fMRI Identifies the Right Inferior Frontal Cortex as the Brain Region Where Time Interval Processing is Altered by Negative Emotional Arousal

Micha Pfeuty,^{1*} Bixente Dilharreguy,¹ Loïc Gerlier,² and Michèle Allard^{1,2,3}

¹University of Bordeaux, INCIA Department, CNRS UMR 5287, F-33000, Bordeaux, France

²CHU de Bordeaux, Service de Médecine Nucléaire, Bordeaux, France

³EPHE, Département de Neurobiologie Intégrative et Adaptative, Bordeaux, France

Abstract: The reason why human beings are inclined to overestimate the duration of highly arousing negative events remains enigmatic. The issue about what neurocognitive mechanisms and neural structures support the connection between time perception and emotion was addressed here by an event-related neuroimaging study involving a localizer task, followed by the main experiment. The localizer task, in which participants had to categorize either the duration or the average color of visual stimuli aimed at identifying the neural structures constitutive of a duration-specific network. The aim of the main experiment, in which participants had to categorize the presentation time of either neutral or emotionally negative visual stimuli, was to unmask which parts of the previously identified duration-specific network are sensitive to emotionally negative arousal. The duration-specific network that we uncovered from the localizer task comprised the cerebellum bilaterally as well as the orbitofrontal, the anterior cingulate, the anterior insular, and the inferior frontal cortices in the right hemisphere. Strikingly, the imaging data from the main experiment underscored that the right inferior frontal cortex (IFC) was the only region within the duration-specific network whose activity was increased in the face of emotionally negative pictures compared to neutral ones. Remarkably too, the extent of neural activation induced by emotionally negative pictures (compared to neutral ones) in this region correlated with a behavioral index reflecting the extent to which emotionally negative pictures were overestimated compared to neutral ones. The results are discussed in relation to recent models and studies suggesting that the right anterior insular cortex/IFC is of central importance in time perception. *Hum Brain Mapp* 36:981–995, 2015. © 2014 Wiley Periodicals, Inc.

Key words: time perception; emotion; functional magnetic resonance imaging (fMRI); inferior frontal cortex; anterior insular cortex

*Correspondence to: Micha Pfeuty, Aquitaine Institute for Cognitive and Integrative Neuroscience (UMR CNRS 5287), University of Bordeaux, 146 rue Leo Saignat, 33076 Bordeaux, France.

E-mail: micha.pfeuty@u-bordeaux.fr

Received for publication 6 May 2014; Revised 10 October 2014; Accepted 21 October 2014.

DOI: 10.1002/hbm.22680

Published online 4 November 2014 in Wiley Online Library (wileyonlinelibrary.com).

INTRODUCTION

It is a commonplace to say that human beings have an innate ability to perceive time and estimate its passage and that their perception of time is affected by their emotional states. Such a capacity, which individuals continually use to plan any future action, is essential indeed in their everyday life for helping them make appropriate decisions and adapt to their ever-changing environment.

Yet, the neurocognitive mechanisms that underlie the interplay between time perception and emotions as well as the neural structures that support their connection are still mysterious. Access to this stimulating field of research in time psychology has opened only recently owing to the methodical listing and characterization of standardized affect-stimulating devices [Droit-Volet and Gil, 2009]. Numerous studies actually have shown that the duration of highly arousing negative, whether visual [Angrilli et al., 1997; Grommet et al., 2011], or auditory stimuli [Mella et al., 2011; Noulhiane et al., 2007], or facial expressions [Droit-Volet et al., 2004; Tipples, 2008] is subjectively perceived as longer than that of neutral stimuli. This effect could be explained within the “pacemaker-accumulator” model of interval timing [Gibbon, 1977] which states that the perceived duration of an event correlates with the number of time units discharged by a “pacemaker” emitting pulses with a certain frequency and gathered into an “accumulator” via a “switch” that closes and opens at the onset and the end of the event to be timed, respectively. Accordingly, time overestimation of highly arousing negative stimuli would primarily result from the acceleration of a pacemaker-mediated internal clock [Droit-Volet and Meck, 2007]. It is unclear, however, how such an effect might be generated at the neural level.

Neuroimaging techniques have been of considerable help to visualize brain areas that become activated during timing tasks. These include notably the cerebellum, the basal ganglia and cortical structures, such as the supplementary motor area (SMA) and the prefrontal cortex [Wiener et al., 2010 for a meta-analysis]. According to this meta-analysis, the SMA and the right inferior frontal cortex (IFC) are the only structures presenting significant voxels across a broad diversity of timing conditions [Wiener et al., 2010]. Although both regions are frequently activated in neuroimaging studies of time perception, more attention has been focused on the SMA (or the pre-SMA) which, together with the basal ganglia [Alexander et al., 1986], has been proposed to serve as the neural substrate of the clock mechanisms currently postulated in models of time processing [Pouthas et al., 2005]. The detection of timing deficits in patients suffering from pathologies associated with a deregulation of the dopaminergic (DA) network such as Parkinson’s disease (PD) [Harrington et al., 1998a; Pastor et al., 1992], schizophrenia [Carroll et al., 2009; Elvevåg et al., 2003], and attention deficit disorder [Rubia et al., 2009] together with experiments using DA antagonists or agonists in humans [Rammsayer, 1993, 1997, 1999] and animals, [Maricq and Church, 1983; Meck, 1996], concur indeed to implicate this network in time perception [Coull et al., 2011, for review]. As to the IFC, it has long been neglected as a potentially influential neural substrate for time processing, possibly due to the lack of lesion studies providing direct evidence of temporal processing impairment following damages to this brain region. This view has recently changed following the divulgation of a number of brain imaging studies regularly reporting

the participation of the IFC, usually in association with the anterior insular cortex (AIC) in a diversity of timing tasks [Kosillo and Smith, 2010, for review]. In addition, two recent studies reported disturbance in temporal processing following lesions in the right IFC [Gooch et al., 2011] or in the right AIC/IFC region [Monfort et al., 2014]. In one particularly instructive fMRI study [Livesey et al., 2007], participants had to execute two nearly identical experiments, both consisting in comparing either the duration or the color of two successive, flickering stimuli—the same in the two tasks—but differing in the difficulty of the control (color) task. In this way, the authors aimed to dissociate brain areas whose activation during the timing task truly reflected a time-directed neural activity from those reflecting some other task-related cognitive demands (e.g., memory and decision making). They could thus identify three time-related areas of activation: (i) a small region at the confluence of the IFC and the AIC, bilaterally, (ii) a small portion of the left supramarginal gyrus, and (iii) the putamen. However, they found that the pre-SMA was more active in the control than in the duration condition when the control task was harder, which implies that this structure is not specifically concerned with timing. The results of a temporal reproduction task in the range of several seconds also deserve to be evoked [Wittmann et al., 2010b]. The authors reported that neural activation was greater in the posterior insula during the encoding phase and, further, that it steadily increased to peak at the end of the stimulus, which is typical of an accumulation process. In contrast, neural activation in the SMA followed an inverse U-shape pattern. These findings led the authors to propose that the posterior insular cortex would represent the temporal accumulator unit postulated in the “pacemaker-accumulator” model of interval timing. Furthermore, a greater activation was observed both in the AIC/IFC region and the pre-SMA during the reproduction phase, hinting that these structures would cooperate in the storage and recovery of the representation of the memorized time interval. In other words, during the encoding of a duration, a representation of that duration would build-up in the posterior insula on which, then, would be founded our experience of time. However, an explicit judgment of that duration during the reproduction phase, which entails a deeper mental investment of the subject, would be formed in the AIC/IFC region after processing of the information stored in the posterior insula along their progression from the posterior to the anterior insula.

Remarkably, the conclusions from these experiments validate a recent model which proposes that the AIC (with the neighboring IFC) serves as a neural substrate for awareness of the passage of time because of its unique location at the convergence point of all types of emotional, interoceptive as well as exteroceptive, stimuli [Craig, 2009b]. Craig suggests that, at each instant, primary interoceptive representations collected in the dorsal posterior insula are integrated, along their posterior-to-anterior progression throughout the insula, with activities related to

salient environmental conditions captured in other parts of the brain, to produce “global emotional moments” that are associated with awareness. According to Craig, the duration of an event is evaluated through the accumulation of “global emotional moments”—a time interval corresponding to a series of “global emotional moments.” However, because the storage capacity of these “global emotional moments” is finite [Craig, 2009b], their rate of accumulation would be highly sensitive to the type of emotionally charged environmental cues. A subject exposed for a given period of time to an emotionally arousing negative event would overestimate the duration of that event because the “global emotional moments” would be filled and, thus, built up more rapidly in this condition than those building up in a closely similar, but emotionally neutral, condition. Assuming furthermore that activity in the insula during timing-related tasks reflects the rate of accumulation of “global emotional moments,” then, increased activity in this brain locus should correlate with a subjective impression of accelerated time course. This hypothesis is supported by the fact that, during the encoding of a temporal interval in the millisecond range (600 and 1,000 ms), the hemodynamic response of the mid-insula correlates with the length of the reproduced interval [Bueti and Macaluso, 2011].

The main objectives of this study was to try, first, identifying the neural network that participates in time processing and, next, extracting from this network the brain structures that suffer alteration under the influence of emotional stimuli, leading participants to perceive highly arousing negative stimuli as lasting longer than neutral ones. Such an emotion-induced distortion of time perception has been reported for durations from hundreds of milliseconds to a few seconds using different timing tasks, especially discrimination tasks [Droit-Volet and Meck, 2007]. In this investigation, we used a categorization task, in which a standard duration of 1,500 ms was to be memorized during the encoding phase and test stimuli were to be categorized as “shorter” or “longer” than the standard duration during the comparison phase. An event-related neuroimaging study was conducted that comprised a localizer task followed by the main experiment. The localizer task involved a procedure similar to a previously described one [Coull et al., 2004; Livesey et al., 2007; Morillon et al., 2009] in which visual stimuli consisting in shades of quickly varying colors were presented to participants whose task was to categorize either the duration or the average color of the stimuli. The participants were instructed to pay full attention to either the duration or the color along the whole stimulus duration to equate the attentional load in the two conditions. By subtracting from the neural network activated during the duration test the brain areas activated during the color test, we expected to be able to identify the brain areas that are truly concerned by time processing in our duration categorization tasks. In the main experiment, participants had to categorize the presentation time of either neutral or emotionally negative visual stimuli as shorter or longer than a stand-

ard duration. This experiment was expected to allow for the identification of brain areas that, among those pertaining to the duration-specific network (identified although the localizer task), would be sensitive to negative emotional arousing.

MATERIAL AND METHODS

Participants

Twenty nine right handed healthy volunteers (18 females, mean age 23 years, SD 4 years) without any previous history of neurological/psychiatric disorder and with normal or corrected-to-normal vision gave written informed consent to participate in the study, which was approved by the local ethics committee. One participant (1 female) was not included in the study because of movement artefacts during functional magnetic resonance imaging (fMRI) recordings. In addition, two participants (2 males) were excluded from the analyses of the localizer task due to technical problems and one participant (1 male) was excluded from the analyses of the main experiment because of abnormal performance in the emotional rating task.

fMRI Protocol

The localizer task and the main experiment were designed on E-prime 2.0 (Psychology Software Tools, Pittsburgh, PA) and run with a PC computer outside the scanner room. The stimuli were projected in the scanner room onto a computer screen via fiber optic cables. The participants watched the screen using a mirror mounted on the MRI headcoil. Their responses were recorded via an MRI-compatible box (fORP device, Current Designs, Philadelphia, PA). For the training session and the recognition and rating tasks performed outside the MRI, the visual stimuli were presented on a laptop computer screen and participants had to use the keyboard or the mouse to respond.

The Localizer Task: Duration vs. Color Categorization

The localizer task involved contrasting a time interval with a color categorization task. The experiment began with an encoding phase in which a central, circular, and uniform purple disk was presented six times with a delay of 2,000 ms at a standard duration of 1,500 ms. Participants had to memorize the duration and the color of the stimulus. This phase was followed by a comparison phase comprising 160 trials in which, at each trial, a disk of varying color was presented for a duration 20 % shorter (1,200 ms) or longer (1,800 ms) than the standard duration with a pseudo-random delay (2,000–5,200 ms) between each trial. Five different shades of colors from red to blue (red, brown, purple, indigo, blue) were rapidly (50 ms) and alternately presented [Coull et al., 2004]. The relative

Figure 1.

a: Schematic representation of the two first trials corresponding to a duration block and to a color block of the localizer task. **b:** Schematic representation of two trials of the main experiment run. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

proportion of each shade was either 1/4 red, 1/4 brown, 1/6 purple, 1/6 indigo, and 1/6 blue giving an overall perception of brown or 1/6 red, 1/6 brown, 1/6 purple, 1/4 indigo, and 1/4 blue giving an overall perception of indigo. Thus, there were two possible comparison stimuli for the color task (overall brown and overall indigo) as for the duration task (short and long).

For the duration categorization task, 80 trials were performed in which participants had to estimate whether the presentation time of the disk was shorter or longer than the standard duration of 1,500 ms. For the color categorization task, 80 trials were performed in which participants had to estimate whether the average shade of the disk was bluer or redder than the previously memorized purple disk. Participants were instructed to press on a MRI-compatible

response box the index finger or the middle finger of their right hand depending on whether their response was "bluer" ("shorter") or "redder" ("longer"), respectively. They were asked to respond as accurately as possible within less than 2,000 ms. To avoid switching processes, the localizer task was divided into eight blocks of 20 trials (four blocks per task). The beginning of each block was signaled by visual presentation of the task instruction during 2,000 ms: "Durée" for duration and "Couleur" for color. In addition, the letters "Du" or "Co" were presented on the top of the screen all along the blocks (Fig. 1a). Each block consisted of 20 trials. Duration and color blocks were presented alternately. There were two versions of the localizer task beginning with either a duration or color block. The total duration of the localizer task was 774 s (about 13 min).

A brief training session which consisted in two blocks for each categorization task, each comprising eight trials, was organized outside the MR scanner. Participants were asked to respond as accurately as possible within less than 2,000 ms, followed by a feedback of 1,000 ms.

The Main Experiment: Duration Categorization Task with Negative vs. Neutral Pictures

The main experiment involved contrasting negatively charged emotional pictures with neutral ones during a duration categorization task. The task began with an encoding phase in which a gray square was presented to participants six times with a delay of 2,000 ms at a standard duration of 1,500 ms for memorization. It was followed by a comparison phase of 160 trials in which, at each trial, an emotionally negative or neutral picture was presented at random for a duration 20% shorter (1,200 ms) or longer (1,800 ms) than the standard duration with a pseudo-random delay (2,000–5,200 ms) between each trial. Participants were instructed to estimate whether the duration was shorter or longer than the previously memorized standard duration and to respond as accurately as possible within less than 2,000 ms. The emotional charge of the pictures (negative/neutral) and the durations (shorter/longer) were randomized (Fig. 1b). Eighty pictures were used from the international pictures system [IAPS; Lang et al., 2008] rated from 1 to 9 on the arousal and valence scales (1 corresponding to “very low arousal level” or “very negative valence” and 9 to “very high arousal level” or “very positive valence”). Forty pictures were unpleasant and 40 pictures were neutral. Unpleasant pictures had an arousal level higher than 5 (mean: 6.24) and a valence level lower than 4 (mean: 2.66). However, the most unpleasant pictures (e.g., mutilated persons) were not included in the study because they could have been highly shocking for the participants. Neutral pictures had an arousal level lower than 4 (mean: 3.34) and an intermediate valence level between 4 and 6 (mean: 5.06). The pictures were presented twice, new and repeated pictures were intermixed and two presentations of the same picture were separated by one to 15 trials. There were two versions of the main experiment: the trial order of neutral and negative pictures in the second version was inversed compared to the trial order in the first version. In addition, two emotionally negative and two neutral stimuli were presented at the beginning of the experiment and two emotionally negative and two neutral stimuli were again presented at the end of the experiment. These additional stimuli were introduced to avoid serial position (primacy and recency) effects for the memory task performed at the end of the MRI session. The total duration of the main experiment was 806 s (about 13 min).

A training session, which consisted in two sessions comprising 20 trials with neutral pictures only (<arousal> 3.46, <valence> 5.01), was organized outside the MR

scanner. Participants were asked to respond as accurately as possible within less than 2,000 ms, followed by a feedback of 1,000 ms.

The level of anxiety was measured by the State-Trait Anxiety inventory [Spielberger et al., 1983] just before the MRI session because this parameter has been shown to modulate the effects of emotion on time perception [Bar-Haim et al., 2010]. A second evaluation of the state anxiety was made at the end of the MRI session to detect a possible change due to the MRI session. Furthermore, two additional tasks were performed after the MRI session to evaluate the recognition and emotional rating of the pictures presented in the main experiment. The eighty pictures (40 emotionally negative and 40 neutral) included in the main experiment were presented among 40 new pictures: 20 new emotionally negative (<arousal> 6.19, <valence> 2.92) and 20 new neutral (<arousal> 3.74, <valence> 5.07). Participants were asked to respond whether each picture presented was old or new and, then, to rate its emotional value from 1 to 9 on arousal and valence scales using the Self-Assessment Manikin procedure [Lang, 1980].

fMRI Acquisition

The MRI acquisition was performed on a 3T Achieva MRI system (Philips Medical System, Best, The Netherlands) equipped with an eight-element phased-array head coil. For each participant, a total of 360 volumes (for the run of the localizer task) and 375 volumes (for the run of the main experiment) were acquired using a T2*-weighted single shot echo-planar imaging sequence (Field of View = $240 \times 117 \times 240$; matrix size = 80×80 ; repetition time = 2,150 ms; echo time = 30 ms; flip angle = 80° ; sense factor = 2), with 39 axial slices covering the whole brain (slice thickness = 3 mm; no gap). The orientation of the slices was parallel to AC-PC (Anterior Commissure–Posterior Commissure) line. Four dummy scans were used to reach steady-state magnetization. In addition, high resolution T1-weighted anatomical images were acquired for each participant for anatomical reference (180 slices parallel to AC-PC with a resolution of $1 \times 1 \times 1$).

Behavioral Analysis

In the localizer task, the percentage of correct responses (% CR) and the mean response time of correct responses (RT) were calculated for the two tasks (duration and color) whatever the stimuli and, then, they were calculated separately for each type of stimulus. First, *t*-tests were performed to evaluate the effect of the task (duration, color) on the % CR and on the mean response time of correct responses (RT). Then, a 2×2 ANOVA with the factors of color (bluer, redder) and presentation time (shorter, longer) was performed for each measure and each task. Furthermore, a Pearson correlation analysis was conducted to

TABLE I. Behavioral data of the localizer task and of the main experiment

	Short presentation time (1,200 ms)		Long presentation time (1,800 ms)	
	% Correct (SE)	RT in ms (SE)	% Correct (SE)	RT in ms (SE)
Localizer Task				
Color task	75 (1)	696 (18)	79 (2)	619 (16)
Duration task	83 (2)	710 (16)	83 (2)	619 (26)
Main experiment				
Emotionally-neutral	92 (1)	703 (24)	78 (2)	602 (29)
Emotionally-negative	88 (2)	729 (26)	79 (2)	596 (24)

Localizer task: Mean and standard error (SE) of the percentage of correct responses (% CR) and the mean response time of correct responses (RT) obtained for each task (color and duration) and each presentation time (short and long). Main experiment: Mean and standard error (SE) of the percentage of correct responses (% CR) and the mean response time of correct responses (RT) obtained for each emotion (neutral and negative) and each presentation time (short and long).

examine whether the % CR obtained in the duration task was correlated with that obtained in the color task to establish whether common or separate mechanisms are involved in the two tasks.

In the main experiment, the % CR and the RT were measured for each emotion and each presentation time. A 2×2 ANOVA with the factors of emotion (negative, neutral) and presentation time (shorter, longer) were performed for each measure (% CR, RT). Assuming that emotionally negative pictures are perceived longer than neutral ones, an interaction effect was expected to be found between emotion and presentation time, that is, a higher % CR and a faster RT for emotionally negative than for neutral pictures in the case of longer stimuli and, conversely, a lower % CR and a slower RT for emotionally negative than for neutral pictures in the case of shorter stimuli.

The recognition and emotion rating tasks conducted after the MRI session were also analyzed. Regarding the recognition task, *t*-tests were carried out to examine the effect of emotion (negative, neutral) on the percentage of recognition ("old" responses), separately for new and old pictures. Regarding the emotion rating task, *t*-tests were carried out with each participant on the set of old pictures presented in the main experiment to check whether emotionally negative pictures were rated as more arousing and more unpleasant than neutral ones.

fMRI Analysis

Functional imaging data were analyzed using Statistical Parametric Mapping (SPM8, Wellcome Department of Imaging Neuroscience, University College London). For each run, all volumes were slice time corrected and realigned to the first scan of the time series. Images were then normalized into the Montreal Neurological Institute brain template using DARTEL approach with transformation parameters derived from segmentation of the T1-weighted anatomical coregistered to the mean fMRI image. The resulting functional images were then spatially smoothed

using a 8-mm full-width at half-maximum isotropic Gaussian kernel.

For each participant, the general linear model approach was used to model the data including a high-pass filter with a cutoff of 128 s and correction for nonindependence between adjacent scans by use of AR-model. In the localizer task, two effects (Duration and Color) were modeled as delta functions based on trial onsets convolved with the canonical hemodynamic response function. The contrasts ([Duration]>[Color]) and ([Color]>[Duration]) were entered in a second level random-effect one sample *t*-test analysis. The statistical threshold was set to $P < 0.05$ [family-wise error (FWE) corrected for multiple comparisons] with an extent threshold of 100 voxels. Anatomical localization was performed using the Automated Anatomical Labeling (AAL) atlas [Tzourio-Mazoyer et al., 2002]. In the main experiment, two effects (Negative and Neutral) were modeled as delta functions based on trial onsets convolved with the canonical hemodynamic response function. The aim of the main experiment was to identify, among the brain regions involved in time processing, those that were activated to a greater extent by the processing of emotionally negative stimuli than by the processing of neutral ones. Using MarsBar [Brett et al., 2002], the clusters showing significant activation in the contrast ([Duration]>[Color]) of the localizer task were defined as regions of interest (ROIs). For each participant and for each emotional condition (neutral, negative) of the main experiment, the mean activation was computed within each ROI (cluster). Then for each ROI, *t*-tests were performed to compare activations between the negative and the neutral condition. Bonferroni corrections were applied to adjust for the number of ROIs.

RESULTS

Behavioral Data

Table I presents the mean and standard error (SE) of the % CR and of the mean response time of correct responses

TABLE II. fMRI data of the localizer task. [Color > Duration]: Brain regions that presented a greater activity during the color task than during the duration task. [Duration > Color]: Brain regions that presented a greater activity during the duration task than during the color task.

Anatomical structure	<i>x, y, z</i> coordinates (mm)	Z score
<i>[Color > Duration]</i>		
L mid/sup occipital cortex	-28, -69, 26	7.15
R angular gyrus/sup parietal cortex	28, -61, 44	6.25
R fusiform cortex	36, -52, -22	6.10
L fusiform cortex	-40, -57, -13	5.90
L inf/sup parietal cortex	-22, -62, 43	5.69
<i>[Duration > Color]</i>		
R cerebellum_8	13, -60, -33	6.40
R mid/sup orbitofrontal cortex	36, 46, -8	6.15
R anterior insular cortex	38, 19, 1	6.06
R anterior cingulum	13, 33, 20	5.60
L cerebellum crus1/crus2/7b	-15, -71, -37	5.45
R inferior frontal cortex Oper/Tri	54, 18, 2	5.40

All clusters are significant at $P < 0.05$ (FWE-corrected for multiple comparisons) with an extent threshold of 100 voxels.

(RT) obtained in the localizer task for each task and each presentation time. The % CR was higher for the duration (83%) than for the color (77%) task ($t_{25}=3.45$, $P < .005$), while the RT did not differ between the two tasks (664 and 658 ms for the duration and the color task, respectively). Furthermore, the Pearson correlation analysis did not reveal any significant correlation between the % CR obtained in the duration categorization task and that obtained in the color categorization task ($r_{24} = 0.09$, $P > 0.10$).

In the duration task, no significant effect of color nor of presentation time was observed on the % CR but a major effect of presentation time was observed on the RT, which was faster in the case of longer (619 ms) than of shorter (710 ms) presentation times ($F_{1,25}=19.47$, $P < 0.001$). There was no interaction effect between color and presentation time for both the % CR and the RT. In the color task, the % CR was higher for longer (79%) than for shorter (75%) presentation times ($F_{1,25} = 5.79$, $P < 0.05$) and tended to be higher for redder (79%) than for bluer (75%) stimuli ($F_{1,25} = 2.94$, $P = 0.10$). The RT were faster for longer (619 ms) than for shorter (696 ms) presentation times ($F_{1,25} = 53.82$, $P < 0.001$) and tended to be faster for redder (643 ms) than for bluer (672 ms) stimuli ($F_{1,25} = 3.48$, $P = 0.07$). There was no interaction effect between color and presentation time for both the % CR and the RT.

Table I presents the mean and SE of the % CR and of the mean response time of correct response (RT) obtained in the main experiment for each emotion and each presentation time. The % CR was higher for shorter (90%) than for longer (79%) stimuli ($F_{1,26} = 15.52$, $P < 0.005$) but did

not differ between emotionally negative (84%) and neutral (85%) pictures ($F_{1,26} < 1$). The % CR was significantly lower for emotionally negative (88%) than for neutral (92%) pictures in the case of shorter presentation times ($t_{26} = 2.56$, $P < 0.05$) while no significant difference was observed in the case of longer presentation times (negative vs. neutral: 79% vs. 78%, $t_{26} < 1$). Contrary to our hypothesis, the interaction between emotion and presentation time was only a trend toward significance ($F_{1,26} = 4.14$, $P = 0.05$).

The RT was faster for longer (599 ms) than for shorter (716 ms) presentation times ($F_{1,26} = 43.58$, $P < 0.001$) but did not differ between emotionally negative (662 ms) and neutral (652 ms) pictures ($F_{1,26} = 1.77$, $P > 0.10$). As expected, there was a significant interaction between emotion and presentation time ($F_{1,26} = 6.07$, $P < 0.05$). The RT was significantly slower for emotionally negative (729 ms) than for neutral (703 ms) pictures in the case of shorter presentation times ($t_{26} = 3.17$, $P < 0.005$) while no significant difference was observed in the case of longer presentation times (negative vs. neutral: 596 ms vs. 602 ms, $t_{26} < 1$).

In the recognition task, the percentage of old pictures correctly recognized as "old" did not significantly differ between emotionally negative (79%) and neutral (79%) pictures ($t_{26} < 1$) but the percentage of new pictures wrongly recognized as "old" was larger for emotionally negative (18%) than for neutral (9%) pictures ($t_{26} = 4.56$, $P < 0.001$). The emotional rating task performed with the set of old pictures presented in main experiment revealed that emotionally negative pictures were rated as significantly less pleasant and more arousing than neutral pictures by all but one participant, who was excluded from group analyses. As expected, emotionally negative pictures were credited high arousal (5.30) and low valence (2.71) values whereas neutral pictures were credited low arousal (2.39) and intermediate valence (5.47) values.

Participants presented an average score of state anxiety of 29 ± 7 and an average score of trait-anxiety of 37 ± 8 . The score of state anxiety was marginally higher after than before the MRI session (30 vs. 28, $t_{26} = 1.95$, $P = 0.06$). Further analyses did not reveal any significant correlation between anxiety (state and trait) levels and the effects of emotion on temporal judgments in the main experiment.

fMRI Data

The functional analysis of the localizer task revealed that, on the one hand, color (vs. duration) processing activated the fusiform gyrus bilaterally, the left mid/superior occipital cortex, the left inf/superior parietal cortex, and the right angular gyrus/superior parietal cortex (Table II and Fig. 2). On the other hand, the duration (vs. color) processing activated the cerebellum bilaterally as well as the mid/superior orbitofrontal, the anterior cingulate, the anterior insular, and the inferior frontal cortices on the right hemisphere (Table II and Fig. 2).

LFuC left fusiform cortex; LSOC right superior occipital cortex; LSPC left superior parietal cortex; RFuC right fusiform cortex; RSPC right superior parietal cortex.

LCb left cerebellum; RCB right cerebellum; RACC right anterior cingulate cortex; ROFC right orbitofrontal cortex; RAIC right anterior insular cortex; RIFC right inferior frontal cortex.

Top left: right lateral view; Top middle: anterior view; Top right: dorsal view

Bottom left: left lateral view; Bottom middle: posterior view; Bottom right: ventral view

Figure 2.

Brain regions (in red) that, in the localizer task, presented a greater activity during the duration task than during the color task and, (in green) that, inversely, presented a greater activity during the color task than during the duration task. All clusters are significant at $P < 0.05$ (FWE-corr) with an extent threshold of 100 voxels.

The six clusters showing significant activation in the contrast ([Duration > Color]) of the localizer task were defined as ROIs for the analysis of the main experiment (Fig. 3): the left cerebellum (LCb: $[-15, -71, -37]$), the right cerebellum (RCb: $[13, -60, -33]$), the right anterior cingulate cortex (RACC: $[13, 33, 20]$), the right orbitofrontal cortex (ROFC: $[-30, 46, -8]$), the right anterior insular cortex (RAIC: $[38, 19, 1]$), and the right inferior frontal cortex (RIFC: $[54, 18, 2]$). The t -tests performed to compare, within each ROI, the mean activation between the negative and the neutral condition, revealed that the right IFC was the only ROI to be more intensively activated in the presence of emotionally negative than of neutral pictures ($t_{26} = 3.87$, $P < 0.005$ after Bonferroni correction; Fig. 4a). No ROI was significantly more activated in the presence of neutral than of emotionally negative pictures.

Pearson correlation analyses were then performed to determine whether the mean activations of the contrast ([Negative > Neutral]) computed within each ROI for each participant were correlated with the impact of emotion on the behavioral performance. Four behavioral indexes were

computed: The first index is the interaction term of the 2×2 ANOVA performed on the % CR $\{[(\%CR_{Lg})_{Ng} - (\%CR_{Lg})_{Nt}] - [(\%CR_{Sh})_{Ng} - (\%CR_{Sh})_{Nt}]\}$, which reflects the fact that the proportion of “long” responses is higher for negative than for neutral pictures. The second index is the global difference of % CR between neutral and negative pictures $[(\%CR)_{Nt} - (\%CR)_{Ng}]$ which reflects the fact that the proportion of correct responses is higher for neutral than for negative pictures (for shorter and longer presentation times pooled together). The third index is the interaction term of the 2×2 ANOVA performed on RT $\{[(RT_{Sh})_{Ng} - (RT_{Sh})_{Nt}] - [(RT_{Lg})_{Ng} - (RT_{Lg})_{Nt}]\}$ which reflects the fact that response times are slower for negative than for neutral pictures in the case of shorter presentation times but not in the case of longer presentation times. The fourth index is the global difference of RT between negative and neutral pictures $[(RT)_{Ng} - (RT)_{Nt}]$, which reflects the fact that response times are slower for negative than for neutral pictures (for shorter and longer presentation times pooled together). Bonferroni corrections were applied to adjust for the number of ROIs. If a ROI is

Figure 3.

Coronal, sagittal and axial views of the six ROI used for the analysis of the main experiment. These ROIs were defined from the clusters showing significant activation in the contrast ([Duration > Color]) of the localizer task. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Figure 4.

a: Mean activation values (beta) computed within each ROI for the emotionally negative and neutral conditions of the main experiment (***: $P < 0.005$, after Bonferroni correction). **b:** Pearson correlation between the value (beta) of the contrast ([Negative > Neutral]) within the right IFC ROI and the differential

between shorter and longer picture exposition of the difference in response time between emotionally negative and neutral pictures $\{[(RT_{Sh})_{Ng} - (RT_{Sh})_{Nd}] - [(RT_{Lg})_{Ng} - (RT_{Lg})_{Nd}]\}$ (*: $P < 0.05$, after Bonferroni correction).

involved in the subjective lengthening of perceived duration induced by emotionally negative pictures, mean activation of the contrast ([Negative > Neutral]) in this region should be correlated with the indexes 1 and/or 3. By contrast, if a ROI is involved in the general interference of negative pictures on the duration task, mean activation of the contrast ([Negative > Neutral]) in this region should be correlated with the indexes 2 and/or 4.

The results revealed that the mean activation of the contrast ([Negative > Neutral]) in the right IFC was correlated with the index 3 ($[(RT_{Sh})_{Ng} - (RT_{Sh})_{Nt}] - [(RT_{Lg})_{Ng} - (RT_{Lg})_{Nt}]$; $r_{25} = 0.52$, $P < 0.05$ after Bonferroni correction; Fig. 4b), which corresponds to the differential between shorter and longer picture exposition of the difference in response time between emotionally negative and neutral pictures. It was not correlated with the other indexes. The mean activations of the contrast ([Negative > Neutral]) in the five other ROIs were not significantly correlated with any behavioral index.

DISCUSSION

The first aim of this study was to identify, using the fMRI technique, the neural structures that participate in the human capacity to perceive time and estimate the duration of events with an accuracy that depends on their emotional charge. It is well-acknowledged indeed that highly arousing negative stimuli are perceived as lasting longer than emotionally neutral stimuli [Droit-Volet and Meck, 2007]. We set up a protocol in which participants had to perform a localizer task followed by the main experiment. The localizer task involved a procedure [Coull et al., 2004; Livesey et al., 2007; Morillon et al., 2009] in which visual stimuli consisting in shades of quickly varying colors were presented to participants who had to categorize either the duration or the average color of the stimuli. This localizer task was expected to allow for the identification of a duration-specific neural network after subtracting from the neural activation pattern obtained during the duration-directed task that obtained during the color-directed task. In the main experiment, participants had to categorize the presentation time of either neutral or emotionally negative visual stimuli as shorter/longer than a standard duration. This experiment was expected to allow for the identification of brain areas that, among those belonging to the duration-specific network (identified through the localizer task), would be sensitive to emotionally negative arousal.

The Localizer Task

The behavioral results of the localizer task disclosed that the % CR was higher in the duration task than in the color task although the response times were identical in both tasks, suggesting a higher difficulty in the execution of the color task. In both tasks, the response time was faster for

long than for short stimulus exposition, possibly because, for long exposition, the decision process initiated before the exposition stopped. Remarkably too, the % CR was higher for long than for short exposition in the color task, hinting that attention was caught during the full stimulus exposition and that the performance was improved as more time was available to treat the visual stimulus content. Finally, a Pearson correlation analysis revealed no significant correlation between the % CR obtained in the duration task and that obtained in the color task, which is in line with previous studies [Gilaie-Dotan et al., 2011; Wiener et al., 2014] and suggests that separate mechanisms are involved in temporal and color processing.

The imaging results of the localizer task uncovered the existence of two distinct neural networks that were specifically activated, one, during the color task contrasted to the duration task and, the other, during the duration task contrasted to the color task. The former network was delineated by the presence of an increased activity in the fusiform gyrus bilaterally, close to area V4, which corresponds to the brain area specialized in color processing, and also in the left superior occipital cortex and the superior parietal cortex bilaterally which, reportedly, are activated in visuo-spatial attention. The color task required participants to concentrate on color changes and, thus, to invest a larger amount of visuo-spatial attention during this task than during the duration task in which color variations were to be ignored. The posterior parietal cortex is suspected to participate in quantity processing [Walsh, 2003]. To execute the color task, participants had to compute the relative quantity of red and blue, letting suppose that quantity processing was more demanding in the color than in the duration task and making the color task more difficult.

As to the latter network activated during the duration task contrasted to the color task it included the cerebellum bilaterally, as well as the orbitofrontal, the anterior cingulate, the anterior insular, and the inferior frontal cortices on the right hemisphere. The issue about where the neural structures that support time perception do precisely reside in the human brain is still a matter of debate. At the sub-cortical level, our study revealed an activation in the cerebellum, a structure which has been repeatedly shown to be involved in temporal processing [Coull et al., 2011, for review] using various types of approaches (lesion, stimulation and functional neuroimaging studies). Interestingly, the cerebellum has been proposed to be used to predict events in the temporal dimension [O'Reilly et al., 2008]. Such a cerebellar function would certainly be of great help to categorize a test duration as shorter or longer than a memorized standard. Remarkably too, our data further suggest that the role of the cerebellum in temporal processing is not limited to subsecond intervals as it is generally assumed [Ivry, 1996; Lee et al., 2007]. In our study, cerebellar activation was notably located in the lobule VII (Crus 1 and 2) of the left hemisphere which, together with the right prefrontal cortex, is assumed to participate in

executive functions [O'Reilly et al., 2010]. Color processing is probably more automatic than duration processing and participants would most likely have to inhibit color processing during the duration task whereas the reverse would not necessarily be true. The greater activation observed in the left cerebellum and the right prefrontal cortex during the duration task as compared to the color task could, therefore, reflect the higher participation of inhibitory processing in the former task. Intriguingly, there was no activation in the basal ganglia, which is at odds with the numerous studies showing the participation of this region (especially the dorsal striatum) in temporal processing [Coull et al., 2011, for review]. It has been proposed, however, that the basal ganglia could be more specifically involved in the storage of stimulus duration [Coull et al., 2008; Rao et al., 2001]. Thus, the lack of activation in the basal ganglia in our study could possibly be explained by the fact that fMRI activations were examined during the categorization (comparison) but not during the storage (encoding) of durations.

An exhaustive meta-analysis recently identified the SMA and the right IFC as the brain regions the most regularly activated across a wide diversity of timing tasks [Wiener et al., 2010]. By contrast, our own study did not find any significant activation in the SMA. This finding reminds that of the aforementioned study [Livesey et al., 2007] in which, by manipulating the difficulty of a duration discrimination task relative to that of a control task, the authors demonstrated that the SMA was more active in the control than in the duration condition when the control task was harder, hinting that this structure does not directly participate in timing function. The lack of activation within the SMA for the contrast ([Duration > Color]) in this study could, thus, be due to the fact that the color categorization task was indeed more difficult than the duration categorization task.

An area that passed the task-difficulty test of Livesey et al. [2007] was a small region at the confluence of the IFC and the anterior insula, bilaterally. In this study, activations were located in both the IFC and the AIC on the right hemisphere. Activations in these two regions have repeatedly been documented in the literature on time perception [Ferrandez et al., 2003; Lewis and Miall, 2003a,b; Nenadic et al., 2003; Pouthas et al., 2005; Rao et al., 2001], preferentially on the right hemisphere [Kosillo and Smith, 2010]. Furthermore, disturbance in temporal processing has recently been reported following lesion in the right IFC [Gooch et al., 2011] or in the right AIC/IFC region [Monfort et al., 2014]. The significance of the connection between this brain locus and time processing, however, remains unclear: it has been proposed to be involved in the representation of temporal information in memory [Pouthas et al., 2005], in the recovery of encoded durations from memory [Lewis and Miall, 2006], as well as in intertemporal decisions [Wittmann et al., 2010a]. It is worthwhile here to recall that the insular cortex appears as the most prominent

receptive brain area for all physiological states of the body where all emotional feelings are produced. Hence, it may serve as a neural substrate for the construction of all subjective feelings and play a fundamental role in human awareness [Craig, 2009a]. In view of the results of functional imaging studies, Craig further proposed that the AIC (with the neighboring IFC) contains a critical neural device enabling humans to perceive time and estimate its passage [Craig, 2009b]. Craig hypothesizes that primary interoceptive informations collected in the posterior insula are progressively integrated, as they move throughout the insula, with a set of neural activities induced by salient environmental conditions (emotional and physical) in other brain areas, to ultimately create within the AIC (and the IFC) a "global emotional moment," that is associated with self-awareness. According to this scheme, the duration of an event would be estimated through the counting of the "global emotional moments" gathered during the event. Such a model would account for the results of the above-described temporal reproduction task in the range of seconds [Wittmann et al., 2010b] showing that, during the encoding phase, neural activation was greater in the posterior insula, steadily increasing to peak at the end of the stimulus. By contrast, a greater activation was observed in the AIC/IFC region during the reproduction phase. The authors inferred that, during the encoding of a duration, a representation of that duration would build-up in the posterior insula whereas its explicit judgment that entails a deeper mental engagement of the subject would be formed in the AIC/IFC region during the reproduction phase. In this study, we failed to detect activation in the posterior part of the insular cortex. This may be because the durations we used were much shorter than those used in the study by Wittmann et al. [2010b].

The duration-responsive neural network presently identified also included the right orbitofrontal as well as the right anterior cingulate cortex (ACC) that is coactivated with the AIC in most but not all neuroimaging studies and that is supposed to be the initiation site for motor function [Craig, 2009a]. The right hemispheric bias concerning the involvement of the frontal structures in our study is in concordance with the results of EEG [Monfort et al., 2000; Pouthas et al., 2000], fMRI [Lewis and Miall, 2006; Pouthas et al., 2005] and neuropsychological [Funnell et al., 2003; Harrington et al., 1998b; Morin et al., 2005] studies suggesting a predominance of the right hemisphere in timing tasks. Reportedly, implicit and explicit temporal processing would take place in the left and right frontal regions, respectively [Coull and Nobre, 2008; Coull et al., 2013]. An implicit temporal processing could possibly have occurred during the color task since the response times were faster for the long than for the short stimulus presentation. This could explain why the contrast between the duration-selective and the color-selective neural networks encompassed only brain areas engaged in explicit temporal processing.

The Main Experiment

Assuming that the presentation time of an emotionally negative picture is perceived longer than that of a neutral one, we expected, in the main experiment, to obtain a greater proportion of “long” responses for emotionally negative than for neutral pictures. In other words, the % CR was expected to be higher for neutral than for negative pictures in the case of shorter presentation times, but, to be higher for emotionally negative than for neutral pictures in the case of longer presentation times. Indeed, in the case of shorter presentation times, the proportion of “long” responses (i.e., errors) was significantly higher for emotionally negative than for neutral pictures, while in the case of longer presentation times, the proportion of “long” responses (i.e., correct responses) was not markedly different between the two emotion conditions. However, the interaction between emotion and presentation time was barely significant. This lack of meaningful interaction effect could be due to the fact the temporal interval was very large between the two test durations (1200 and 1800 ms), which, thus, were easy to categorize as “short” or “long” (the rate of errors was <16%). A relatively large proportion of errors were probably attributable to general factors, like distraction, which could have partially masked the contribution of emotion. Using a larger set of test durations (e.g., 1,200, 1,400, 1,600, and 1,800 ms) would certainly have allowed to improve the sensitivity of the behavioral data but, in return, mixing multiplying trials of variable difficulty could have generated noise in the fMRI data.

In the context of an easy behavioral task, response times (RT computed for correct responses) give valuable information about behavioral performance. As for the % CR, we expected the responses times to be faster for neutral/negative pictures in the case of shorter/longer presentation times. Indeed, the interaction between emotion and presentation time was significant: the response times were much slower for negative than for neutral pictures in the case of shorter presentation times, while they were not significantly different between the two emotion conditions in the case of longer presentation times.

Importantly, neither the analysis performed on the % CR, nor that performed on the response times revealed a main effect of emotion. Thus, emotion did not interfere globally with the performance in the duration categorization task, but affected selectively the categorization of the shorter stimuli that were much harder to detect (lower % CR and slower response times) in the case of emotionally negative than in the case of neutral pictures, while there was no effect of emotion on the detection of longer stimuli.

On the whole, the results of the behavioral analyses performed both on the % CR and on the response times concur to suggest that the presentation times of emotionally negative pictures were subjectively perceived as lasting longer than those of neutral ones although the effects were

modest, maybe because we did not select the most arousing and unpleasant pictures (e.g., pictures of mutilated persons) of the IAPS database. Nonetheless, the emotion rating task uncovered that, for all participants, emotionally negative pictures were perceived as more unpleasant and more arousing than neutral ones. At last, the performance in the recognition task was not better in the case of emotionally negative pictures than of neutral ones, refuting a possible memory-enhancing effect of emotion.

Strikingly, the imaging data obtained from the main experiment brought to the fore that the right IFC was the only region within the duration-specific neural network (identified through the localizer task) whose activity was amplified in the face of emotionally negative pictures as compared to neutral ones. This increased activation of the right IFC with increasing emotional charge could be related either to a global effect of emotion on the duration task or to the fact that the presentation times of the pictures were subjectively perceived as longer with higher emotional charge. Two arguments tend to privilege the second hypothesis over the first one: First, the behavioral results showed that emotion affected selectively the categorization of the shorter stimuli, hinting that it did not globally impact the duration task. Secondly, the extent of neural activation induced by the emotionally negative pictures (compared to neutral ones) within the right IFC was not correlated with the two indexes reflecting the global interference of emotion on the duration task (correct responses and responses times). By contrast, it was correlated with the interaction term of the 2×2 ANOVA performed on responses times, an index which indirectly reflects the extent to which emotionally negative pictures were overestimated compared to neutral ones.

Two recent fMRI studies have explored how the timing network is modulated by emotional arousal [Dirnberger et al., 2012; Tipples et al., 2013]. One study [Dirnberger et al., 2012] was designed to test the hypothesis that distortion of time perception induced by emotional events correlates with enhanced recognition memory for these events. Participants presented with successive pairs of pictures (neutral-neutral, aversive-neutral) for either 1.8 s (“short”) or 2.2 s (“long”) had to judge which one of the two pictures was presented for a longer/shorter time. Importantly, when a short aversive picture was presented before a long neutral one, its subjective duration increased in relation to the following neutral picture. A recognition test performed afterwards indicated that aversive pictures were more readily recognized than neutral ones, albeit, only in trials in which their presentation time was also subjectively overestimated. A region-of-interest fMRI analysis performed in parallel revealed a greater activation of the right amygdala, the right insula, and the right putamen in trials in which the presentation time of aversive pictures was overestimated but not in trials in which they were correctly estimated. At last, the authors found that the extent of activation in the right anterior insula and in the right putamen correlated with the extent of memory

enhancement by emotion. They suggested that the processing of aversive pictures would be accelerated, which would provide advantages to the memorization process but at the expense of time estimation performance. The other study [Tipples et al., 2013] investigated the effect of facial emotion on short time interval perception using a duration bisection task. Participants had to judge whether the presentation times (varying from 400 to 1,600 ms) of neutral, angry, and happy faces were closer in duration to the short (400 ms) or to the long (1,600 ms) previously memorized standard. Time was overestimated for both angry and happy face expressions compared to neutral ones. Using a region-of-interest fMRI analysis, the authors showed that the neural activity in the right SMA and the right AIC/IFC region was enhanced for angry and happy faces compared to neutral faces only for the 700 ms test duration (for which the temporal decision was the most difficult and reaction times, the longest).

The findings of these two studies converge to some extent with our own data, clearly pointing the right AIC/IFC region as a critical part of the timing network whose activity is consistently enhanced by emotional arousal. However, the methodology used in these studies is different from ours. Notably, in these earlier works, the analyses were restricted to ROIs selected from the literature on time perception. In our study, the ROIs were obtained starting from a preliminary localizer task (duration vs. color categorization) whose aim precisely was to identify the duration-selective network of interest for our main experiment (duration categorization with negative vs. neutral stimuli). The different methodological approaches used to define the ROIs could explain in part the slight differences observed between the three studies about where exactly in the right AIC/IFC region emotion appears to interfere with temporal processing: the right AIC [Dirnberger et al., 2012], the junction of the right AIC and IFC [Tipples et al., 2013], the right IFC (our study). Finally, because neither study applied to the whole brain, it cannot be excluded, therefore, that changes in neural activity in other brain regions might also have occurred under the pressure of emotional arousal and contributed to the distortion in time perception observed in each experimental setting.

The functional significance of the emotionally induced activity enhancement observed in the right AIC/IFC region remains to be clarified. It is actually uncertain whether it reflects an acceleration of information processing leading to a subjective lengthening of the perceived duration [Dirnberger et al., 2012], or a difficulty in temporal decision making [Tipples et al., 2013]. Our own data tend to support the first hypothesis since the extent of the emotionally induced activity enhancement in the right IFC was correlated with a behavioral index indirectly reflecting the extent to which emotionally negative pictures were overestimated compared to neutral ones. Such an explanation also agrees with the model proposed by Craig [2009b] according to which, increasing the emotional charge of a stimulus should lead to a faster accumulation of “global

emotional moments” in the AIC/IFC region whose activity should then increase in proportion to the perceived duration of the stimulus. The model of Craig further stipulates that the AIC would function asymmetrically: sympathetic and parasympathetic signals would promote activation in the right and the left AIC, respectively; that is, negative arousing feelings would activate the right AIC and positive affiliating feelings would activate the left AIC [Craig, 2005, 2009b]. This well accounts for our right-lateralized effect.

This functional interpretation, however, should be taken cautiously. First, in the model of Craig [2009b], the AIC emerges as the pivotal region where “emotional moments” would be produced and where emotion would interfere with temporal judgment, whereas our own data suggest that emotionally negative stimuli enhance activation of the right IFC, but not of the right AIC. Further studies are clearly needed to determine the differential role of the very close AIC and IFC brain areas in temporal processing. Secondly, the behavioral index which correlated with the emotionally induced activity enhancement in the right IFC, was based on the response time. Certainly, the evidence would be stronger if the correlation had been obtained with the proportion of “long” responses. Finally, it is still obscure at which stage of temporal processing (pacemaker, attention, memory, or decision) the interference effect between emotion and temporal judgment exactly occurs [see Ivry and Scherf, 2008, for a review of the role of nontemporal factors on perceived duration]. Furthermore, in the study by Dirnberger et al. [2012] and ours, the effect of emotion was explored by comparing highly arousing negative pictures with neutral ones making impossible to distinguish the role of arousal from that of emotional valence, while the study by Tipples et al. [2013] investigated the influence of arousal, independently of the valence. The influence of emotion on temporal processing is not as yet clearly understood at the behavioral level. For instance, the presentation of low-arousing negative pictures is perceived as lasting shorter than that of neutral pictures [Gil et al., 2009], hinting that the valence differentially affects subjective time perception depending on the arousal level [Droit-Volet and Meck, 2007]. It is conceivable that judging the duration of an event in relation to another would not rely only on the difference in the information processing speed (or rate of accumulation of “global emotional moments”) in the two situations. It could also depend for instance on the difference in the attention selectively paid to the time dimension in the two situations [Droit-Volet and Meck, 2007; Gil et al., 2009].

CONCLUSION

Our present neuroimaging investigation identified the right IFC as the only brain region, within a duration-specific network identified through a localizer task, which, during a duration categorization task, was more activated

by highly arousing negative pictures than by neutral ones. Importantly, the extent of neural activation induced by emotionally negative (compared to neutral) pictures in this brain region correlated with a behavioral index of the extent to which emotionally negative pictures were overestimated compared to neutral ones. Together, these findings lend a strong support to the hypothesis that the right IFC stands as the primary neural region where emotion interferes with temporal processing, possibly by accelerating the rate of information processing, or alternatively by interfering with temporal decision processes. Further studies on time perception combining neuroimaging and neuropsychological approaches and involving healthy subjects as well as brain-damaged and psychiatric (e.g., with anxiety disorders) patients and different panels of emotional factors are needed to extend the present results.

ACKNOWLEDGMENT

We are most grateful to participants for kindly willing to cooperate in this experiment.

REFERENCES

- Alexander GE, DeLong MR, Strick PL (1986): Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annu Rev Neurosci* 9:357–381.
- Angrilli A, Cherubini P, Pavese A, Mantredini S (1997): The influence of affective factors on time perception. *Percept Psychophys* 59:972–982.
- Bar-Haim Y, Kerem A, Lamy D, Zakai D (2010): When time slows down: The influence of threat on time perception in anxiety. *Cogn Emotion* 24:255–263.
- Brett M, Anton J, Valabregue R, Poline J (2002): Region of interest analysis using an SPM toolbox. *NeuroImage* 16:1140–1141.
- Bueti D, Macaluso E (2011): Physiological correlates of subjective time: Evidence for the temporal accumulator hypothesis. *NeuroImage* 57:1251–1263.
- Carroll CA, O'Donnell BF, Shekhar A, Hetrick WP (2009): Timing dysfunctions in schizophrenia span from millisecond to several-second durations. *Brain Cogn* 70:181–190.
- Coull J, Nobre A (2008): Dissociating explicit timing from temporal expectation with fMRI. *Curr Opin Neurobiol* 18:137–144.
- Coull JT, Vidal F, Nazarian B, Macar F (2004): Functional anatomy of the attentional modulation of time estimation. *Science* 303:1506–1508.
- Coull JT, Nazarian B, Vidal F (2008): Timing, storage, and comparison of stimulus duration engage discrete anatomical components of a perceptual timing network. *J Cogn Neurosci* 20:2185–2197.
- Coull JT, Cheng R-K, Meck WH (2011): Neuroanatomical and neurochemical substrates of timing. *Neuropsychopharmacology* 36:3–25.
- Coull JT, Davranche K, Nazarian B, Vidal F (2013): Functional anatomy of timing differs for production versus prediction of time intervals. *Neuropsychologia* 51:309–319.
- Craig AD (2005): Forebrain emotional asymmetry: A neuroanatomical basis? *Trends Cogn Sci* 9:566–571.
- Craig AD (2009a): How do you feel—Now? The anterior insula and human awareness. *Nat Rev Neurosci* 10:59–70.
- Craig ADB (2009b): Emotional moments across time: A possible neural basis for time perception in the anterior insula. *Philos Trans R Soc Lond B Biol Sci* 364:1933–1942.
- Droit-Volet S, Gil S (2009): The time-emotion paradox. *Philos Trans R Soc Lond B Biol Sci* 364:1943–1953.
- Droit-Volet S, Meck WH (2007): How emotions colour our perception of time. *Trends Cogn Sci* 11:504–513.
- Droit-Volet S, Brunot S, Niedenthal PM (2004): Perception of the duration of emotional events. *Cogn Emotion* 18:849–858.
- Dirnberger G, Hesselmann G, Roiser JP, Preminger S, Jahanshahi M, Paz R (2012): Give it time: Neural evidence for distorted time perception and enhanced memory encoding in emotional situations. *NeuroImage* 63:591–599.
- Elvevåg B, McCormack T, Gilbert A, Brown GDA, Weinberger DR, Goldberg TE (2003): Duration judgements in patients with schizophrenia. *Psychol Med* 33:1249–1261.
- Ferrandez AM, Hugueville L, Lehericy S, Poline JB, Marsault C, Pouthas V (2003): Basal ganglia and supplementary motor area sub-tend duration perception: An fMRI study. *NeuroImage* 19:1532–1544.
- Funnell MG, Corballis PM, Gazzaniga MS (2003): Temporal discrimination in the split brain. *Brain Cogn* 53:218–222.
- Gibbon J (1977): Scalar expectancy theory and Weber's Law in animal timing. *Psychol Rev* 84:279–325.
- Gil S, Rousset S, Droit-Volet S (2009): How liked and disliked foods affect time perception. *Emotion* 9:457–463.
- Gilaie-Dotan S, Kanai R, Rees G (2011): Anatomy of human sensory cortices reflects inter-individual variability in time estimation. *Front Integr Neurosci* 5:76.
- Gooch CM, Wiener M, Hamilton AC, Coslett HB (2011): Temporal discrimination of sub- and suprasecond time intervals: A voxel-based lesion mapping analysis. *Front Integr Neurosci* 5:59.
- Grommet, EK, Droit-Volet S, Gil S, Hemmes NS, Baker AH, Brown BL (2011): Time estimation of fear cues in human observers. *Behav Processes* 86:88–93.
- Harrington DL, Haaland KY, Hermanowicz N (1998a): Temporal processing in the basal ganglia. *Neuropsychologia* 12:3–12.
- Harrington DL, Haaland KY, Knight RT (1998b): Cortical networks underlying mechanisms of time perception. *J Neurosci* 18:1085–1095.
- Ivry RB (1996): The representation of temporal information in perception and motor control. *Curr Opin Neurobiol* 6:851–857.
- Ivry RB, Schlerf JE (2008): Dedicated and intrinsic models of time perception. *Trends Cogn Sci* 12:273–280.
- Kosillo P, Smith AT (2010): The role of the human anterior insular cortex in time processing. *Brain Struct Funct* 214:623–628.
- Lang PJ (1980): Behavioral treatment and bio-behavioral assessment: Computer applications. In Sidowski JB, Johnson JH, and Williams TA, editors. *Technology in Mental Health Care Delivery Systems*. Norwood, NJ: Ablex Publishing. Pp 119–137.
- Lang PJ, Bradley MM, Cuthbert BN (2008): International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8. Gainesville, FL: University of Florida.
- Lee K-H, Egleston PN, Brown WH, Gregory AN, Barker AT, Woodruff PW (2007): The role of the cerebellum in subsecond time perception: Evidence from repetitive transcranial magnetic stimulation. *J Cogn Neurosci* 19:147–157.
- Lewis PA, Miall RC (2003a): Distinct systems for automatic and cognitively controlled time measurement: Evidence from neuroimaging. *Curr Opin Neurobiol* 13:250–255.

- Lewis PA, Miall RC (2003b): Brain activation patterns during measurement of sub- and supra-second intervals. *Neuropsychologia* 41:1583–1592.
- Lewis PA, Miall RC (2006): A right hemispheric prefrontal system for cognitive time measurement. *Behav Processes* 71:226–234.
- Livesey AC, Wall MB, Smith AT (2007): Time perception: Manipulation of task difficulty dissociates clock functions from other cognitive demands. *Neuropsychologia* 45:321–331.
- Maricq AV, Church RM (1983): The differential effects of haloperidol and methamphetamine on time estimation in the rat. *Psychopharmacology* 79:10–15.
- Meck WH (1996): Neuropharmacology of timing and time perception. *Brain Res Cogn Brain Res* 3:227–242.
- Mella N, Conty L, Pouthas V (2011): The role of physiological arousal in time perception: Psychophysiological evidence from an emotion regulation paradigm. *Brain Cogn* 75:182–187.
- Monfort V, Pouthas V, Ragot R (2000): Role of frontal cortex in memory for duration: An event-related potential study in humans. *Neurosci Lett* 286:91–94.
- Monfort V, Pfeuty M, Klein M, Collé S, Brissart H, Jonas J, Maillard L (2014): Distortion of time interval reproduction in an epileptic patient with a focal lesion in the right anterior insular/inferior frontal cortices. *Neuropsychologia* 64:184–194.
- Morillon B, Kell CA, Giraud A-L (2009): Three stages and four neural systems in time estimation. *J Neurosci* 29:14803–14811.
- Morin C, Guigot J, Manai R, Vu P, Guérin N, Samson Y, Pradat-Diehl P, Touitou Y (2005): Impairment in clock-time estimation following right hemisphere ischemic damage. *Brain Res Cogn Brain Res* 22:305–307.
- Nenadic I, Gaser C, Volz H-P, Rammsayer T, Häger F, Sauer H (2003): Processing of temporal information and the basal ganglia: New evidence from fMRI. *Exp Brain Res* 148:238–246.
- Noulhiane M, Mella N, Samson S, Ragot R, Pouthas V (2007): How emotional auditory stimuli modulate time perception. *Emotion* 7:697–704.
- O'Reilly JX, Mesulam MM, Nobre AC (2008): The cerebellum predicts the timing of perceptual events. *J Neurosci* 28:2252–2260.
- O'Reilly JX, Beckmann CF, Tomassini V, Ramnani N, Johansen-Berg H (2010): Distinct and overlapping functional zones in the cerebellum defined by resting state functional connectivity. *Cereb Cortex* 20:953–965.
- Pastor MA, Artieda J, Jahanshahi M, Obeso JA (1992): Time estimation and reproduction is abnormal in Parkinson's disease. *Brain* 115:211–225.
- Pouthas V, Garnero L, Ferrandez A-M, Renault B (2000): ERPs and PET analysis of time perception: Spatial and temporal brain mapping during visual discrimination tasks. *Hum Brain Mapp* 10:49–60.
- Pouthas V, George N, Poline J-B, Pfeuty M, VandeMoortele P-F, Hugueville L, Ferrandez A-M, Lehericy S, Lebihan D, Renault B (2005): Neural network involved in time perception: An fMRI study comparing long and short interval estimation. *Hum Brain Mapp* 25:433–441.
- Rammsayer TH (1993): On dopaminergic modulation of temporal information processing. *Biol Psychol* 36:209–222.
- Rammsayer TH (1997): Are there dissociable roles of the mesostriatal and mesolimbocortical dopamine systems on temporal information processing in humans? *Neuropsychobiology* 35:36–45.
- Rammsayer TH (1999): Neuropharmacological evidence for different timing mechanisms in humans. *Q J Exp Psychol B* 52:273–286.
- Rao SM, Mayer AR, Harrington DL (2001): The evolution of brain activation during temporal processing. *Nat Neurosci* 4:317–323.
- Rubia K, Halari R, Christakou A, Taylor E (2009): Impulsiveness as a timing disturbance: Neurocognitive abnormalities in attention-deficit hyperactivity disorder during temporal processes and normalization with methylphenidate. *Philos Trans R Soc Lond B Biol Sci* 364:1919–1931.
- Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA (1983): Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press.
- Tipples J (2008): Negative emotionality influences the effects of emotion on time perception. *Emotion* 8:127–131.
- Tipples J, Brattan V, Johnston P (2013): Facial emotion modulates the neural mechanisms responsible for short interval time perception. *Brain Topogr* 12:1–9.
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002): Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage* 15:273–289.
- Walsh V (2003): A theory of magnitude: Common cortical metrics of time, space and quantity. *Trends Cogn Sci* 7:483–488.
- Wiener M, Turkeltaub P, Coslett HB (2010): The image of time: A voxel-wise meta-analysis. *NeuroImage* 49:1728–1740.
- Wiener M, Lee Y-S, Lohoff FW, Coslett HB (2014): Individual differences in the morphometry and activation of time perception networks are influenced by dopamine genotype. *NeuroImage* 89:10–22.
- Wittmann M, Lovero KL, Lane SD, Paulus MP (2010a): Now or later? Striatum and insula activation to immediate versus delayed rewards. *J Neurosci Psychol Econ* 3:15–26.
- Wittmann M, Simmons AN, Aron JL, Paulus MP (2010b): Accumulation of neural activity in the posterior insula encodes the passage of time. *Neuropsychologia* 48:3110–3120.