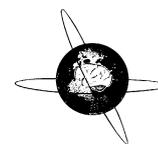


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## Is two better than one? A cross-modal oddball paradigm reveals greater sensitivity of the P300 to emotional face-voice associations

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### ABSTRACT

**Objective:** Studies exploring neurophysiological correlates of main psychiatric disorders have commonly used event-related potentials (ERP) during a visual or an auditory oddball task. The main results concern modulations of the P3b amplitude and/or latency. The present study aims to increase the clinical sensitivity of these P3b modulations by using a more ecological oddball design, using synchronized pairs of audio-visual emotional stimuli.

**Method:** Two groups of healthy participants, one composed of controls and the other of students displaying anxious and depressive tendencies completed visual, auditory and audio-visual (cross-modal) oddball tasks, in which they had to detect deviant happy and sad stimuli among neutral ones as quickly as possible. Behavioral performance and P3b ERP data were analyzed.

**Results:** Subjects displaying anxious and depressive tendencies exhibited lower P3b amplitude than the controls, but only in the cross-modal oddball task.

**Conclusions:** Although the two groups of subjects differed in their levels of co-morbid anxiety and depression, unimodal visual and auditory oddball tasks did not allow us to detect this difference by P3b amplitude modulations, but the cross-modal task did.

**Significance:** These results suggest that a cross-modal oddball design should be used in future studies to increase the sensitivity of the P300 amplitude differences between healthy participants and those with clinical symptoms.

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### 1. Introduction

The specialty of electrophysiology is to offer tools that can monitor the brain's electrical activity with a high temporal resolution (up to 1 ms). Cognitive event-related potentials (ERPs) allow us to monitor brain activity, ranging from sensory to higher cognitive processes, during the entire information-processing stream. Therefore, during a cognitive task, ERPs allow the electrophysiological component representing the onset of a dysfunction to be identified, and then the impaired cognitive stages to be inferred (Rugg and Coles, 1995). Today a growing literature shows that specific psychiatric disorders exhibit abnormal ERPs' components in particular conditions (e.g., Polich and Herbst, 2000) and at different latencies (e.g., Campanella and Philippot, 2006). Numerous studies have identified a number of early and late neuroelectric features that

seem to be anomalous in various psychiatric populations. Indeed, for instance, many studies have investigated whether early deficits can be evidenced on the information-processing stream in schizophrenia. In keeping with this, schizophrenic patients showed a reduction of the mismatch negativity (MMN) (Javitt et al., 1994), a negativity over fronto-central brain regions, recorded around 200 ms in response to auditory stimuli presenting a physical deviance (loudness, duration, frequency) as compared to a standard one, which is independent of attention and seems to reflect an automatic deviance detecting process of the auditory sensory cortex (see Näätänen et al., 2007, for a review). This indicates that a neurophysiological deficit in schizophrenia can be found already at the level of the sensory cortex. Moreover, this is also true in the visual domain, as a study of ours (Campanella et al., 2006) confirmed earlier results obtained by Foxe et al. (2001) showing that early visual components, such as the P100, the N100 and the N170, displayed reduced amplitude and longer latencies in schizophrenic patients. However, in many of these studies, the primary and most reported finding is P300 abnormalities (see Hansenne, 2006 for a review).

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P300 (or P3) is a long-lasting positive component that occurs between 300 and 700 ms after the onset of stimulation (Sutton et al., 1965; Desmedt et al., 1965). The P300 response is not a single phenomenon but can be divided into two main subcomponents: P3a and P3b (Squires et al., 1975). The P3b is the component recorded in response to task-relevant targets. It has a more parietal distribution and a longer latency, usually between 280 and 600 ms. The P3a component occurs after novel events, independent of task relevance, i.e., even when the subject is ignoring (has not been asked to attend to) rare stimuli. It has a more frontal distribution and its latency usually ranges from 220 to 280 ms (Hansenne, 2000). At a functional level, P3a is thought to reflect initial signal evaluation (and is particularly modulated by stimulus novelty) (Knight, 1991), whereas P3b is associated with a decisional “response-related stage”, representing the end of the cognitive information-processing stream, indexing diverse functions such as memory updating (Polich and Herbst, 2000) or cognitive closure (Verleger, 1988), and involving the activation of inhibitory processes over widespread cortical areas (Tomberg and Desmedt, 1998). Overall, the P300 and its underlying subprocesses are thought to reflect rapid neural inhibition of ongoing activity to ease transfer of stimulus/task information from frontal (P3a) to temporal-parietal (P3b) locations, in order to heighten memory operations (Polich, 2007).

The ERP task most frequently used to elicit the P300 is the ‘oddball task’, in which participants are confronted with a train of repeated ‘standard’ stimuli (e.g., a sound of 1000 Hz, which occurs 80% of the time), and a few ‘deviant’ stimuli (e.g., a sound of 2000 Hz, 20% occurrence rate). They have to detect the deviant stimuli as quickly as possible (typically by pressing a button or by mental counting). In healthy individuals, the P3b occurs following the presentation of the target stimulus, and is of maximum amplitude over the parietal area with a peak latency of about 300–350 ms when auditory stimuli are used, and 350–450 ms in the visual modality (see Linden, 2005 for a review). With this in mind, a large number of ‘ERP oddball’ studies have been carried out to investigate this neurophysiological marker in the main psychiatric disorders. Diverse cognitive functions, such as attention and memory, are affected by psychiatric disorders (e.g., Bearden et al., 2006 for depression; Evans et al., 1997 for schizophrenia; Noël et al., 2001 for alcoholism), and a reduction of P3b amplitude and prolongation of P3b latency are common and logical findings in these situations (e.g., Bruder et al., 1991 for major depression; Duncan et al., 1987 for schizophrenia; Porjesz and Begleiter, 2003 for chronic alcoholism). These findings show that, when appropriate procedures are used, P3b brain potential can provide a highly useful means to monitor the efficiency of the cognitive information-processing stream (Polich, 1998, 2004).

Interesting data have also been obtained on the use of this P3b component as a biological marker of psychopathological disorders. Indeed, there is general agreement that a reduction of P3b amplitude is (1) a state marker of depression, i.e., a biological marker that is altered during the disease but that stabilizes after clinical remission (Karaaslan et al., 2003); (2) a trait marker of schizophrenia, i.e., a biological parameter that is changed during and after the disease (Mathalon et al., 2000); (3) a vulnerability marker of alcoholism, i.e., a biological variable that is altered before the emergence of the disease (high-risk children of alcoholic parents) (e.g., Hill et al., 1999).

Although a large number of studies have provided evidence of the relevance of P3b for its use as a biological marker, its clinical sensitivity has been hampered by the fact that its parameters (amplitude, latency) are diagnostically unspecific and not reliable enough to be useful for individual patients (Pogarell et al., 2007). In other words, although differences in P3b amplitude and latency can indicate the severity of a clinical state and its possible

evolution, its clinical value as a diagnostic index is low, mainly due to its considerable inter-individual variations, its functional heterogeneity (P3a vs. P3b) and its distributed neural generation (Campanella and Philippot, 2006). Therefore, a current and important challenge for neurophysiologists is to discover novel and appropriate procedures to enhance the applicability and sensitivity of the P3b component in clinical settings.

In everyday life, sensory events are not experienced in isolation. Indeed, human beings are constantly confronted with multiple stimuli that are integrated into a unitary perception of the environment (see, for example, Calvert, 2001; Joassin et al., 2004). Nevertheless, because the sensory modalities have usually been explored separately in the fields of psychology and neuroscience, the mechanisms leading to cross-modal integration have only been explored during the last decade (see Campanella and Belin, 2007 for a review). They require additive ‘associative’ processes to integrate unimodal events (for instance, a visual happy face with an auditory happy voice) into a single perception. Interestingly, this complex activity has been shown to be performed differently in psychopathological populations, such as schizophrenics (Surguladze et al., 2001) and chronic alcoholics (Maurage et al., 2008).

This is particularly important because (1) although most empirical studies have used unimodal stimuli, multimodal stimuli, and, in particular, auditory–visual stimuli, are more common in everyday life; (2) the cross-modal activities involved in complex integrative processes are different from those implicated in unimodal (visual or auditory) ones, and may therefore be specifically altered in some clinical afflictions. Our aim in the present study was to explore these cross-modal findings by adapting the classical ERP oddball design, which has been used to work with a single modality.

The ubiquity of cross-modal interactions is particularly evident in the field of emotion processing because the perception of emotions is often based in our everyday life on several sensory aspects, including principally emotional facial expression (visual modality) and emotional prosody (auditory modality) (unless in some particular circumstances, such as during a phone call or when we’re listening to radio or watching a silent movie). Unimodal exploration of emotion is thus nowadays considered insufficient to comprehend the complexity of ‘normal’ and ‘pathological’ emotion processing (Ethofer et al., 2006). Variants of the classical ‘unimodal’ oddball paradigm (using, for instance, ‘neutrality’ as the frequent stimulus and different emotions such as fear, happiness and sadness as the deviant stimuli) have proved to be useful to show P3b abnormalities in clinical psychopathological populations. This is true in both the visual modality (e.g., Campanella et al., 2006; Maurage et al., 2007a) and the auditory one (e.g., Kaustio et al., 2002; Kawasaki et al., 2007). This is also true for subclinical populations, i.e., for people showing ‘clinical tendencies’ (e.g., psychopathic tendencies) without the full-blown symptoms (Campanella et al., 2005). Synchronized congruent visual–auditory stimulations (e.g., a happy face with a happy voice) are more realistic than incongruent ones. As the cross-modal processing needed to integrate the products of unimodal processes into a single emotional representation may be specifically altered in psychopathological populations, we felt that using an emotional cross-modal oddball design might enhance the sensitivity of the procedure by increasing the observable P3b differences between healthy and psychopathological groups of participants.

To test this hypothesis, we selected two groups of healthy participants for the present study, with one composed with people displaying anxious and depressive tendencies. A recent study by Rossignol et al. (2008) showed, by means of a visual oddball emotional paradigm, that healthy subjects displaying depressive tendencies with co-morbid anxiety did not differ from healthy participants on the P3b component. The authors suggested that this absence of effect is probably due to the subclinical level of

the symptoms, and/or to a 'smoothing' effect due to the co-morbidity between non-clinical depression (which is known to increase P3b latencies) and anxiety (which is known to decrease them).

We suggest that this lack of effect may actually be due to a lack of sensitivity in the unimodal visual oddball design, and that, as our brain is intrinsically multimodal (Campanella and Belin, 2007), using a cross-modal oddball design may help to increase the sensitivity of the test, so that psychopathological differences can be detected, even at a subclinical level. In the present experiment, all the subjects were asked to complete a visual oddball task, an auditory oddball task and a cross-modal (visual–auditory) oddball task. We hypothesized that P3b differences between the healthy and subclinical participants would be observable in the cross-modal task, but not in the unimodal (visual and auditory) situations.

## 2. Methods

### 2.1. Participants

Thirty students were selected from a group of 100 students at the University of Louvain on the basis of their scores on the Spielberger Trait Anxiety Inventory (STAI-T, Spielberger et al., 1983) and the 13-item Beck Inventory Depressive Scale (BDI, Beck and Steer, 1987). All the participants were right-handed, between the ages of 18 and 24, with normal/corrected vision, normal hearing, no medication and no history of neurological disease. We used median splits on the STAI-T and BDI scores to create standardized scores for anxiety and depression (median: STAI-T = 50; BDI = 6). We then created two groups of 15 subjects each, a control group (CG) of healthy participants, and an experimental group (EG) of healthy students displaying depressive and anxious tendencies<sup>1</sup> (BDI:  $t(28) = -11.297$ ;  $p < .001$ ; STAI-T:  $t(28) = -4.311$ ;  $p < .001$ ). We matched the groups on age ( $t(28) = -0.616$ ; N.S.) and gender (as gender differences in event-related potentials (ERPs) for emotional processing have already been shown to occur, see Campanella et al., 2004) ( $\chi^2(1) = 0.536$ ; N.S.). The group characteristics are reported in Table 1.

### 2.2. Task and procedure

All the participants carried out three emotional oddball tasks (visual, auditory, and cross-modal), in which they were confronted with one regularly repeated standard neutral stimulus and two deviant stimuli which they had to detect as quickly as possible by clicking on a button with the right forefinger. This set-up is similar to that used by Maurage et al. (2007a). In the visual oddball task, the standard stimulus was a neutral face and the deviant stimuli were the same face displaying happiness or sadness. In the auditory oddball task, the standard stimulus was a neutral voice pronouncing the word 'papier' (French for 'paper') and the deviant stimuli were the same voice pronouncing the same word with an emotional prosody of happiness or sadness. In the cross-modal auditory–visual oddball task, pairs of synchronized and congruent faces and voices were displayed to participants (frequent stimulus: a neutral face and a neutral voice; deviant stimuli: a happy face with a happy voice, and a sad face with a sad voice).

For the visual oddball task, four different faces (two male and two female) each displaying neutral, happy and sad expressions were selected from Ekman & Friesen's set of standardized pictures (1976). Each face was used for one block, comprising a total of 110

**Table 1**

The means and standard deviations (in parentheses) of the control (CG) and experimental (EG) groups' scores on the BDI and STAI-T psychological tests.

	Gender (M/F)	Age	BDI	STAI-T
CG	9/6	19.7 (1.86)	2.2 (1.74)	45.1 (8.0)
EG	7/8	20.1 (1.68)	9.3 (1.71)	56.8 (6.8)

stimuli (86 frequent neutral, 12 deviant happy and 12 deviant sad). In the visual condition, all the subjects completed four blocks (440 stimuli), with the order of the blocks (i.e., the face used) being counterbalanced across participants.

Similarly, in the auditory oddball task, four different voices (two male and two female) each pronouncing the word 'papier' in a neutral, a happy and a sad way were chosen from the validated battery of vocal emotional expressions (Maurage et al., 2007b). All the subjects then completed four blocks (110 auditory stimuli in each block), with the order of the blocks being counterbalanced across participants. Finally, in the cross-modal auditory–visual oddball task, each visual stimulus was combined with an auditory stimulus in order to create 12 auditory–visual stimuli (always congruent on gender and emotion; e.g., male face A neutral with male voice A neutral; male face A happy with male voice A happy; male face A sad with male voice A sad; and so on with male face B and female faces C and D). As in the visual and auditory oddball tasks, the subjects each completed four blocks (440 bimodal stimuli in total), and the order of the blocks varied between participants.

Overall, each participant completed 12 blocks of stimuli (4 visual, 4 auditory, and 4 cross-modal). Each block took around 3 min; during the intervals between blocks, the participants were informed about what kind of block they would encounter next (visual, auditory or cross-modal). The order of the 12 blocks was counterbalanced across subjects.

During the ERP recordings, each participant individually sat in a darkened room on a chair placed one meter from the screen, with his or her head restrained in a chin rest. The visual stimuli subtended a visual angle of  $3^\circ \times 4^\circ$ . The auditory stimuli were presented binaurally via headphones. Each stimulus (face alone; voice alone; or synchronized face-voice) was presented for 700 ms. A black screen was displayed between stimuli, for a random duration of between 500 and 1000 ms. From the onset of the stimulus, the participants had at least 1200 ms to answer. Response times and error rates were recorded. There were two categories of error. Omission (i.e., not pressing the answer key when a deviant stimulus appeared) and false recognition (i.e., pressing the answer key when a standard stimulus appeared). Participants were told that speed was important but not at the cost of accuracy. Only correct answers (i.e., deviant stimuli for which the subject pressed the answer key) were used in the analysis of reaction times and ERPs.

### 2.3. EEG recording and analysis

The EEG was recorded by 32 electrodes mounted in an electrode Quick-Cap. Electrode positions included the standard 10–20 system locations and intermediate positions. Recordings were made with a linked mastoid physical reference but re-referenced using a common average (Bertrand et al., 1985). The EEG was amplified by battery-operated A.N.T.<sup>®</sup> amplifiers with a gain of 30,000 and a band-pass of 0.01–100 Hz. The impedance of all the electrodes was kept below 20 k $\Omega$ . The EEG was continuously recorded (sampling rate 500 Hz, A.N.T. Eeprobe software) and trials that were contaminated by EOG artifacts (mean of 15%) were eliminated off-line, using the procedure developed by Semlitsch et al.

<sup>1</sup> The STAI-T scores grouped the participants as follows: less than 36, very low; 36–45, low; 46–55, normal; 56–65, high; more than 65, very high. A cut-off score of 10 was used on the BDI to signify students displaying a clinical level of depression (Furlanetto et al., 2005).

(1986), which consists in computing for each individual participant an average artefact response based on a percentage of the maximum eye movement potential (generally recorded on prefrontal electrodes). The EOG response was therefore subtracted from the EEG channels on a sweep-by-sweep, point-by-point basis in order to obtain ocular artefact-free data. Epochs beginning 200 ms prior to the stimulus onset and continuing for 800 ms were created. Three parameters were coded for every stimulus (1) the modality of the task (visual; auditory, cross-modal); (2) the type of stimulus (rare happy, rare sad, frequent); (3) the response type (keypress for deviant stimuli, no keypress for frequent ones). Data were filtered with a 30 Hz low-pass filter.

For each modality and each subject, the component of interest (the P3b) was investigated by gathering individual values of maximum peak amplitudes and peak latencies. These data were obtained from the classical electrodes used to define the P3b component and onto which the maximum amplitudes were recorded for this component (P3, Pz, P4) and by computing the classical 'Deviant minus Frequent' subtraction (e.g., Polich, 2004). The data were explored using repeated measures of analysis of variance (ANOVA), with the Greenhouse–Geisser correction applied when appropriate, and two-tailed Pearson correlations, using S.P.S.S. 17.02®.

### 3. Results

#### 3.1. Behavioral data

The participant's responses were 98% correct, and only the correct response latencies were statistically analyzed. The data are summarized in Table 2. A  $2 \times 3 \times 2$  ANOVA on reaction times (RTs) for correct responses was computed, with group (CG, EG) as the between-subject factor, and modality (visual, auditory, cross-modal) and emotion (happy, sad) as the within-subject variables. The following results were significant at the  $p < .05$  level:

(1) A main effect of modality ( $F(2, 56) = 80.877, p < .001$ ) and a main effect of emotion ( $F(1, 28) = 195.329, p < .001$ ). Post hoc Bonferroni tests showed that while the auditory and cross-modal tasks did not differ significantly ( $p = .098, N.S.$ ), the reaction times were longer for the visual task than for the auditory ( $p < .001$ ) and the cross-modal ( $p < .001$ ) ones. Moreover, mean reaction times suggest that happiness was detected more quickly than sadness (416 ms vs. 448 ms,  $p < .001$ );

(2) A significant modality  $\times$  emotion interaction ( $F(2, 56) = 14.237, p < .001$ ). Paired  $t$  tests suggest that, independent of the group, the response latencies were shorter for happiness than for sadness in each modality, with the largest difference in the auditory condition (visual difference: 17.36 ms,  $t(29) = -5.004, p < .001$ ; cross-modal difference: 32.86 ms,  $t(29) = -7.59, p < .001$ ; auditory difference: 45.73 ms,  $t(29) = -12.55, p < .001$ ).

#### 3.2. ERP data

##### 3.2.1. P3b latencies

P3b latencies were analyzed in a  $2 \times 3 \times 3 \times 2$  ANOVA, with group (CG, EG) as a between-subjects factor, and modality (visual, auditory, cross-modal), electrode (P3, Pz, P4) and emotion (happy, sad) as within-subject variables. The results matched those found for RTs (see Table 2):

(1) A significant main effect of modality ( $F(2, 56) = 55.748, p < .001$ ) and a significant main effect of emotion ( $F(1, 28) = 50.734, p < .001$ ). Post hoc Bonferroni tests showed that the visual condition generates longer P3b latencies than the auditory ( $p < .0001$ ) and cross-modal ( $p < .0001$ ) ones, and that the P3b latencies were shorter for happiness than for sadness (380 ms vs. 402 ms,  $p < .0001$ ).

(2) A modality  $\times$  emotion interaction ( $F(2, 56) = 4.537, p = .016$ ) was also present, suggesting that the difference between the happiness and sadness emotions was, independently of the group, larger in the auditory (difference: 36.13 ms,  $t(29) = -3.949, p < .001$ ) than in the visual (difference: 17.16 ms,  $t(29) = -3.004, p < .001$ ) or the cross-modal (difference: 26.93 ms,  $t(29) = -4.0095, p < .001$ ) condition.

##### 3.2.2. P3b amplitudes

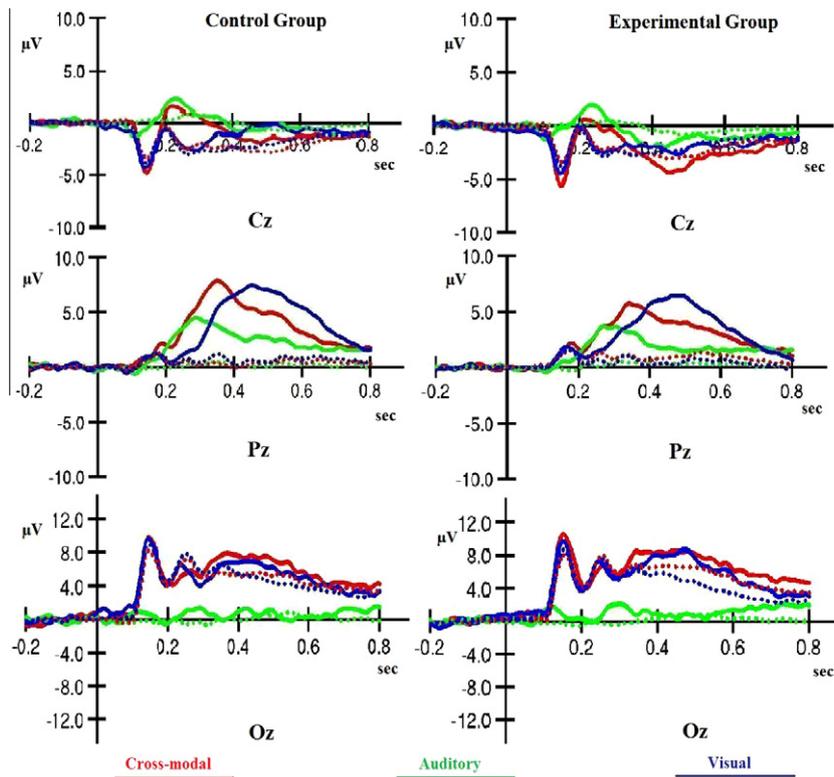
We computed a  $2 \times 3 \times 3 \times 2$  ANOVA on P3b amplitude values, with group (CG, EG) as the between-subjects factor, and modality (visual, auditory, cross-modal), electrode (P3, Pz, P4), and emotion (happy, sad) as within-subjects variables. Our hypothesis was that the difference between CG and EG would be enhanced in the cross-modal task. In keeping with this, we obtained a significant main effect of modality ( $F(2, 56) = 45.428, p < .001$ ) and a significant modality  $\times$  group interaction ( $F(2, 56) = 3.464, p = .038$ ) (see Figs. 1 and 2 for illustration). This interaction was independent of the emotion displayed by the deviant stimuli and of the electrode (emotion  $\times$  modality  $\times$  group:  $F(2, 56) = 0.720, N.S.$ ; electrode  $\times$  modality  $\times$  group:  $F(4, 112) = 0.726, N.S.$ ; electrode  $\times$  emotion  $\times$  modality  $\times$  group:  $F(4, 112) = 0.625, N.S.$ ).

In order to better define the modality  $\times$  group interaction, we performed independent  $t$  tests on the P3b amplitude values (means of happy and sad deviant stimuli) at the Pz electrode. The Pz electrode was the location where the P3b displayed the maximum amplitude (main effect of electrode:  $F(2, 56) = 17.894, p < .001$ ). The results show a significant difference between the CG and the EG on the cross-modal task ( $t(28) = 2.098, p = .04$ ), but not on the visual ( $t(28) = 0.459, N.S.$ ) or the auditory ( $t(28) = 0.960, N.S.$ ) ones (Table 3).

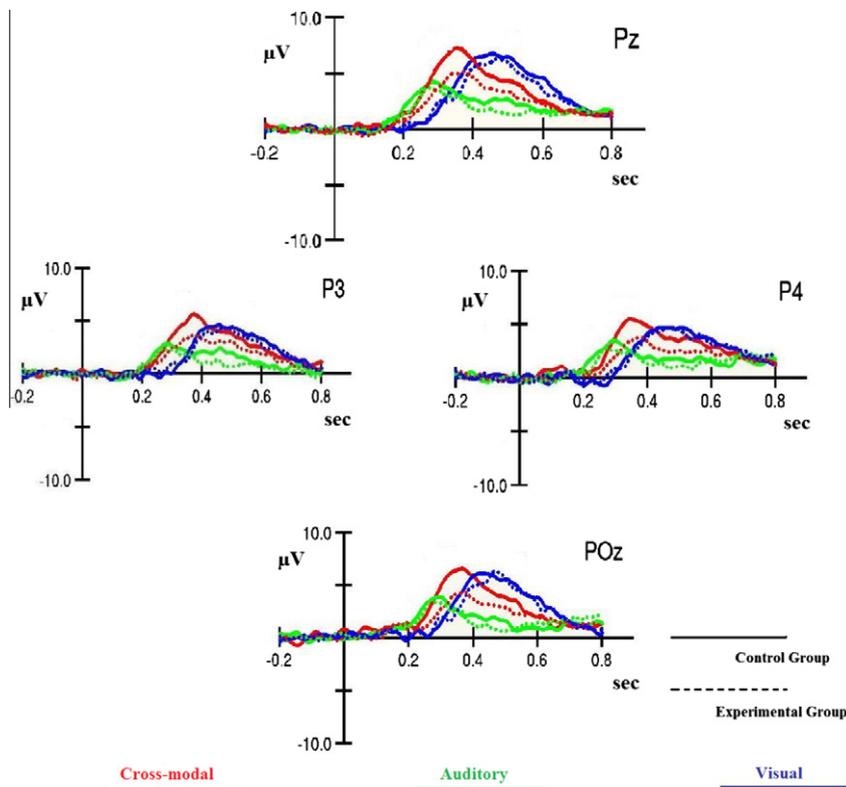
Finally, Pearson correlations were performed to test the idea that this difference between the groups on the cross-modal task is linked to the experimental group's subclinical scores on the BDI and STAI-T. The results show that the higher the BDI and

**Table 2**  
The means and standard deviations (in parentheses) of the reaction times (ms) and P3b latencies (ms) for deviant stimuli detection as a function of group (control (CG), experimental (EG)) and modality (visual (V), auditory (A), cross-modal (AV)).

	V – happy	V – sad	A – happy	A – sad	AV – happy	AV – sad
CG RTs	457 (43)	473 (37)	364 (79)	409 (81)	383 (66)	410 (52)
EG RTs	490 (36)	510 (34)	390 (58)	436 (63)	412 (36)	451 (33)
CG P3b lat	431 (41)	457 (41)	303 (83)	323 (100)	356 (38)	387 (59)
EG P3b lat	451 (35)	459 (40)	306 (59)	328 (79)	374 (63)	397 (66)



**Fig. 1.** Illustration of the base waveforms (thick lines, oddball stimuli; dashed lines, frequent ones) on three midline scalp electrodes (Cz, Pz, Oz) for each modality in the control and experimental groups.



**Fig. 2.** The mean difference amplitude ( $\mu\text{V}$ ; subtraction rare-frequent) of the P3b component on four parietal electrodes (P3, Pz, POz, P4) for each modality in the control and experimental groups.

**Table 3**

The means and standard deviations (in parentheses) of the P3b amplitudes ( $\mu\text{V}$ ) recorded by the control (CG) and experimental (EG) groups in each modality.

	Visual	Auditory	Cross-modal
CG	7.51 (2.14)	5.09 (2.35)	7.89* (2.72)
EG	7.12 (2.50)	4.34 (1.88)	5.98* (2.21)

\* Significant at  $p < .05$ .

STAI-T scores, the lower the P3b amplitude—but only on the cross-modal task (see Table 4).

#### 4. Discussion

The main objective of the present study was to compare the P300 differences observed thanks to the use of classical unimodal visual and auditory oddball tasks, with those obtained from a new kind of oddball paradigm, based on the presentation of synchronized emotional audio-visual stimuli.

To this end, we selected two groups of healthy participants, one composed of controls and the other of students displaying anxious and depressive tendencies. Each participant had to complete three oddball tasks—one visual, one auditory and the third a cross-modal audio-visual task. On each task, the participants had to detect the stimuli showing happiness or sadness from a stream of neutral stimuli.

Overall, it is important to emphasize that the results show perfect congruency between the RTs and the P3b latencies. As in previous studies using emotional oddball designs (e.g., Campanella et al., 2005, 2006), faster RTs and earlier P3b latencies were found with happy stimuli than with sad ones. This difference was greatest in the unimodal auditory condition. Moreover, the two groups of participants did not differ significantly in their RTs or P3b latencies when detecting deviant stimuli. This suggests that oddball tasks are simple enough for subjects displaying a subclinical level of anxious and depressive tendencies not to differ from the healthy controls in their speed and accuracy in detecting deviant emotional stimuli amongst neutral ones.

This absence of differences on RTs and P3b latencies is an important finding of the present study. Although the most common result associates a delay in P3b with clinical depression (Bange and Bathien, 1998; Kayser et al., 2000), our results are supported by those of a recent study investigating subclinical levels of depression associated with co-morbid anxiety by means of an emotional (visual) oddball design (Rossignol et al., 2008) which found no significant differences in P3b latencies between the control and the experimental group. To replicate this absence of effect, we intentionally selected two groups of people as similar as possible in age and gender, in order to increase the possibility that they would not show any significant differences on RTs and P3b latencies when performing a simple oddball task. Nevertheless, these two groups were different: even if composed with healthy participants, i.e., people free from clinically significant symptoms, one was composed of participants displaying anxious and depressive

symptoms, albeit at a non-clinical level. Our main argument is that, as ERPs have the potential to detect even minor neurocognitive restrictions (Rugg and Coles, 1995; Maurage et al., 2009), the use of more elaborate experimental designs should allow these subtle differences between groups to emerge.

With this in mind, we opted for a new variant of the commonly used oddball design (classically using unimodal visual or auditory stimuli), in which we used synchronized pairs of audio-visual stimuli. The rationale for this choice was mainly based on the fact that cross-modal situations are highly ecological (Brefczynski-Lewis et al., 2009), and that it has already been shown that the processing of emotional cross-modal situations may be impaired by some psychopathological disorders (Surguladze et al., 2001; Maurage et al., 2008). The main result of the present study is that a significant P3b amplitude difference was found, on the cross-modal oddball task only, between the control (CG) and experimental (EG) groups. P3b amplitude modulations are a classical finding when healthy participants are compared to clinical populations (e.g., Kayser et al., 2000; Campanella et al., 2005; Maurage et al., 2007a). We have now shown that when the two groups of subjects differ in their subclinical level of co-morbid anxiety and depression, unimodal visual and auditory oddball tasks may not allow us to detect this difference using P3b amplitude modulations, but a cross-modal task has greater power.

The cross-modal processing of multimodal information involves complex associative processes, including the integration of unimodal visual and auditory products into a single, coherent representation. This is especially true in the emotional domain (see Campanella and Belin, 2007 for a review). For instance, it is known that the neural processes involved in the processing of a happy face and a happy voice are functionally segregated, but human brains can form a unique representation of this 'happy' stimulation by means of associative processes. Interestingly, although neurobiologists have traditionally assumed that multisensory integration is a higher order process that occurs after extensive sensory signals processing, recent findings demonstrate multisensory convergence in low level cortical structures that were generally believed to be unisensory in function (e.g., Schroeder and Foxe, 2005). For our purpose, it is important to note that these emotional integrative processes can be specifically and independently impaired in psychopathology. For instance, de Jong et al. (2009) have recently shown that cross-modal interactions between faces and voices were impaired in schizophrenic patients, while the unimodal processing of faces and voices seemed to be preserved. By using an emotional cross-modal oddball design, which is more ecological and requires additional associative processes, the present study has helped to evidence differences that were not observable either at a behavioral level, or by using a classic unimodal oddball procedure.

This result may be particularly important in the area of clinical neurophysiology. In our experiment there was no significant difference between the two groups at the behavioral level (i.e., on RTs). This absence of behavioral differences was matched at the neurophysiological level, as no P3b latency effect was evidenced on the unimodal tasks. Despite these similarities, we know that our participants were different, based on the experimental group's anxious and depressive tendencies. A cross-modal procedure allowed us to detect this difference, which manifested itself as a significant P3b amplitude modulation in the subclinical group. This suggests that the P3b is sensitive even to subclinical symptoms.

Obviously, these results are preliminary and should be replicated on clinical populations. For example, it would be interesting to investigate whether there are P300 differences between healthy and clinical subjects on cross-modal oddball designs. If so, this might enable several steps of clinical severity to be defined, for

**Table 4**

Pearson correlations between the BDI and STAI-T scores and the P3b amplitude.

	Visual	Auditory	Cross-modal
BDI/P3b amplitude	$r = -.194$	$r = -.325$	$r = -.460^*$
STAI-T/P3b amplitude	$r = -.301$	$r = -.263$	$r = -.457^*$

\*  $p = .011$ .

example if a greater P300 difference is linked to more severe clinical symptoms. In order to increase the ecological validity of face-voice pairs, dynamic stimuli (not a static face, but a moving image pronouncing a word) could be used (Schweinberger et al., 2007). It would also be important to investigate whether the present results are potentiated by the fact that we used an emotional cross-modal task, or if bimodal stimulations are sufficient per se to generate such results. Finally, as suggested in the introduction, we would like to outline that we are totally aware that such P300 deficits may be due to earlier components, may obviously affect subsequent processing stages (such as for instance, N400 component), and that all these ones should certainly be taken into account in further “cross-modal” studies. Although further work is still needed to refine our results, we think that our empirical data deserve attention, and should be tested to see if they represent an appropriate procedure for enhancing the applicability and sensitivity of the P3b measurement in clinical settings.

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