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6 **Error-related Negativity Relates to the**
7 **Neural Processing of Brief Aversive Bodily Sensations**

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Abstract

The error-related negativity (ERN) is an event-related potential occurring in the electroencephalogram (EEG) within 100ms after the commission of an error. The ERN is thought to partially reflect emotionally aversive aspects of error commission, however, it has thus far not been related to the neural processing of other aversive events, such as brief aversive bodily sensations. Therefore, the present study investigated the links between the ERN and the N1 amplitudes of respiratory-related evoked potentials (RREP) and somatosensory evoked potentials (SEP). During the acquisition of high-density EEG, 41 healthy participants performed a Flanker task to evoke the ERN, while RREP and SEP were separately elicited, using inspiratory occlusions and electrocutaneous stimulation of the wrist. Significant positive correlations were observed between the amplitudes of the ERN and the N1 of RREP and SEP, suggesting relationships between the neural processing of different emotionally aversive events, namely errors and bodily sensations.

Keywords: aversive events, electroencephalography, error processing, error-related negativity, respiratory-related evoked potentials, somatosensory evoked potentials

Word count (not counting in-text references, captions, funding information, author contribution, and reference list): 1550

Introduction

The ability to adjust one's behavior to sudden changes greatly depends on the timely detection of errors, enabling quick adaptations of goal-directed behavior (Weinberg, Dieterich, & Riesel, 2015). A popular measure for studying the neural processing of errors is the error-related negativity (ERN; Hajcak, 2012), a negative deflection in the electroencephalogram (EEG). The ERN is usually identified at fronto-central electrodes within 100ms after error commission in cognitive tasks (Olvet & Hajcak, 2009b; Weinberg, Riesel, & Hajcak, 2012), and is thought to mainly originate in the anterior cingulate cortex (Dehaene, Posner, & Tucker, 1994; Ullsperger & von Cramon, 2001).

Despite the wealth of literature, cognitive and emotional processes represented by the ERN are not clear-cut. Apart from conflict (Yeung, Botvinick, & Cohen, 2004) and performance monitoring (Steinhauser & Yeung, 2010), the ERN was suggested to reflect motivational and emotional aspects of error commission (Hajcak & Foti, 2008), a perspective supported by findings of increased ERN in mood disorders (Hajcak & Foti, 2008; Hajcak, McDonald, & Simons, 2003; Riesel, 2019; Weinberg et al., 2012). In this view, the ERN at least partially reflects early emotional processing of an error as a sudden, aversive, and threat-signaling event. However, literature is lacking in exploring this aspect of the ERN in terms of relationships with the neural signatures of other events fitting this description, such as brief aversive bodily sensations. Instances of such EEG markers of bodily sensations include respiratory-related evoked potentials (RREP; Chan & Davenport, 2010), and somatosensory evoked potentials (SEP; Liu et al., 2018), both constituting stable and consistent evoked potentials that, like the ERN, are known to be affected by anxious states and trait negative affect (Chan, von Leupoldt, Bradley, Lang, & Davenport, 2012; Cheng et al., 2016; Chenivresse et al., 2014; Goffaux et al., 2011).

Therefore, we examined potential links between the ERN and the neural correlates of brief, aversive respiratory and somatosensory events in healthy young adults. We used a Flanker task to elicit the ERN (Sucec, Herzog, Van Diest, Van den Bergh, & von Leupoldt, 2019; Tan, Vandeput, Qiu, Van den Bergh, & von Leupoldt, 2019), and evoked RREP and SEP using brief inspiratory occlusions and brief electrocutaneous stimulation, respectively. We focused on the respective N1 amplitudes, the negative-going RREP/SEP components with comparable latency/topography to the ERN (Chan & Davenport, 2010; Cheng et al., 2016), and hypothesized positive relationships between the mean amplitudes of the ERN and N1 of RREP/SEP.

Materials and Methods

Participants

After providing written informed consent, 41 participants were included (32 female; mean age 21.4 years, $SD(40)=4.50$), to whom none of the following applied: current/former somatic, neurological, or psychiatric conditions, intoxication in the prior 24h, smoking, not-corrected impaired vision, insufficient spirometry-measured lung function, and pregnancy. All procedures were approved by the local ethics committee.

Procedure

The order of the below-described procedures was semi-counterbalanced, with the bodily stimulation blocks counterbalanced across participants but both preceding the Flanker task. Participants were able to take a pause in-between blocks as well as procedures.

Inspiratory occlusions. During two 5-minute blocks, participants breathed through a breathing circuit while wearing a nose-clip (for details see Herzog, Sucec, Van Diest, Van den Bergh, & von Leupoldt, 2019). While participants fixated the cross on the screen, brief paired inspiratory occlusions (150ms, ISI=500ms) were manually administered once every second to fifth breath at the start of altogether 40 inspirations (von Leupoldt, Chan, Bradley, Lang, & Davenport, 2011), based on the continuous analog mouth pressure signal (Herzog, Sucec, Van Diest, Van Den Bergh, et al., 2018). After each block, participants rated intensity and unpleasantness of the occlusions on a scale from 0 (unnoticeable) to 10 (highest imaginable).

Electrocutaneous stimulation. A bar electrode filled with electro-conductive gel was attached to the participants' posterior left wrist. A constant-current stimulator (DS7, Digitimer Limited, Hertfordshire, UK) delivered 40 brief paired electrocutaneous stimuli (2ms, ISI=500ms), once every 5-30s. The stimulation intensity (mean: 1.7mA, $SD(40)=0.83$) was constant and individually calibrated to keep the subjective stimulus unpleasantness comparable to the unpleasantness of inspiratory occlusions. As with occlusions, intensity/unpleasantness ratings were taken after each 5-minute block.

Flanker task. An established Flanker procedure was used to elicit the ERN, with five arrowheads horizontally aligned in the center of the screen (e.g. >><>>) at the visual angle of 1.5° vertically and 6° horizontally (Olvet & Hajcak, 2009b; Sucec et al., 2019). On each trial, participants indicated the direction of the central arrowhead by pressing the left or right mouse button. Each arrowhead combination was pseudo-randomly presented ~60 times,

resulting in 240 trials split into four ~4-minute blocks. The arrowheads were presented for 200ms after which 1000ms was allowed for the response. Inter-trial interval varied randomly at 800 ± 200 ms (Pontifex et al., 2010).

EEG Recording and Analysis

EEG was recorded using a 129-channel system (Philips Electrical Geodesics Inc., Eugene, USA) with a sampling rate of 250Hz (reference: Cz, impedance $< 50k\Omega$).

Offline analyses were conducted with BESA Research 6.0 (BESA GmbH, Gräfelfing, Germany) using filter cut-offs of 0.1Hz and 30Hz, and a notch filter (50Hz). Non-repetitive artifacts were manually rejected. Repetitive artifacts (resulting from eye movements/blinks) were detected using principal component analysis, and subsequently corrected. Noisy electrodes were interpolated using a spherical spline procedure, with $< 10\%$ interpolated electrodes. Electrodes were re-referenced to the average reference.

Flanker error trials were segmented into [-500,1000ms] response-locked epochs. Trials were averaged across the epoch, with the [-500,-300ms] interval used for baseline correction (Jackson, Nelson, & Proudfit, 2015). RREP and SEP data were segmented into [-200,1000ms] stimulus-locked epochs and averaged (Herzog, Sucec, Van Diest, Van den Bergh, et al., 2018). For both RREP and SEP, only the first stimulus in each pair was used for the current analysis, using a baseline correction interval of [-150,-50ms]. Before averaging, an additional semi-automatic artifact rejection was performed, with the following parameters: maximum amplitude $< 200\mu V$, minimum amplitude $> 0.01\mu V$, and a maximal gradient of $75\mu V/\partial T$ (Tan et al., 2019). For trial numbers entered into averaging, see Table 1.

Trial type	<i>M (SD)</i>
ERN	19.2 (14.08)
RREP	35.0 (2.73)
SEP	35.4 (1.89)

Table 1 Mean (SD) values of trial numbers included into averaging for each of the three ERPs

The ERN was defined as mean amplitude at FCz in the [0,100ms] interval relative to the erroneous response (Godefroid, Pourtois, & Wiersema, 2016; Sucec et al., 2019). As in previous studies, individual N1 amplitudes were defined as mean amplitudes, in standard intervals of [80,125ms] relative to the stimulus onset for RREP (von Leupoldt et al., 2010), and [90,135ms] for SEP (Clauwaert, Torta, Danneels, & Van Damme, 2018), with both

amplitudes calculated as the mean amplitude at three neighboring individual hotspot electrodes, chosen using semi-automatic peak detection (Herzog, Sucec, Van Diest, Van den Bergh, et al., 2018).

Data Analysis

Five participants were excluded from the ERN analysis due to insufficient error counts (<6; Olvet & Hajcak, 2009a), and two participants from SEP analysis due to electrical artifacts.

Statistical data analyses were performed in RStudio v1.1.383 (RStudio Team, 2015). To test our hypotheses, we calculated bivariate Pearson correlations for the ERN and RREP N1 ($N=36$) and ERN and SEP N1 ($N=35$), using a threshold of $\alpha < 0.05$. This allowed for detection of effects larger than 0.4 at power of 0.82 for RREP and 0.81 for SEP using one-tailed t-tests.

Results

The mean amplitudes measured for the ERN: $-2.45\mu\text{V}$ ($N=36$, $SD=2.24$), for RREP N1: $-2.89\mu\text{V}$ ($N=41$, $SD=3.05$), and for SEP N1: $-1.11\mu\text{V}$ ($N=39$, $SD=1.34$). For grand average waveforms, see Figure 1A/B.

Correlational analyses (Figure 1C/D) demonstrated significant positive relationships between mean amplitudes of the ERN and RREP N1 ($r = 0.55$, $N=36$, $p < 0.001$), between mean amplitudes of the ERN and SEP N1 ($r = 0.41$, $N=35$, $p < 0.05$), and between mean N1 amplitudes of RREP and SEP ($r = 0.57$, $N=39$, $p < 0.001$). The ERN-RREP correlation remained significant ($r = 0.36$, $N=35$, $p < 0.05$) after the exploratory exclusion of the single RREP outlier. The average ratings of intensity/unpleasantness of bodily stimuli are summarized in Table 2. These ratings showed no further significant correlations with ERN, RREP N1 or SEP N1.

Rating	<i>M (SD)</i>
Inspiratory occlusion intensity	2.23 (1.02)
Inspiratory occlusion unpleasantness	2.15 (1.39)
Electrocutaneous stimulation intensity	1.88 (0.94)
Electrocutaneous stimulation unpleasantness	1.58 (1.27)

Table 2 Mean (SD) ratings of intensity and unpleasantness of the bodily sensations used to evoke RREP and SEP, on a scale from 0 (not noticeable/not unpleasant) to 10 (highest imaginable intensity/unpleasantness)

Figure 1 A) Grand average ERN (N = 36) with topography. B) Grand average RREP (N = 41) and SEP (N = 39) with topographies. C) Scatterplot showing a positive correlation (N = 36) of ERN and RREP. D) Scatterplot showing a positive correlation (N = 35) of ERN and SEP [2-column fitting image, in color both online and in print]

Discussion

The present study tested for relationships between the early neural processing of error commission, as reflected by the ERN, and early neural processing of aversive bodily sensations, operationalized as N1 amplitudes evoked by inspiratory occlusions and electrocutaneous stimulation. We expected positive relationships, as previous studies have suggested the ERN to partially reflect the emotional aversiveness of error commission (Hajcak & Foti, 2008; Meyer et al., 2015), supporting a potential relationship to other aversive events. The current results showed such significant correlations, thereby supporting our hypotheses, and demonstrating for the first time a relationship between the neural processing of errors and different bodily sensations. These findings extend previous studies on

1 the interoceptive ERN (Tan et al., 2019), and the links of the ERN with interoceptive
2 accuracy (Sueyoshi, Sugimoto, Katayama, & Fukushima, 2014). Together, the results suggest
3 that different categories of emotionally aversive events (cognitive, respiratory,
4 somatosensory) trigger partially comparable neural responses during approximately 130ms
5 post-event, indicating similarities in the neural processing across different aversive stimuli.
6 This is in line with earlier studies demonstrating that similar, emotion-related brain areas
7 process different aversive bodily sensations within the same individuals, e.g. pain and
8 breathlessness (von Leupoldt et al., 2009), and pain and tinnitus (Vanneste, To, & De Ridder,
9 2019). Notably, these brain areas include the anterior cingulate cortex, also a main generator
10 of the ERN (Dehaene et al., 1994).

11 Aside from the perspective of errors as emotionally salient events, the current results
12 are consistent with viewing aversive bodily sensations as homeostatic or bodily errors. This
13 interpretation might be particularly relevant for the processing of inspiratory occlusions
14 (RREP N1), as respiration normally occurs outside consciousness. A sudden inspiration
15 interruption (and the resulting mouth pressure change) could constitute a motor prediction
16 error, resulting in respective cortical activation (Chan & Davenport, 2010). Recently, it has
17 been suggested that the ERN could relate to an N1 elicited by balance perturbations (Payne,
18 Ting, & Hajcak, 2019), which, if shown empirically, could complement the present results
19 from the bodily-error perspective. If replicated/extended, these findings could not only have
20 significant implications for the understanding of the ERN but also of the perceptual and
21 attentional processes captured by the bodily N1. Moreover, future research is needed to clarify
22 possible factors underlying the observed relationships, for example by manipulating
23 emotional context or event salience.

24 The present study is not without limitations. The sample, though comparable in size or
25 larger than other ERN studies (Olvet & Hajcak, 2009a; Sueyoshi et al., 2014), consisted
26 mainly of young, healthy women, limiting generalization to other populations. Furthermore,
27 including a non-aversive neutral stimulus/condition might have provided further information
28 on whether the observed relationships ultimately arose due to shared aversive character of the
29 stimuli. Moreover, the average number of errors is fairly low and trial number variability high
30 (see Table 1). While it has been shown that ERN amplitudes are sufficiently reliable using as
31 few as six trials (Olvet & Hajcak, 2009b), higher trial numbers could yield more stable and
32 reliable ERPs. Additionally, excluding participants due to low error count and/or artifacts
33 likely reduced our statistical power. Finally, the applied bodily sensations had a rather mild

aversive character, thus requiring future studies using more intense aversive stimuli, and preferably extending to other bodily systems (e.g. gastrointestinal, musculoskeletal).

Nevertheless, the present study provides support for the motivational/emotional perspective of the ERN, and suggests potential relationships between the neural processing of errors and bodily sensations, prompting further research.

Funding Information

This work was supported by the grants from the Research Fund KU Leuven, Belgium (STRT/13/002), a PhD grant from the Research Foundation – Flanders, Belgium (FWO/11G1320N), an infrastructure grant from the Herculesstichting, Belgium (AKUL/13/07), and by the “Asthenes” long-term structural funding Methusalem grant (METH/15/011) from the Flemish Government, Belgium.

Author Contributions

V.J., D.M.T., and A.vL. identified the research problem and designed the study. V.J. and A.vL. constructed the experiment. V.J. collected the data. V.J., D.M.T. and A.vL. developed the analysis strategy, analyzed and interpreted the data. V.J., D.M.T., I.VD. and A.vL. wrote the paper. Special thanks are extended to Dr. Mathijs Franssen and Jeroen Clarysse, for their technical expertise and assistance in the construction of the experiment and conduction of analyses.

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