, Corbera, Nuñez, 2003). This distracting effect is reduced when WM load is imposed on the task (SanMiguel et al., *submitted*), also when both the distracting and task features of the stimuli are auditory (Berti & Schröger, 2003). The purpose of these studies was to test the replicability of these effects on a different task setting, using a delayed memory recognition task to impose load on WM, rather than doing so in an n-back fashion. Also different conditions of load were compared, as opposed to having only a load vs. no-load comparison.

b. Study I

Goals: To replicate the distraction and distraction attenuation effects of SanMiguel et al. (*submitted*) using a delayed memory recognition task; to investigate these effects under increasing amounts of load.

Methods: Eight healthy university students participated in this experiment (18-27 years; mean age 19.4; 2 male). Subjects gave informed consent after the nature of the study was explained to them and received course credits for their participation. They were presented with and auditory-visual distraction and working memory task with three conditions of load: no-load, load 1 and load 3. The two load conditions were randomised within the same block, whereas the no-load condition was presented in a separate block. Each trial (Figure 1) consisted of an initial fixation cross for 1,2 s, then the fixation cross became red for 1s. Immediately after, the memory array was presented for 2 s, consisting of four images organized around a black fixation cross, which could either be three faces and a scrambled image in the load 3 condition, one face and three scrambled images in the load 1, or four scrambled images on the no-load condition. Faces were randomly selected from a set of six faces and eight scrambled faces, their location was randomised and they were never repeated in the same memory array. A 1 s retention interval was presented after the memory array and finally a test face in the load 1 and load 3 conditions, or alternatively a face or a scrambled face in the no-load condition was presented for 2 s. Only responses within 900 ms from the test face were accepted. In the load 1 and load 3 conditions subjects had to respond, as accurately and fast as possible, whether the test face was present or absent on the memory array; in the no-load condition, they had to respond whether the test stimuli was a face or not. Responses were accomplished by pressing either one of two response buttons with the index and middle finger of the right hand. In half of the trials in the load 1 and load 3 conditions the face was present and on the other half it was absent. In the no-load condition half of the trials presented a face and half of them presented a scrambled image. During the whole duration of the trial, sounds were presented through headphones (ATA 1118) every 1200 ms. Sounds were either repetitive standard tones (600 Hz, 200 ms) or environmental novel sounds selected from a sample of 100 different exemplars, such as those produced by a drill, hammer, rain, door, telephone ringing, etc. The novel sounds were digitally recorded, low-pass filtered at 10,000 Hz, and edited to have a duration of 200 ms, including rise and fall times of 10 ms. Six sounds were presented in each trial, and in half of the trials a novel sound was presented 300 ms prior to the test stimuli, thus the actual probability of a novel sound was 1/12. The other 5 sounds on the novel trial were standard tones. The other half of the trials were standard trials, presenting 6 standard tones. Randomly, one out of nine trials was a “catch trial” in which the novel sound was presented at a different position, 300 ms after the start of the memory array. Each condition consisted of 150 trials and the total duration of the experiment was 60 minutes, allowing for pauses every 3,5 minutes. All participants performed the no-load condition first, in order to become equally familiar with all the faces before the memory conditions. Ten practice trials were performed before the start of each condition.

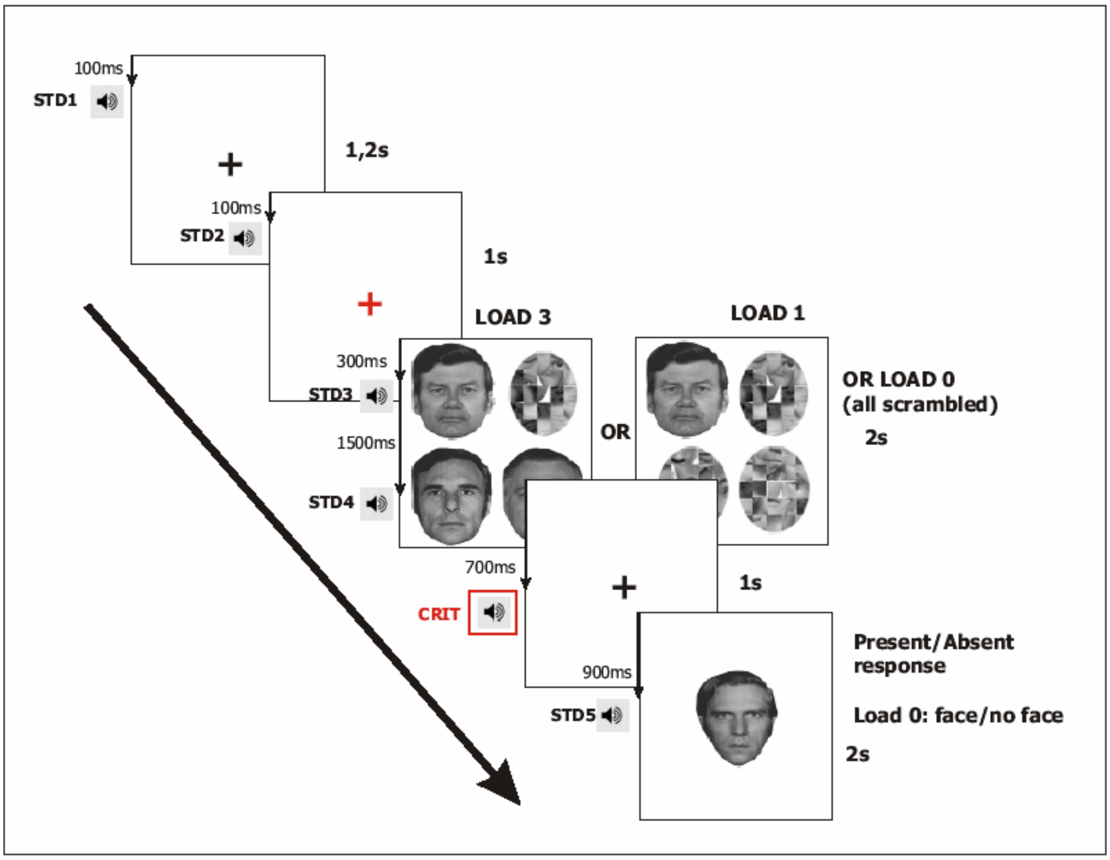

Figure 1. Trial structure for study 1. In the no-load condition all images on the memory array were scrambled faces. Visual stimulus duration is indicated on the right. Location of the sounds is indicated on the left, arrows indicate the location of the sound, from the start of the corresponding visual stimulus.

Results: A repeated measures ANOVA on reaction time (RT) with set size (0, 1, 3) and trial type (novel, standard) as factors revealed a main effect of set size $F(2,14)=41,83$, $p<0.001$. RT increased progressively with increasing load. There was also a main effect of trial type $F(1,7) = 14,88$, $p= 0,006$, showing a facilitation effect by novel sounds. The set size x trial type interaction did not reach significance ($p=0,076$). Paired comparisons revealed that the facilitation effect was only significant in the no-load condition $t(7)= -4,59$, $p=0,003$. The facilitation effect in the no-load condition differed only marginally from the load 1 $t(7)= 2,03$, $p=0,082$, and it differed significantly from the load 3 condition $t(7)=2,41$, $p=0,047$. There were no differences in facilitation between loads 1 and 3. A subsequent analysis comparing the no-load versus the load situations collapsed together revealed a set size x trial type interaction $F(1,7)=7,413$, $p=0,03$, showing that the facilitation effect found in the no load situation was attenuated in the load conditions, becoming non-significant.

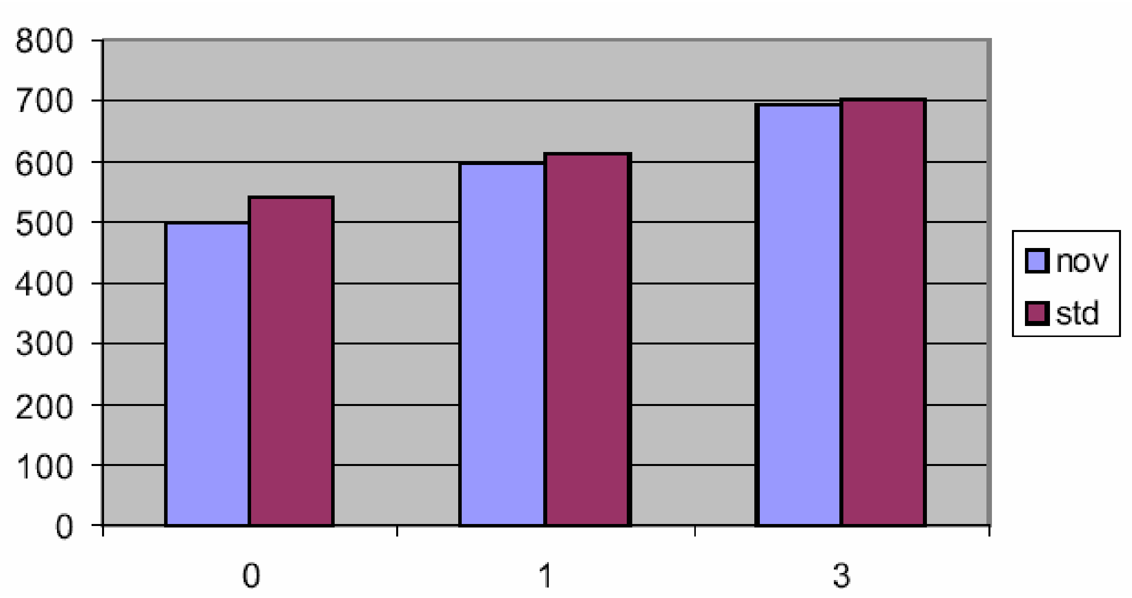

Figure 2. RT in the no-load, load 1 and load 3 conditions for novel and standard trial types.

The repeated measures ANOVA on hit rate (HR) revealed a main effect of set size F(2,14)= 36,21, p<0,001. There were no main trial type effects but there was a significant set size x trial type interaction F(2,14)= 5,419, p=0,02. Paired comparisons revealed that there was a facilitation effect in novel trials only in the load 1 condition t(7)= 3,806, p=0,007.

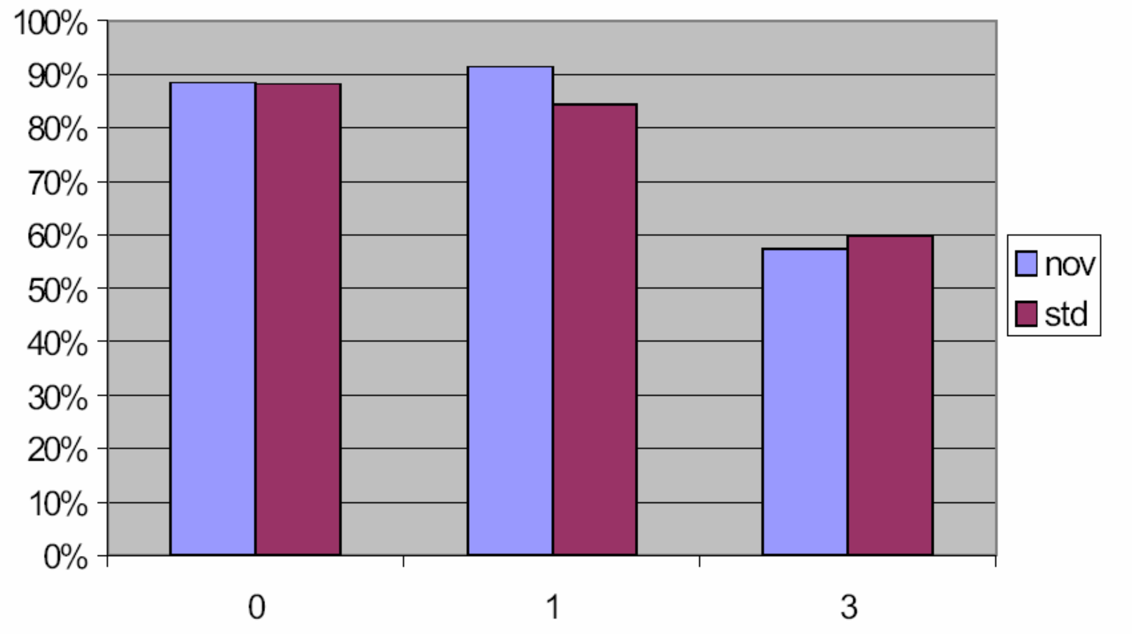

Figure 3. HR in the no-load, load 1 and load 3 conditions for novel and standard trial types.

Discussion: Task setting dramatically affected the effect of irrelevant sounds on task performance. When the sounds were presented during a delayed memory recognition task, facilitation by novel sounds occurred as opposed to distraction. This facilitation effect was of great magnitude when no load was imposed on the task, whereas imposing load on the task reduced the effect to the point of making it disappear. Increasing amounts of load seemed to progressively reduce the facilitation effect, although these effects did not reach statistical significance.

c. Study II

Goals: To study the effects of irrelevant sounds presented at different phases of the delayed-memory recognition task.

Methods: Eight healthy university students participated in this experiment (17-47 years; mean age 22; 3 male). Subjects gave informed consent after the nature of the study was explained to them and received course credits for their participation. The same task as in study 1 was used, but the timing of the trial was slightly changed to introduce a novel sound 300 ms prior to the encoding phase on 1/3 of the trials. Each trial (Figure 4) consisted of an initial fixation cross for 1 s, then the fixation cross became red for 600ms. Immediately after, the memory array was presented for 2,3 s, followed by a 1,3 s retention interval and finally a test face in the load 1 and load 3 conditions, or alternatively a face or a scrambled face in the no-load condition was presented for 2 s. Sounds were presented through headphones every 1200 ms. One third of the trials were standard trials (all sounds were standard tones), one third were encoding novel trials (a novel sound was presented 300 ms prior to the encoding array), and one third were retrieval novel trials (a novel sound was presented 300 ms prior to the test face). The overall probability of a novel sound was thus 11%. Each condition consisted of 225 trials and the total duration of the experiment was 84 minutes, allowing for pauses every 3 or 4 minutes. Ten practice trials were performed before the start of each condition. Participants performed this task in combination with the task of study 3 and the order of the tasks and conditions within task were counterbalanced.

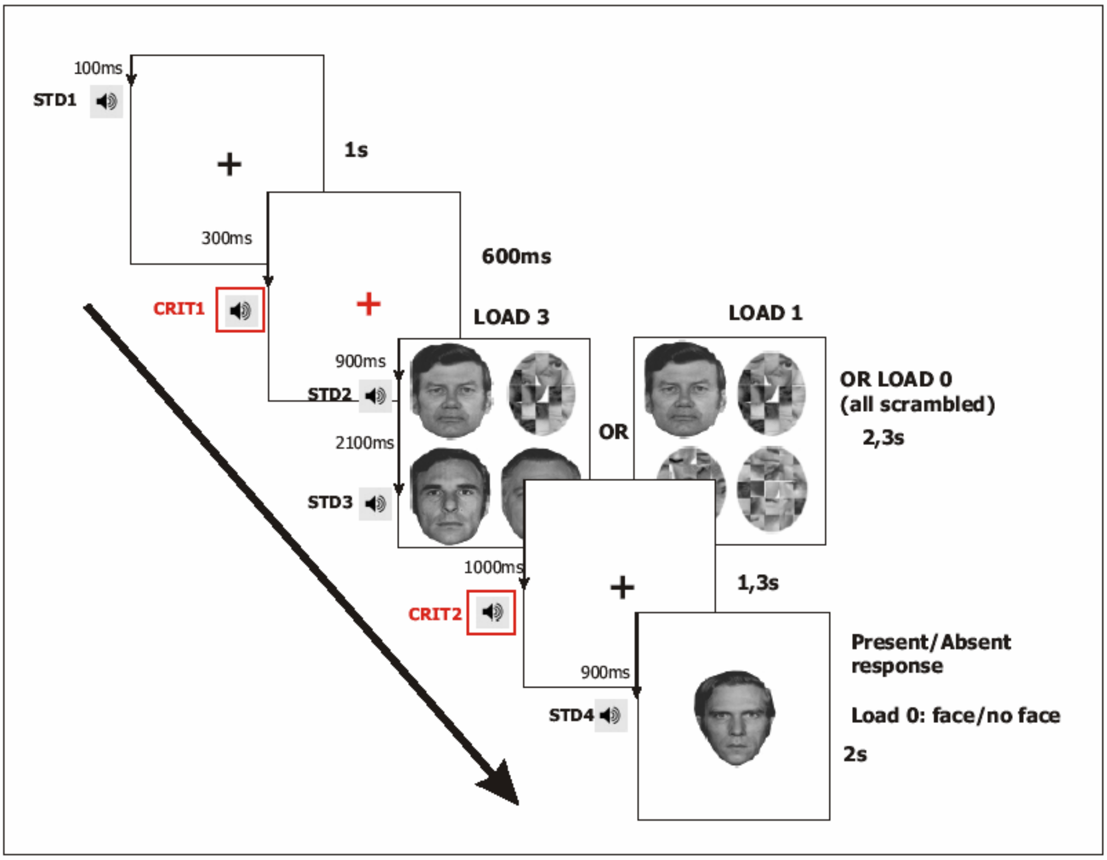

Figure 4. Trial structure for study 2. In the no-load condition all images on the memory array were scrambled faces. Visual stimulus duration is indicated on the right. Location of the sounds is indicated on the left, arrows indicate the location of the sound, from the start of the corresponding visual stimulus.

Results: RT increased progressively with increasing load F(2,14)=47,12, p<0,001 and HR decreased progressively F(2,14)=39,81, p<0,001. The effects of encoding and retrieval novels were analysed separately against the standard trials. Encoding novels did not affect either RT or HR to the test stimuli. Facilitation effects caused by retrieval novels were replicated as in study 1. A repeated measures ANOVA on RT revealed a main effect of set size F(2,14)=44,320, p<0,001 and a main effect of trial type (standard vs. retrieval novel) F(1,7)=10,356, p=0,015. No interaction effects were found. However, paired comparisons revealed that there was a significant facilitation effect only for the no-load condition t(7)=3,25, p=0,014. A subsequent repeated measures ANOVA comparing the no-load vs. the load situations collapsed together revealed also a significant set size x trial type interaction F(1,7)=6,953, p=0,034. Thus, the facilitation effect was only significantly present in the no-load condition and disappeared in both load1 and load3.

Retrieval novels did not have and effect on HR to test stimuli.

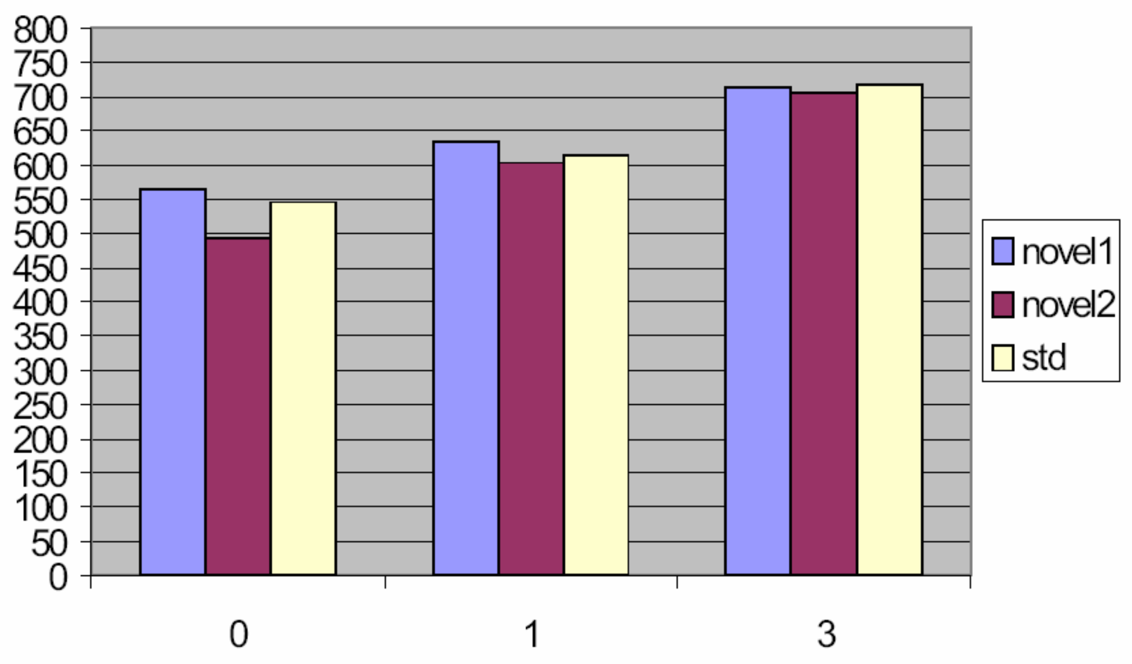

Figure 5. RT in standard, novel 1 (encoding) and novel 2 (retrieval) trials for the no-load, load 1 and load 3 conditions.

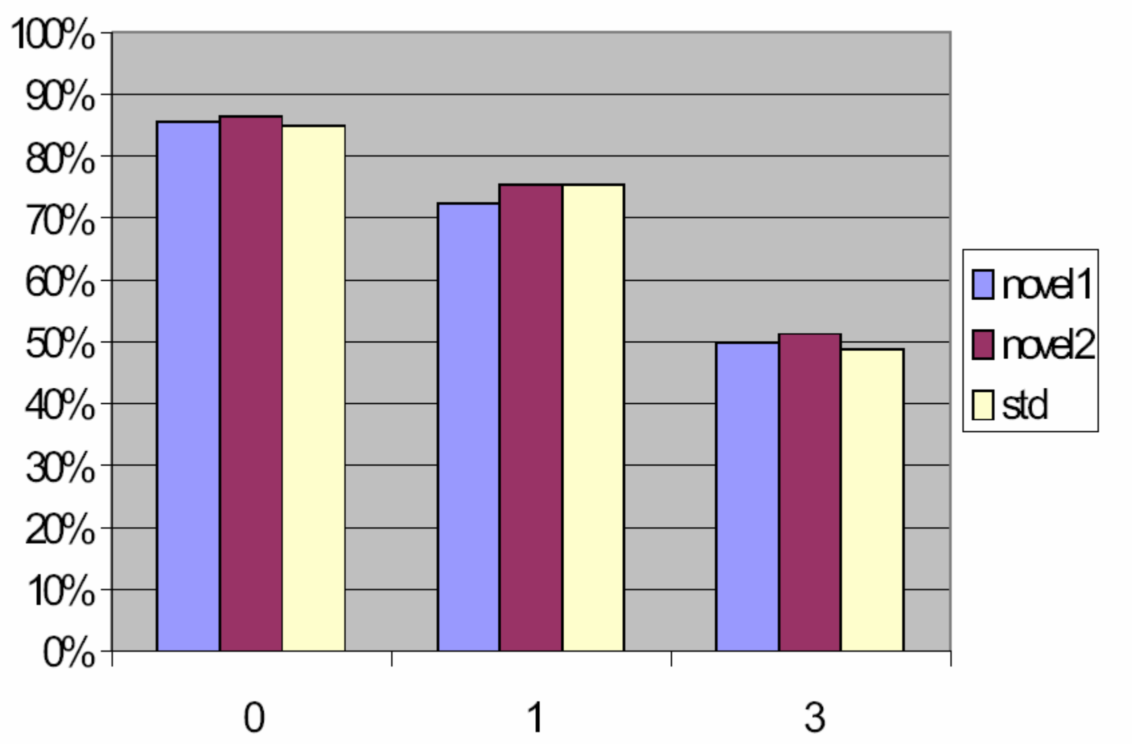

Figure 6. HR in standard, novel 1 (encoding) and novel 2 (retrieval) trials for the no-load, load 1 and load 3 conditions.

Discussion: Novel sounds presented prior to the encoding phase of the task did not have an effect on task performance, even in the no-load situation, where no memory is involved in the task. However, the facilitation effect caused by novel sounds presented prior to the retrieval phase were replicated.

d. Study III

Goals: To compare the effects of irrelevant sounds on the same subjects varying only the trial structure while keeping the sound-task stimuli relation equal and performing the same task.

Methods: Seven of the participants from study 2 students participated in this experiment (18-47 years; mean age 22,7; 3 male). Subjects gave informed consent after the nature of the study was explained to them and received course credits for their participation. They were presented with a visual discrimination task (figure 7) in which they had to answer as accurately and fast as possible whether the image presented at the centre of the screen was a face or not by making the corresponding button press with the index and middle finger of the right hand. Response buttons were counterbalanced across participants. Randomly, half of the trials presented a face and half presented a scrambled face. Only responses within 900 ms from the presentation of the visual stimulus were accepted. In each trial, a either a standard tone (p=0.8) or a novel sound (p=0.2) was presented via headphones 300 ms before the visual stimulus. Sounds and visual stimuli were identical to those used in study 1 and had a duration of 200 ms. The total duration of the experiment was 7 min., divided into three blocks allowing a short rest between blocks. The first four trials of each block were always standard trials and standard trials immediately following a novel trial were automatically discarded from any analysis. All subjects performed ten practice trials without sounds before starting the experiment.

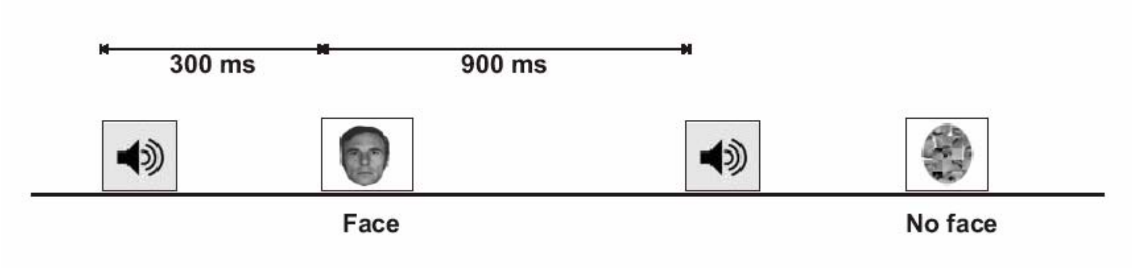

Figure 7.

Results: Participants were distracted by the occurrence of a novel sound, showing increased RTs in novel trials as compared to standard trials t(8)=2,878, p=0,028. No differences in HR were found between standard and novel trials.

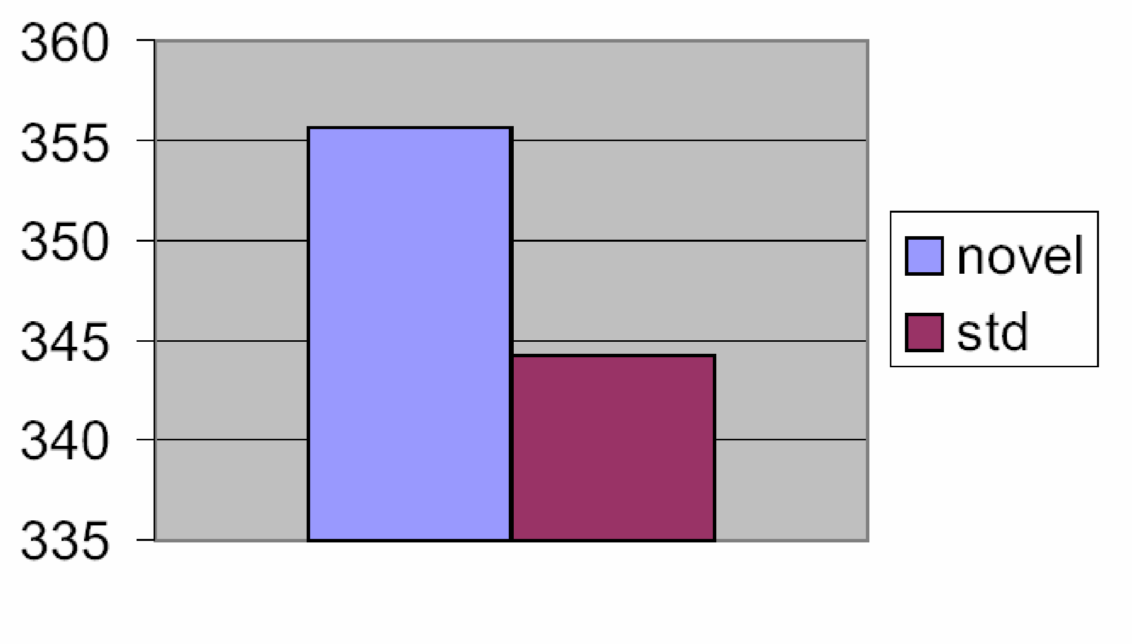

Figure 8. RT for novel and standard trials.

Discussion: When the trial structure was simplified while keeping all other elements of the task equal, the effect of irrelevant novel sounds on task performance was inverted on the same subjects, showing here the well-established distraction effect as expected.

e. General discussion

Surprisingly, a facilitation effect by novel sounds was found when using a delayed memory recognition task. This effect appeared to be very reliable and was replicated in study II. The control experiment performed in study III revealed that this is a top-down effect, dependent on the complex trial structure of studies I and II, as using the same task, under a simplified trial situation the well-established distraction effect by novel sounds appeared. Thus, this new top-down facilitation effect is of great interest, and was further studied using the combined ERP and fMRI approach, in order to describe also its electrophysiological and anatomical features.

4. Combined ERP and fMRI experiment

a. Introduction

Based on the results of the behavioral tests, a new task was created in order to study the newly found facilitation effect with the combined ERP and fMRI approach. This approach allows to further investigate the brain events related to this facilitation (its spatio-temporal dynamics) and also the mechanism leading to the modulation of this facilitation effect by working memory load.

b. Procedure

Thirteen healthy volunteers participated in this experiment (18-32 years; mean age 22.5; 5 male). All subjects performed separate ERP and fMRI sessions. Eight participants started with the ERP session and the other 5 started with the fMRI session. Subjects gave informed consent after the nature of the study was explained to them and received £35 for their participation. They were presented with and auditory-visual distraction and working memory task with two conditions: no-load and load 1. The two conditions were presented in separate blocks, their order counterbalanced across subjects. Each trial (Figure 9) started with an initial fixation cross for 1,7 s. Immediately after, either a face in the load 1 condition or a scrambled image in the no-load condition was presented for 2,3 s. Faces were randomly selected from a set of six faces and eight scrambled faces. This was followed by a 1,3 s retention interval and finally a test face in the load 1 condition, or alternatively a face or a scrambled face in the no-load condition was presented for 1,9 s.. In the load 1 condition subjects had to respond, as accurately and fast as possible, whether the test face the same or a different face to the one presented previously; in the no-load condition, they had to respond whether the test stimuli was a face or not. Responses were accomplished by pressing either one of two response buttons with the index and middle finger of the right hand. Response buttons were counterbalanced across participants. In half of the trials in the load 1 condition the face was present and on the other half it was absent. In the no-load condition half of the trials presented a face and half of them presented a scrambled image. During the whole duration of the trial, sounds were presented through headphones every 1200 ms. Sounds were either repetitive standard tones (600 Hz, 200 ms) or environmental novel sounds selected from a sample of 100 different exemplars, such as those produced by a drill, hammer, rain, door, telephone ringing, etc. The novel sounds were digitally recorded, low-pass filtered at 10,000 Hz, and edited to have a duration of 200 ms, including rise and fall times of 10 ms. Six sounds were presented in each trial, and in half of the trials a novel sound was presented 300 ms prior to the test stimuli, thus the actual probability of a novel sound was 1/12. The other 5 sounds on the novel trial were standard tones. The other half of the trials were standard trials, presenting 6 standard tones. Randomly, one out of nine trials was a "catch trial" in which the novel sound was presented at a different position, 200 ms before the start of the memory face or initial scrambled image. These trials were discarded from further analyses. Ten practice trials were performed for each condition before the start of the experiment in both the ERP and fMRI sessions.

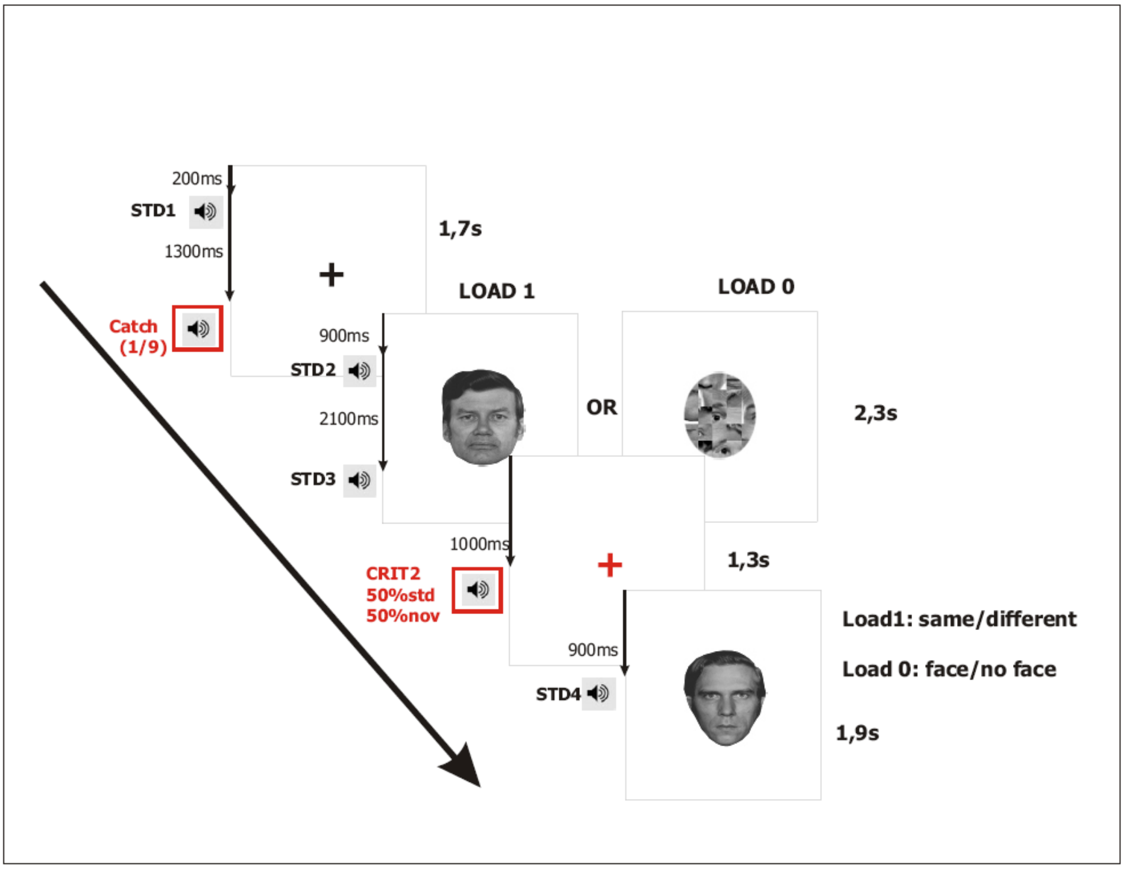

Figure 9.

c. ERP methods

The ERP session had a duration of 68 minutes, divided into two blocks, one for each condition, and with frequent participant-controlled pauses every four minutes

approximately. In each condition block, 244 trials were presented, half novel trials and half standard trials. Only responses within 900 ms from the test face were accepted.
The electroencephalogram (EEG) was continuously digitized at a rate of 500 Hz (band pass DC-250Hz) from 64 electrodes placed on the scalp. The electro-occulogram was recorded from the electrodes Nz (between the eyebrows) and IO1 and IO2 (below each eye). The electrodes were mounted in an elastic cap, and the common reference electrode for all electrodes was placed on Cz.
ICA-based blink correction was performed for all subjects using the BrainVision Analyzer package. All further analyses were performed using Eeprobe (ANT software). The continuous EEG data was filtered offline between 0.1 and 30 Hz. All trials exceeding +/- 100 uV on any channel were excluded from further analyses. Standard and novel trials were averaged separately for each condition, with an epoch of 700 ms, using a 100 ms pre-stimulus baseline. Novel minus standard difference wave were calculated for each condition.

d. fMRI methods

The fMRI session had a duration of 45 min, divided into four runs of 10 minutes each, and five minutes of anatomical scan (1mm slice thickness, TR=13, TE=3, in plane resolution 1x1x1, FOV 256), which was always performed at the beginning of the session. Each run included 80 trials and 320 volumes were acquired (TR= 1,8 s, 18 slices, 5mm slice thickness, TE= 50 ms, matrix 64^2, pixel size 3x3). All participants practiced the task outside the scanner immediately before the session started. Response time was prolonged to 1200 ms due to longer RTs inside the scanner.
Data analysis was performed using the BrainVoyager package; however, to the date only the preprocessing of the fMRI data has been performed.

e. Results

Behavioral results: A two-factor ANOVA including WM load (0,1) and stimulus type (novel, standard) revealed that the WM load condition was harder to perform as indexed by lower HRs (ERP: $F(1,13)=13{,}57$, $p=0{,}003$; fMRI: $F(1,13)=10{,}06$, $p=0{,}007$) and slower RTs (ERP: $F(1,13)=28{,}73$, $p<0{,}001$; fMRI: $F(1,13)=26{,}97$, $p<0{,}001$). There was a facilitation effect also in both the fMRI ($F(1,13)=5{,}78$, $p=0{,}032$) and the ERP

(F(1,13)=29,42, p<0,001) sessions, showing faster RTs in novel trials. The interaction did not reach significance; however, there was a trend towards the facilitation effect being smaller in the load 1 condition compared to the no-load condition.

ERPs: On the difference wave, the N1/MMN, P3a and RON components could be identified, even when no behavioral distraction but rather a facilitation effect was present in this task. This is an interesting result that calls for a re-interpretation of these components.

The P3a component seemed to be attenuated under WM load; however, this result is pending from further statistical analyses which still have to be performed.

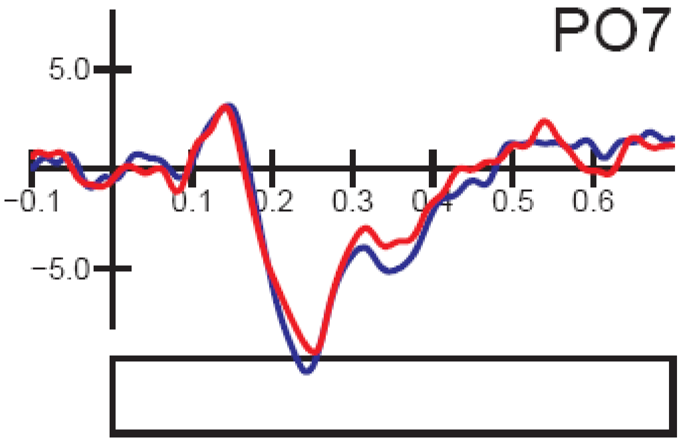

Figure 10. Difference waves for condition WM1 (red) and WM0 (blue) on PO7.

5. Future work

This project is still in process and further work needs to be done in order to accomplish the established objectives. The ERP and fMRI data will be analyzed separately first and later also in combination, in order to more precisely describe the spatio-temporal dynamics of the effects found.

6. References

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