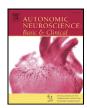
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Heart evoked potential triggers brain responses to natural affective scenes: A preliminary study****



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ABSTRACT

The relationship between ongoing brain interoceptive signals and emotional processes has been addressed only indirectly through external stimulus-locked measures. In this study, an internal body trigger (heart evoked potential, HEP) was used to measure ongoing internally triggered signals during emotional states. We employed high-density electroencephalography (hd-EEG), source reconstruction analysis, and behavioral measures to assess healthy participants watching emotion-inducing video-clips (positive, negative, and neutral emotions). Results showed emotional modulation of the HEP at specific source-space nodes of the fronto-insulo-temporal networks related to affective-cognitive integration. This study is the first to assess the direct convergence among continuous triggers of viscerosensory cortical markers and emotion through dynamic stimuli presentation.

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1. Introduction

Emotions have been claimed to interact with visceral-interoceptive signals (Garfinkel and Critchley, 2013). Cardiac interoceptive afferents project to structures involved in visceral perception (Pollatos et al., 2005a) which modulate complex behavior. While several studies have supported this view indirectly, using external stimulus-locked measures as triggers (Critchley et al., 2004; Pollatos et al., 2007a; Terasawa et al., 2013b), no one has explored the direct coupling of online brain–cardiac interoceptive signals during emotional experience.

Literature linking cardiac interoception to emotional responses (Wiens, 2005) suggests that bodily states intensify emotional feelings (Garfinkel and Critchley, 2013) and interoceptive-emotional

networks share neural hubs (Feinstein et al., 2013; Lane et al., 2009). The heartbeat is one of the key sources of interoceptive signals related to emotion. Heartbeat detection (HBD) tasks (Khalsa et al., 2008) – the moment-to-moment perception of heartbeat signals – activate the IC and the ACC (Canales-Johnson et al., 2015; Couto et al., 2015; Critchley et al., 2004; Pollatos et al., 2005a, 2007b; Sedeno et al., 2014). Moreover, performance in these tasks correlates with the volume of the right alC – as do negative affective states (Bechara and Naqvi, 2004; Critchley et al., 2004).

Emotional processing has also been associated with interoception. Autonomic changes, such as increase in heart rate, trigger emotional modulations. This suggests that interoceptive processes are involved in emotional self-assessment (Lee and Siegle, 2012). Indeed, a proportional relationship exists between emotional experience and interoceptive sensitivity (Critchley et al., 2004; Pollatos et al., 2005b; Werner et al., 2009), indexed by IC activity (Critchley et al., 2004). Activations associated to interoceptive and emotional processes have been shown to overlap in the alC and the ACC (Craig, 2002; Critchley et al., 2001; Damasio et al., 2000; Terasawa et al., 2013b). These are among the most consistently activated areas in the emotion literature (Kober

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et al., 2008). Overall, this evidence highlights interoception as a key element for emotional processing.

Thus cardiac signals would modulate emotional recognition. Further, we hypothesized that such modulation would predominantly involve a fronto-insulo-temporal network (Couto et al., 2013a; Ibáñez and Manes, 2012) responsible for the processing of external and internal signals during cognitive–affective integration (Uddin et al., 2014). To address the above issues, here we relied on the heart-evoked potential (HEP), an event related potential (ERP) triggered by internal body signals, rather than external stimulus locked markers (Pollatos et al., 2007a). The HEP is a cortical correlate of interoceptive afferents to the cortex (Pollatos and Schandry, 2004) related to behavioral performance. Thus, it represents a suitable measure to track ongoing cardiac signatures during induced affective states.

We measured the HEP and estimated its cortical sources while showing affectively-laden video-clips inducing positive, negative, and neutral emotions. This procedure allowed us to observe whether properties of the HEP, including its amplitude and topographical distribution, reflect signatures of internal bodily responses to emotional stimuli.

2. Materials & methods

2.1. Participants

Participants were recruited by advertisements in the community. In a telephone screening we verified criteria for eligibility. Subsequently, those participants that met the criteria underwent a psychiatric and neurological examination to confirm their neurotypical profile. We assessed ten healthy participants (eight women, two men; mean age = 41.3; SD = 14.95; mean education level = 18.5 years; SD = 2.6, 8) with no history of neurological or psychiatric conditions, and with normal or corrected to normal vision. The study was approved by the institution's ethics committee, and all participants provided written informed consent.

2.2. Experimental task design

2.2.1. Emotion induction procedure

While recording high-density electroencephalography (hd-EEG), each participant watched nine affectively-laden clips (Feinstein, 2012) aimed to induce specific emotions classified as positive, negative, and neutral. Each clip was chosen according to previously published criteria; including brevity, self-containment, intensity, and specificity (Feinstein, 2012) (see Supplementary data, Section 1.1).

The pre-test questionnaire of basic emotional features is summarized in Table 1. Before each video, participants performed a one-minute relaxation exercise, and completed baseline questions about their current level of basic emotions. Clips were presented in a pseudo-randomized order (see Supplementary data, Section 1.1.1). Immediately after each clip, participants answered two questions: one regarding emotion recognition, and one about peak intensity of the

Table 1Pre-test questionnaire of emotional features.

	Mean	SD
Average happiness	74%	10%
Percent of time happy	51.5%	22.4%
Percent of time unhappy	14%	9.37%
Percent of time neutral	34.5%	17.55%
How emotionally introspective are you?	41.2%	8%
Level of pleasantness	57%	17%
Level of arousal	52%	18.7%
Satisfaction with the way of life chosen	25%	6.22%

SD: standard deviation; % indicates degree of participants' emotional features at baseline (before the experiment, 1% = null and 100% = full).

experienced emotion. Subsequently, they offered ratings of the current emotion level, choosing from a 100-point modified visual analogue scale (VAS) (see Supplementary data, Section 1.1.2) using the arrows of a computer keyboard. These ratings were repeated every 30 s with a total of 4 ratings over a 2 minute period. Finally, they completed a self-report questionnaire, and rated the arousal level for each clip on a scale from 0 to 8.

2.3. Hd-EEG recording and HEP

Hd-EEG and electrocardiography (EKG) signals were simultaneously registered with a Biosemi Active-two 128-channel system. Data were preprocessed following standard procedures (see Supplementary data, Section 1.2). The HEP was obtained by sampling EEG epochs corresponding to emotional clips, time-locked to each participant's EKG-Rwave (see Supplementary data, Section 1.3). Segments for each subject and clip were collapsed into three valence types (positive, negative, and neutral emotion) according to a previous report (Feinstein, 2012).

2.4. Data analysis

To assess emotional valence, both behavioral and EEG data from each emotion were collapsed into three categories (Feinstein, 2012): (a) positive emotion (clips 4th and 9th), (b) negative emotion (1st, 3rd, 5th, 6th, and 8th), and (c) neutral clips (clips 2nd and 7th). Given that the number of videos in each valence category is not the same, weighted estimation algorithm and z-scores were calculated for each condition during ERP and source reconstruction analysis before statistical comparisons.

2.4.1. Behavioral assessments

A factorial ANOVA was conducted to test the interaction between emotion category and time interval on the emotion ratings, in order to determine whether there were general differences among the arousal generated by each condition (i.e., positive, negative, and neutral emotion) across the five time intervals in which arousal was measured. We then applied a post-hoc Tukey's HSD test to conduct bivariate comparisons among the three conditions.

2.4.2. Heartbeat-evoked potential analysis

The HEP analysis was performed after EEG data preprocessing following previous reports of our group (Couto et al., 2013b; Ibanez et al., 2013). We performed Monte Carlo permutation tests aimed at estimating the null distribution of the test statistics, by generating and analyzing surrogate data that is similar to the original data (Eklund et al., 2011) and compared the experimental conditions of the HEP within five regions of interest (ROIs, see Supplementary data, Section 1.4.1). We first selected an anterior ROI, where classical arousal effects are reported (Olofsson et al., 2008), from three frontal channels (ROI1: left C27, C28, C29; ROI2: central C17, C18, C19; ROI3: right C14, C15, C16). We then averaged a posterior ROI, commonly associated with valence effects, from three posterior channels (ROI4: left A5, A17, A18; ROI5: right A30, A31, A32). These sites coincide with both anterior-posterior HEP locations, (Gray et al., 2007) and resemble ERPs related to emotional valence (LPP and EPN) (Hajcak et al., 2010; Olofsson et al., 2008).

2.4.3. Source reconstruction analysis

The statistical framework used throughout the analysis of the source space is similar to what we previously described (Chennu et al., 2013). Cortical current density maps of ERPs for each clip were reconstructed using an inverse model through a weighted minimum-norm estimation (wMNE) algorithm (Baillet et al., 2011) from the BrainStorm package. Statistics were calculated at whole brain and regional levels, the latter using cluster-based permutation tests implemented in FieldTrip (see Supplementary data, Section 1.4.2). For the HEP scouts selection, we

included those most relevant for interoceptive and emotional processing (Destrieux et al., 2010) such as the dorsal anterior insula-fronto opercular (dal-FO), posterior insula-temporal opercular (pl-TO), ventral anterior insula-orbitofrontal (val-OFC), somatosensory cortex (S), temporo-parietal junction (TPJ), anterior cingulate cortex (ACC), lateral orbitofrontal, (l-OFC), insular cortex (IC), and medial temporal lobe (mTL) (Table 3). All these areas have been implicated in cardiac interoception and emotional awareness (Couto et al., 2013a,c; Feinstein et al., 2013; Garfinkel and Critchley, 2013; Pollatos et al., 2005a; Uddin et al., 2014).

3. Results

3.1. Behavioral results

The following summarizes our results regarding valence, the first rating of peak intensity, and ratings 2 to 5 indexing recovery of emotion up to 3 min post-film. An interaction ($F_{(8.348)}=13.613, p<.001$) between category and rating followed by post-hoc comparisons (Tukey HSD, MS=612.57, df=135.93) evidenced differences in positive > neutral emotions (peak intensity: p<.01; rating 1: p<.01; rating 2: p<.01; rating 3: p<.05), with no differences in the last emotion recovery measure (rating 4: p=.39). The comparison between negative > neutral revealed significant differences in peak intensity, and first 2 ratings (peak intensity: p<.01; rating 1: p<.01; rating 2: p<.05), with no differences in ratings 3–4 (rating 3: p=.24; rating 4: p=.99). Finally, there were no differences for the positive–negative comparison (see Fig. 1A).

Additionally, self-report scores on arousal level showed significant differences between the conditions ($F_{(2,5)}=45.82$; p<.001). While there were no differences between positive and negative clips (HSD post-hoc, p=.26), significant differences were observed between positive–neutral (HSD post-hoc, p=.002), and negative–neutral (HSD post-hoc, p<.001). The emotional experience induced by positive and negative scenes extended beyond clips, decreasing with time.

3.2. Heartbeat-evoked potential

Amplitude of the HEP showed significant modulation by clip condition (emotional valence) for negative > neutral, and positive > neutral in the five ROIs studied. Significant differences in the negative > positive comparison were also observed in posterior ROIs (see Supplementary data, Section 2.1, Table 2, Fig. 1B).

Table 2Significant time windows of HEP emotional modulation per region of interest (ROI). Pairwise comparisons between the 3 conditions (neutral, negative and positive).

Region of interest	Neg > Neu (ms)	Pos > Neu (ms)	Neg-Pos (ms)	
1. Left anterior	216-224	204-388	204	
	284-304	_	_	
	324-348		-	
2. Central anterior	280-344	204-268	564-572	
	-	276-356	-	
3. Right anterior	204-264	204-356	-	
	272-384		-	
Left posterior	308-320	224-236	272-276	
	492	316-320	464-476	
	552-572	348-356	600-604	
	-	476-492	644-648	
	-	556-572	-	
Right posterior	248-260	212-216	204-248	
	448-456	220-232	-	
	548	560-568	_	

Neg, negative emotion; Neu, neutral condition; Pos, positive emotion; significance level: p < .05, Montecarlo simulation in bootstrap mode 5000 iterations; ms, milliseconds.

Table 3Significant differences at source location among conditions.

	Positive vs neutral		Negative vs neutral		Negative vs positive	
	Time (ms)	p-Value	Time (ms)	p-Value	Time (ms)	p-Value
Scout 1 (pI-TO) L	225-270	0.03	480-800	0.01		
			445-468	0.04		
Scout 2 (daI-FO) R	330-410	0.02	475-800	0.005		
	430-450	0.05	310-460	0.02		
Scout 6 (ACC) L	220-320	0.01	330-800	0.001		
	320-380	0.03	192-290	0.02		
Scout 6 (ACC) R			475-800	0.002		
			388-460	0.03		
			180-224	0.04		
Scout 7 (I-OFC) L			275-590	0.005		
			192-208	0.03		
			228-252	0.03		
			615-645	0.03		
Scout 7 (I-OFC) R			315-420	0.01	236-520	0.01
			480-508	0.04		
			430-446	0.04		
Scout 8 (IC) L			478-672	0.002	380-432	0.04
			372-472	0.005		
			344-356	0.02		
Scout 8 (IC) R					300-392	0.01
					450-480	0.04
Scout 9 (mTL) L			625-720	0.008		
			480-552	0.01		
			580-612	0.04		
Scout 9 (mTL) R			580-680	0.01		
			388-456	0.03		
			288-332	0.04		

pl-TO = posterior insula, temporal operculum; dal-FO = dorsal-anterior insula, frontal operculum; ACC = anterior cingulate cortex; l-OFC = lateral orbitofrontal cortex; IC = ICC = ICC

3.3. Source space analysis

Relative to neutral clips, negative clips yielded significantly higher activity (p < .01) in right dal-FO, left pl-TO, bilateral ACC, bilateral l-OFC, bilateral mTL, and left IC scouts. Positive clips, as compared to neutral ones, elicited significant activation increases in left pl-TO, left ACC, and right dal-FO. The positive–negative comparison showed significant clusters (p < .01) in bilateral IC and right l-OFC (see Fig. 1C and Supplementary data, Section 2.2). In line with the above–mentioned behavioral and HEP results, source reconstruction revealed emotional modulation of ongoing cardiac signatures at specific interoceptive regions.

4. Discussion

As compared to neutral clips, both positive and negative clips yielded higher emotional experience extending to post-film periods and decreasing with time. The ongoing cardiac cortical signal was modulated in the 200 and 600 ms windows over frontal electrodes, and to a lesser extent in posterior electrodes. Maximum peak amplitude of the HEP is typically located in anterior electrodes, consistent with the stronger differentiation observed here. Notably, the HEP was modulated by the emotional triggering of a continuous scene, suggesting a possible ongoing interaction of interoception and emotion.

The anterior HEP scalp pattern was modulated by positive and negative valence, confirming the proposed relationship between ongoing cardiac signatures and affective/emotional evaluation (Garfinkel and Critchley, 2013; Pollatos et al., 2005b). Furthermore, the observed scalp modulation resembled the LPP, (Cunningham et al., 2005) which indicates motivational modulation of emotional engagement (Dufey et al., 2011). Emotional processes involving autonomic arousal (Gomez et al., 2008; Palomba et al., 2000), such as evaluative categorization, have been measured through the LPP, which we paralleled by the HEP.

At posterior sites, the HEP showed a small negative-positive modulation that resembles the EPN, which indexes affective qualities

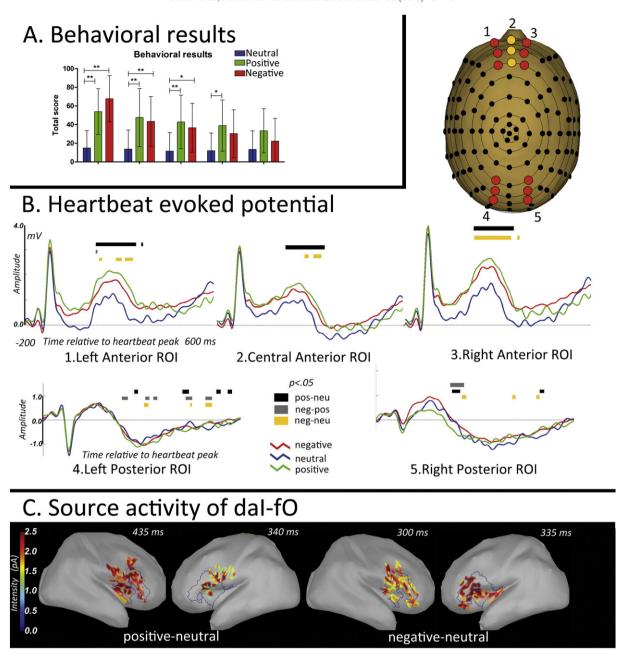


Fig. 1. Main results. A) Behavioral results (for valence and rating). Rating 1: peak intensity of the target emotion experienced while watching the video. Ratings 2 to 5: recovery of emotion up to 3 min post-film. B) HEP at anterior and posterior locations. C) Source space results showing the valence modulation for dorsal anterior insula and frontal opercula. Dal-fO: dorsal anterior insula-frontal opercula.

of stimuli (Ibanez et al., 2012; Olofsson et al., 2008). Note that the EPN also seems to be modulated by non-cardiac bodily signals, such as breathlessness sensation and pain, (Juravle et al., 2014) suggesting a tight connection between interoceptive signaling and affective experience (Feinstein et al., 2013).

Previous HEP source-location studies have indicated activity in the right insula, ACC, prefrontal cortex, and left S2 (Pollatos et al., 2005a). Out of these, we found negative emotional modulation in the right dorsal anterior insular cortex (da-IC), confirming earlier evidence on lateralization of negative affective processing (Critchley et al., 2004). This supports the assumption that the right da-IC is a critical hub for bodily emotional awareness (Craig, 2009). Moreover, negative modulation in the left posterior insula, right ACC, I-OFC, and mTL coincides with networks of emotion processing (Adolphs, 2002; Couto et al., 2013c; Escobar et al., 2014; Feinstein, 2013).

Although earlier emotional modulation for positive rather than negative valence can be expected on the left side (Cunningham et al., 2005), the right a-IC and left ACC pattern merits consideration. This may represent higher arousal for positive than negative clips, consistent with current accounts of positivity bias (Bayer and Schacht, 2014), revealed by more sustained emotional experience over time (Fig. 1A), and higher HEP amplitude (Fig. 1B). Positive emotions modulate perception and memory encoding, possibly playing a role in social interactions (Weinberg and Hajcak, 2010).

Overall, the estimated cortical sources comprised the right anterior insula/fronto-opercular region, left posterior insula, bilateral ACC, and medial temporal lobe. The findings at the levels of HEP amplitude and source space reflect an emotional modulation of ongoing bodily signals processed at specific cortical nodes of the fronto-insulo-temporal network, closely related to integration of

internal-external milieus (Couto et al., 2013a,c; Ibáñez and Manes, 2012; Uddin et al., 2014).

Consistent with meta-analytic investigations of these domains (Lindquist et al., 2012; Phan et al., 2002, 2004; Wager et al., 2008), a network comprising the IC, the ACC, the mPFC, and subcortical regions appears to be the prime candidate for the integration of interoception and emotions. Several studies suggest that we refer to our own bodily state when evaluating our emotional state and that the areas mentioned above serve as common ground (Dunn et al., 2010; Gu et al., 2013b; Pollatos et al., 2005a). Different models propose that the subjective experience of emotion arises from the integration of interoceptive stimuli and external environmental stimuli in the aIC (Craig, 2009; Critchley, 2009; Gu et al., 2013a; Kurth et al., 2010; Terasawa et al., 2013a). Present results support the blending of interoception and emotion and highlight the role of internal cardiac triggers in the rapid encoding of emotional salience.

Limitations of this study are its small sample size, the high femaleto-male ratio, and the bidimensional analysis of emotion through valence and arousal. Future research could benefit from a more detailed multidimensional approach to emotions and multimodal (i.e., auditory and visual) stimuli.

The present study is the first to assess the convergence of cardiac signals and emotion by means of dynamic stimuli and continuous triggers of viscerosensory cortical markers. Our findings may prove relevant to the field of neurocardiology and to models of heart–brain interactions, for both cardiac and psychiatric diseases (Couto et al., 2013b; Critchley and Harrison, 2013; Kemp and Quintana, 2013; Kemp et al., 2010). Also, present results provide a novel approach combining ECG and ERP signals with theoretical implications for the conception of emotions driven by autonomic and bodily sensing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.autneu.2015.06.006.

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