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Increased cortisol and decreased right ear advantage (REA) in dichotic listening following a negative mood induction

Marien Gadea*, Cristina Gómez, Esperanza González-Bono, Raúl Espert, Alicia Salvador

Area de Psicobiologia, Facultat de Psicologia, Universitat de València, Avda. Blasco Ibañez 21, E. 46010 València, Spain

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Summary This study aimed to evaluate neuroendocrine responses and changes in perceptual asymmetry following an induced negative affect. Cortisol increasing in response to negative affect has been reported, while current brain models of emotion processing link negative affect to the right hemisphere. In this study, the Velten Mood Induction Procedure was used to generate neutral or negative affect in 44 healthy subjects. The PANAS scales were used to assess self-reported mood. A consonant-vowel dichotic listening (DL) test was applied after the neutral and negative affect inductions, and levels of salivary cortisol were determined by radioimmunoassay. For the negative affect condition, and congruent with the hypothesis tested, PANAS positive scores diminished ($p<0.001$) and PANAS negative scores increased ($p<0.001$), yielding an inverse correlation between them. A significant increase in cortisol levels was also seen ($p<0.04$). When taking cortisol reactivity into account, PANAS negative scores were higher for high—than for low—cortisol responders ($p<0.02$). Regarding DL, an increase in left ear items ($p<0.04$) and a decrease in right ear items ($p<0.03$) reported for those subjects who obtained a right ear advantage in the neutral condition. An explanation in terms of Kinsbourne's model for attentional-activation influences on DL is postulated and implications for the issue of affective illness are also discussed.

1. Introduction

Cortisol (C) is a glucocorticoid hormone whose secretion is considered as a marker of the activation of the hypothalamic-pituitary-adrenal (HPA) axis. The increase in C secretion in response to a wide range of stressors is a well-documented

* Corresponding author. Tel.: +34-96-3864615; fax: +34-96-3864668.
E-mail address: marien.gadea@uv.es (M. Gadea).

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phenomenon (for a review see Biondi and Picardi, 1999). Commonly applied laboratory stressors are mental arithmetic (al'Absi et al., 1997), speech tasks (Buchanan et al., 1999), emotional films (Hubert and deJong-Meyer, 1992) or interpersonal rejection paradigms (Stroud et al., 2000). Real-life stressors such as anticipation of stressful events (Smyth et al., 1998; Suay et al., 1999; Salvador et al., 2003) or everyday work stress (Hanson et al., 2000) have also been used. However, a great variability in the individual C response to these manipulations has frequently been observed and the subjective perception of the situation seems to be crucial for the psychoendocrine pattern found (Biondi and Picardi, 1999). In fact, experiencing a negative affect or a depressed mood has been suggested to play a mediating role in the relationship between stressful events and C secretion (van Eck et al., 1996; Buchanan et al., 1999; Hanson et al., 2000; Scarpa and Luscher, 2002). In addition, the psychiatric literature often reports an increased activity of the HPA axis in severely depressed patients (Holsboer and Barden, 1996) as well as normalization of the hyperactive HPA system during successful antidepressant pharmacotherapy (Barden et al., 1995).

While the connection between increased C and negative affect seems plausible, its linking with cerebral laterality has not been fully explored, although a special role for the right hemisphere (RH) has been suggested. Animal research has demonstrated that rhesus monkeys with extreme right frontal electroencephalographic (EEG) activity show more fear-related behavior, as well as elevated cortisol concentrations (Kalin et al., 1998). More interesting, the association between right frontal EEG asymmetry with higher cortisol levels and fear or sadness behavior has recently been replicated in a sample of 6-month-old infants (Buss et al., 2003). In adult humans, Wittling and Pfluger (1990) showed increases in C when negatively emotional films were projected to the RH (via left visual hemifield) compared with left hemisphere (LH) presentation. The authors concluded that cortical regulation of C secretion in emotion-related situations is under primary control of the RH. On the other hand, current brain models of emotion processing also link negative affect experience to the RH (Mandal et al., 1996). A recent review of functional neuroimaging of depressed patients has related the right dorsolateral prefrontal cortex to the emotion-cognition interactions that mediate negative mood states (Liotti and Mayberg, 2001). EEG studies have shown a reduced left relative to right frontal activation in depressed or dysphoric individuals (Davidson et al., 2002). For right parietal regions, there is evidence of higher activation in depressed patients having a comorbid anxious disorder, but also of reduced activation in patients with a 'pure' major depression (Bruder et al., 1997). Regarding induced negative affect (INA), Canli et al. (1998) applied functional MRI and demonstrated an overall RH brain reactivity when normal subjects were viewing emotionally negative pictures.

Finally, some studies have explored the cognitive–behavioral outcome of an INA when taking into account the lateralization of the task evaluated. Bartolic et al. (1999) found that dysphoria, generated by means of the Velten Mood Induction Procedure (VMIP) (Velten, 1968) yielded better figural (RH task) than verbal (LH task) fluency outcomes. Van Strien and Morpurgo (1992) demonstrated that the previous presentation of emotionally threatening stimuli enhanced the detection of letters tachistoscopically projected on the left visual field, although this was not replicated in work by Ferry and Nicholls (1997). The above effects could be explained in terms of Kinsbourne's (1970) model of attention and perceptual asymmetry, with the INA increasing RH activation, which in turn facilitated RH tasks and caused an attentional bias to the left hemispace.

In this study, the VMIP was used to induce both a neutral and a negative affect in healthy subjects. Other authors have shown that C increases under the negative compared with the neutral conditions of the VMIP (Brown et al., 1993), so we expected a similar result. A consonant-vowel dichotic listening (DL) test was also applied after each condition. In the light of these studies, a facilitation of left ear performance on the DL task following INA was predicted to occur in this study.

2. Method

2.1. Subjects

Forty-four (22 men/22 women) right handed (Castresana et al., 1989) undergraduated volunteers with a mean age of 21.9 years were recruited from the University community. Participants had no self-reported history of a major depression or other psychiatric disorders, medical illness or chronic pharmacologic treatment. None of them had previous knowledge of the dichotic technique. With regards to the menstrual cycle, only women free from hormonal contraceptives on testing, who previously reported regular menstrual cycles of between 23 and 31 days were selected, in order to carry out the experiment the week after their menses (defined as performing the test into the interval of 1–7 days following the 3rd day of their menstruation). A previous by-phone interview allowed us to schedule the experiment to avoid a reported premenstrual effect of progesterone on perceptual asymmetries (Hausmann and Güntürkün, 2000; Alexander et al., 2002), as well as any possible influence on baseline mood due to subtle signs of premenstrual syndrome. All subjects were treated in accordance with 'Ethical Principles of Psychologists and Code of Conduct' (American Psychological Association, 1992) and received financial compensation for their participation. Hearing acuity was determined by a Lafayette 15014 C screening audiometer. Subjects included were those with no imbalance in hearing levels of more than 10 dB (at the frequencies of 500, 1000, 2000, 3000 and 6000 Hz).

2.2. Procedure

The subjects were told not to eat, drink, smoke or brush their teeth for 1 h prior to testing. On arrival at the laboratory, all subjects were informed that they would be providing saliva for hormonal analyses, and doing some behavioral tasks in a sound-attenuated room in our laboratory. After obtaining informed written consent, the subjects filled in the handedness questionnaire and were tested for hearing acuity. Then, the first session of mood induction started. The neutral and the negative affect induction conditions of the VMIP were completed in a counterbalanced order: for half of men and half of women the experiment started with the neutral condition. The timing of the protocol was: first VMIP (20 min), PANAS questionnaire (5 min), collection of saliva sample directly from mouth to tube—Unitek R (5 min), performance of the DL test (15 min). A short break of maximum 10 min. Then, second VMIP (20 min), PANAS (5 min), saliva sample (5 min), and finally second DL test (15 min). At the end of the experiment subjects were told about the purpose of the experiment, paid, and thanked for participation. All sessions were carried out at the afternoon, starting between 18:00 and 19:00 h. Although subjected to certain individual differences, cortisol has a circadian cycle with peak levels around 08:00 h (Stone et al., 2001). Afternoon sampling was chosen because this is a time when endogenous cortisol levels tend to drop and stabilize, thus maximizing the likelihood that observed cortisol increases are task dependent. All experiments were performed in a 6-month period from October to March (2001/2002). Men and women were assigned to be distributed equally across dates of testing.

2.3. Materials

2.3.1. Induced negative affect (INA): the Velten procedure

A modified Spanish translation of the Velten Mood Induction Procedure (VMIP) (Velten, 1968) was used, with the aim of generating a neutral or negative affect experience. The VMIP is among the most widely used techniques for studying affective influences upon cognitive and behavioral tasks, and it has demonstrated effectiveness in altering subjective emotional states (Clark, 1985; Brown et al., 1993; Bartolic et al., 1999).

The procedure designed to induce a negative affect consisted of 60 self-referent statements gradually progressing from relative mood neutrality ("Today is no different from any other day") to depressed ("I feel terribly tired and indifferent to things today", "Sometimes I've wished I could die", "All of the unhappiness of my past life is taking possession of me") connoting low self-esteem, pessimism, and lack of energy. The neutral induction consisted of 60 statements unrelated to moods or feelings.

In each of the two conditions (neutral versus INA), the subjects were given a loose-leaf binder each page of which contained one of 60 neutral or sad statements. The instructions were to read each statement silently and attempt to experience the mood suggested by the statement. Immediately, subjects closed their eyes and attempted to visualise an appropriate scene. After 20 s the subject was told to go on to the next statement.

2.3.2. Mood questionnaire: PANAS scale

A Spanish translation of the PANAS scales (Watson et al., 1988) was used to assess self-reported mood. The PANAS consists of two 10-item mood scales that comprise positive (PA) and negative (NA) affect states. High PA reflects a state of high energy, full concentration and pleasurable engagement, whereas low PA represents sadness or lethargy. High NA subsumes a variety of aversive mood states including anger, disgust, guilt, fear and nervousness, with low NA being a state of calmness and serenity. The PANAS was rated on a 5-point scale (from not at all to very much) to document the extent to which the subject experienced each mood state immediately after the presentation of the VMIP conditions (neutral versus INA). Psychometric properties of the PANAS scales have shown to have internal consistency, low correlation, and stability over time (Watson et al., 1988; Melvin and Molley, 2000)

2.3.3. Hormonal determinations: salivary cortisol (C)

The salivary samples, which provide an accurate estimate of free unbound cortisol (Kirschbaum and Hellhammer, 1994), were centrifuged and frozen at −20 °C at the end of each experimental session until determination. All samples from a given subject were run in duplicate in the same assay. Hormonal determinations were performed by an experienced radioimmunoassay technician (Central Research Unit, Faculty of Medicine, University of Valencia, Spain) who was unaware of the hypothesis being tested. Salivary cortisol (C) was determined by a commercial kit adapted to salivary levels after dilution of the standard curve in the buffer, as was recommended in the protocol (Orion Diagnostica, Espoo, Finland). The saliva sample (150 μ1) was mixed with ^{125}I-cortisol tracer and the tube coated with high specific antibody. The C antiserum provided in the kit is produced in rabbits by immunizing a BSA conjugate of cortisol-3-carboxymethoxylamine. The tubes were bath incubated at 37 °C for 30 min. Finally, samples were decanted and counted for 1 min. C levels were expressed in nmol/l and internal and external controls were included in the assays. Good precision was obtained with intra-assay variation coefficients below 5% with a sensitivity of 0.8 nmol/l. C mean values are included in the normal range provided in the assay kit.

2.3.4. Perceptual asymmetry: dichotic listening (DL) test

The dichotic stimuli consisted of the six stop consonants paired with the vowel /a/ to form six consonant–vowel syllables (ba, da, ga, ka, pa, ta). The syllables were paired with each other in all possible combinations to form 36 different syllable pairs. From these, the homonymic pairs (ba-ba, etc.) were included in the test as a perceptual control, but they were not considered in the statistical analyses. The other 30 syllables were duplicated and recorded randomly, giving 60 test trials, with a maximum correct score of 60. The DL test used for this study has achieved a test-retest reliability of 0.86 (for details and further descriptions of the DL test see Gadea et al., 2000, 2003). The DL test was replayed to the subjects from a Sony Walkman WM-EX1HG mini cassette player with plug-in type Sennheiser HD545 headphones. Half of the sample (men and women) was asked to change the orientation of the headphones (left channel to right ear) to balance out any possible difference between right and left channels. The output from the cassette player was calibrated at a level of 75 dB.

The subjects were informed that different syllables would be presented to each ear simultaneously and were asked to report only the syllable perceived most clearly. Thus, one response for each trial was emphasized and, if occasionally two responses were given, then the experimenter only counted the first one, since the first response is highly correlated to the overall ear advantage (Boles, 1992). The data were acquired as the number of correctly reported items from the right (RE) and left (LE) ear.

2.4. Statistical analyses

All variables except NA scores of the PANAS were normally distributed (Kolmogorov–Smirnov test >0.05). So, an Analysis of Variance (ANOVA) with repeated measurements and a Student's *t* test for related variables were applied to DL and C measures, respectively. Differences for PANAS scores were tested with the non-parametric Wilcoxon-signed rank test or with the Mann-Whitney *U* test when appropriate. For some comparisons we have included an effect size index using Cohen's *d*. The effect size index (*d*) is the difference in means for the two groups divided by the standard deviation (SD). It provides a standardized measure of the magnitude of group differences that can be compared across samples (Cohen, 1988). Spearman-rank correlations were also performed for all dependent measures separated into the neutral and INA conditions. Previous analyses showed that the variable 'sex' had no significant effect in any of the dependent variables measured, so definite analyses are presented for the whole sample of men and women (except when noted for DL regarding right ear advantage (REA) at the neutral condition, see below). All statistical analyses were performed on a PC, using the SPSS statistical package set. Data are presented as means and SDs.

3. Results

3.1. PANAS scores

As can be seen in Fig. 1, PANAS positive scores (PA) diminished significantly from the neutral to the INA condition ($z=-3.7$, $p<0.001$) while PANAS negative scores (NA) increased significantly ($z=-4.2$, $p<0.001$). These results were seen despite PA being higher than NA for both conditions.

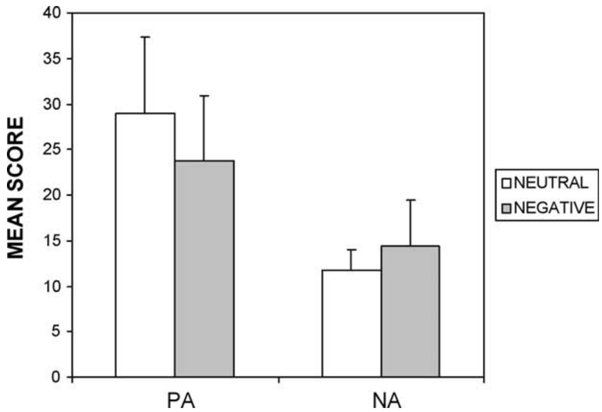

Figure 1 Mean scores for the PANAS scales (PA: positive, NA: negative) depicted for both conditions of induced affect (neutral versus negative affect). Bars: standard deviation. All comparisons were significant ($p<0.001$).

3.2. Cortisol levels

Student's t test for related variables was significant (T (43) $=-2.06$, $p<0.04$) with a (d) index of 0.31, showing an increase in C levels from the neutral (2.6, SD 1.4) to the INA condition (3.1, SD 1.8). Men showed a higher difference in means from the neutral (2.5, SD 1.3) to the INA condition (3.2, SD 2.3) than women (from 2.8, SD 1.6, to 3, SD 1.3) but these differences did not reach statistical significance. The sample as a group obtained a difference in means from the neutral to the INA conditions of 0.5 nmol/l increasing in C. This is more than 15% from the previous value, which would represent a secretory episode (Kirschbaum and Hellhammer, 1989).

3.3. Dichotic listening

A repeated measurements (2×2) ANOVA was carried out with the variables Ear (RE versus LE) and Affect (neutral versus INA conditions). There was a significant main effect of Ear ($F(1, 43)=48.7$, $p<0.001$), indicating a REA in both conditions, and no main effect of Affect ($F<1$). The interaction of Ear×Affect was not significant ($F(1, 43)=2.01$, $p=0.16$) but large enough to suspect that some additional variable could be masking the effects. It was suspected that those who show a left ear advantage (LEA) under the neutral condition could be different from those with a REA. If they were not, one might expect for the entire sample the magnitude of the LEA to increase as RH involvement increases in the INA condition. However, there is general consensus that the emotional prosodic and the linguistic function of speech are organised in a complementary interhemispheric fashion (McNeely and Parlow, 2001). If a complementary arrangement could be possible for a more general processing of emotion versus linguistic functions, then those with a neutral LEA (indicative of a RH representation of language) may show a pattern of data indicating a LH representation of emotion. Therefore, one might expect for those subjects a decreasing of LEA or increasing of REA as LH involvement increases in the INA condition. So, a laterality index ($100\times(RE-LE/RE+LE)$) was applied to the scores obtained under the neutral condition with the aim of including only those subjects who showed a REA (laterality score above zero). Seven subjects (five men and two women) with a LEA in the neutral condition were removed and the above ANOVA was repeated for the 37 REA subjects (84%). The Ear×Affect interaction reached significance ($F(1, 36)=4.5$, $p<0.03$). As can be seen in Fig. 2, the post hoc Student's t tests for related variables showed a significant ((t)=2.1, $p<0.03$) RE decrease from the neutral to the INA condition, with a (d) index of.36, as well as a significant ((t)=−2.1, $p<0.04$) LE increase, with a (d) index of 0.42. These results were shown despite an overall REA (main effect of Ear, $F(1,36)=167.2$, $p<0.001$).

Although knowing that taking data from seven subjects is far from sufficient to obtain statistical power, an ANOVA was applied to their scores for informative purposes. The main effect of Affect was not significant ($F<1$) and for Ear there was a trend to significance ($p=0.09$) due to better performance for the LE (mean 29.8 versus 25.2 for the RE). The Ear×Affect interaction did not reach significance ($p=0.13$), although the mean RE scores increased

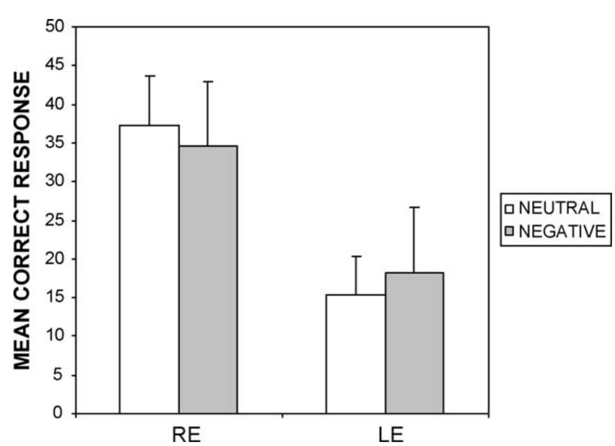

Figure 2 Mean correct responses for both ears (RE: right ear, LE: left ear) obtained for the DL test, and depicted for both conditions of induced affect (neutral versus negative). Results are restricted to those subjects with a REA for the neutral condition. Bars: standard deviation. All comparisons were significant ($p<0.04$ or less).

(21.5, SD 5.7, to 25.3, SD 6.1) and the mean LE scores decreased (32.1, SD 4.8, to 27.5, SD 5.9) from the neutral to the INA condition.

3.4. Correlational analysis

Spearman-rank correlations were performed for all the variables measured (C, RE, LE, PA, NA) separately for the neutral and INA conditions. For the neutral condition, PA and NA were uncorrelated and C did not relate with any of the other variables.

When applying the analysis to the INA condition, PA and NA correlated significantly and inversely to each other ($\rho = -0.48$, $p < 0.001$). NA showed a trend to significance for a positive correlation with C levels ($\rho = 0.25$, $p = 0.09$) but was not related to RE or LE scores.

Given the results obtained for DL, the correlational analysis was repeated, restricted to the sample of 37 REA-neutral subjects, but no different results were found.

3.5. Individual differences

Previous work has documented significant individual differences in cortisol responses to various tasks and stressors (Smyth et al., 1997, 1998) including DL performance (al'Absi et al., 2002). So, we performed an examination of the data taking the results for high and low-cortisol responders to the INA condition into account. A new variable calculated of (INA condition cortisol) minus (neutral condition cortisol) was created. This difference in scores for the two measures of C represents the increasing of C levels from the neutral to the negative affect condition. Then, subjects were classified into high ($n = 23$) and low ($n = 21$) cortisol responders based on a median split of this new variable (al'Absi et al., 1997). Differences for PANAS scores were tested with the non-parametric Mann-Whitney U test, resulting significant for PANAS negative score under the INA condition ($z = -2.3$, $p < 0.02$) due to a higher mean for high cortisol responders (15.6, SD 4.9) than for low cortisol responders (13, SD 4.9). Furthermore, the Spearman-rank correlations between the new continuous variable and PANAS scores also showed a positive relation with PANAS negative score under the INA condition ($\rho = 0.34$, $p < 0.02$). Regarding DL data, we repeated the original ANOVA (with and without the neutral-LEA subjects) adding the new high versus low cortisol responders factor, but no different results were found. And finally, the correlational analysis for DL data and the new continuous variable did not show significant results.

4. Discussion

The main findings of this study were that an INA procedure, applied to healthy subjects, yielded higher salivary C levels, greater self-reported depressed mood, and an increase in LE items reported in DL, as well as lower self-reported elated mood and a decrease in RE items reported in DL.

The analysis of the PANAS scores, which was used to assess self-reported mood, showed not only the above-mentioned effect, but also a significant inverse correlation between PA and NA scales, which appeared only under the negative compared to the neutral affect condition. This replicates previous data from Zautra et al. (1997). These authors, employing the PANAS, found evidence for the hypothesis that the presence of stressful events yields an inverse correlation between PA and NA scales that are uncorrelated otherwise. Zautra et al. (2000) have proposed a model to conciliate opposed proposals in the issue about the degree of independence between states of positive and states of negative affect. Following these authors, one position would point to a univariate model in which the valence of affect would vary along a single continuum from positive to negative, predicting that increases in one affect would correspond to decreases in the other, whereas the alternative view would argue for a bivariate approach, with positive and negative affects being independent and uncorrelated to each other. Zautra et al. (2000) suggested that the degree of relationship between positive and negative affective states might vary with the degree of stress on the person at the time of assessment. Thus, during times of stress, when a narrowing of mental resources may be highly adaptative to allow a more rapid response, a compression of affect dimensions in one could appear, leading to reduced independence and an inverse correlation between PA and NA scales. The results from the present study give additional empirical evidence supporting the model of Zautra et al. (2000).

Regarding C levels, its significant increase when given the INA condition of the VMIP is in agreement with the existing literature (Brown et al., 1993) and supports the view that the experience of negative affect activates the HPA axis. Moreover, individual differences concerning high versus low cortisol responders yielded interesting results to link this hormone to negative affect because the present data pointed to higher reactivity of the HPA axis related to a more pronounced experience of an aversive mood state. In fact, evidence of variability of the neuroendocrine response patterns in HPA axis from one individual to another has been frequently observed in the literature (Kirschbaum et al., 1998).

Therefore, when viewed from the subjective perception and/or from the neuroendocrine response of the subjects, our results indicated that the VMIP was able to generate an experience of a negative affect. The question then was to analyze the consequences of that experience upon perceptual asymmetry when measured with a non-emotional laterality task. The analysis of DL scores under different affect conditions yielded interesting results, since both, a facilitation of LE items and interference on RE items under the INA condition, was observed, but only for those subjects who obtained a REA in the neutral condition. Kinsbourne (1970, 1982) proposed a model for attentional-activation influences on DL performance. Briefly, the model predicts that a secondary task known to be lateralized in one hemisphere is able to alert, activate or 'prime' that hemisphere, which in turns generates an attentional bias to the opposed hemifield, leading to a processing advantage of those items presented there. The model can be tested by analyzing the performance in a primary task (in this case, the DL test) with and without the addition of that secondary task. Manipulations such as judging melodies (Morais and Landercy, 1977) or carrying out a manipulospatial task (Gadea et al., 1997) while performing the DL test have shown to abolish the baseline REA. These data are in accordance with the model considering the processing of music and manipulospatial discriminations as RH tasks. However, to our knowledge, there are only two studies that introduced a negative affect experience and analyzed its consequences on DL performance (Asbjornsen et al., 1992; al'Absi et al., 2002). Asbjornsen et al. (1992) found that the baseline REA lost its significance under the acute stress of electric shock threat for DL errors. The elimination of REA was caused by both an increase in correct LE reports and a drop in correct RE reports, and was explained by arguing a RH dominance for aversive emotional processing in DL. Interestingly, our results resemble these and a similar conclusion can be drawn, except for the fact that the effect of the INA condition was not sufficient to abolish the REA (which appeared significant in both conditions) and, moreover, the results from both ears were observed only for those subjects with a REA under the neutral condition. Methodological manipulations regarding the induction of negative affect might explain these differences, since Asbjornsen et al. (1992) compared conditions of high (shock) versus low (noise) punishment as aversive stimuli to find effects on DL only for the high aversive condition. It could be possible that the VMIP had acted in our sample in an intermediate affective point between the two conditions tested in that study. On the other hand, our results denote the importance of considering different effects regarding the ear advantage obtained initially for a comprehensible analysis of the results. Although limited due to the small sample and so viewed as of heuristic value more than as a conclusion, the results for the subjects with a LEA under the neutral condition were noticeable because they went in an opposite direction (LE decrease and RE increase for the INA condition). A tentative conclusion would suggest a complementary interhemispheric pattern for linguistic and emotional processing that could appear reversed in some individuals. The other mentioned study (al'Absi et al., 2002) applied a rather different design. The authors examined the consequences of two different stressors on cortisol secretion and DL performance with and without attentional instructions (the 'forced attention' paradigm, see Hugdahl, 1995), and took the physiological response of the subjects (high versus low cortisol) into account. For DL performance, al'Absi et al. (2002) found that high cortisol responders focused selective attention better, especially for the right ear in the forced-right attention condition. They interpreted that the results suggesting enhanced sensory intake for those subjects. The present data did not show differences in DL performance for cortisol responders but, given that we did not evaluate DL with forced attention, it is difficult to compare both findings. Moreover, a closer examination of Fig. 1 from the mentioned work, and regarding the non-forced DL condition (the one without explicit attentional instructions and so comparable to our data) shows a non-significant higher mean for LE items in the high cortisol group after the stressor. This result, although non-significant, agrees with our finding of an increasing report of LE items after the INA condition. The scarcity of studies limits conclusions but encourages carrying on with new experiments. Furthermore, these findings can be integrated in a psychophysiological approach through cortisol feedback mechanisms. Cortisol has important sites of feedback to the central nervous system in areas relevant to the processing of incoming stimuli (De Kloet and Reul, 1987). Most important is the amygdala, which on activation during negative affect states may result in cortisol release through its influence on the hypothalamus, and which has important outputs to sensory areas. This could influence the left-right balance of attention-activation to incoming stimuli. However, we also note that a possible limitation of our conclusions is the lack of associations observed between subjective (PA and NA scores) or endocrine (C levels) measures for the INA condition with RE or LE scores.

Gender of the subjects would be another possible source of individual differences in both cortisol reactivity and DL performance. Some studies showed males responding with larger cortisol levels to stress than did women (Smyth et al., 1998) but others (Scarpa and Luscher, 2002) did not find this difference. The present data were in this direction (higher cortisol means for men) but were not statistically significant. Respecting DL, the absence of gender differences is not an unusual feature, and it is compatible with the hypothesis of a weak population-level sex difference that often fails to materialize as a statistically significant finding (see the meta-analytic research on gender of 141 DL experiments by Hiscock et al., 1994).

An additional point can be commented from our data, since we have studied the relationship between lateralization and affect experience in healthy subjects, which raises the question about what this could imply for the issue of affective illness. There is a growing interest in a putative perceptual asymmetry dysfunction as measured with DL in depressed patients, but inconsistent results are frequently reported. Bruder and colleagues found that melancholic depressed patients, depressed patients without a comorbid anxiety disorder, or patients who respond favorably to antidepressive pharmacological treatment, exhibit an abnormally larger REA in verbal DL tasks (Bruder et al., 1989, 1996, 1999). Another study also showed the enhanced REA associated with higher basal plasma C levels in depressed outpatients (Otto et al., 1991). This could indicate that a subgroup of depressive patients might have RH alterations interfering with LE item processing, leading to a higher reporting of RE items due to less competition from LE items, thus leading to an elevated REA. However, other studies have not found such differences (Moscovitch et al., 1981; Johnson and Crocker, 1982; Wale and Carr, 1990; Hugdahl et al., 2003). The observation of a larger REA in some depressed patients is striking when compared to our results of less RE items in normal subjects experiencing a negative affect. Obviously, depression as a syndrome is a qualitatively different entity from a negative affect experienced by a healthy subject, thus making comparisons difficult, but the larger REA reported for depressed patients may well be related to more stable trait differences and therefore both observations do not necessarily conflict. We would like to speculate on some ideas that might conciliate diverging findings. First, there is evidence that anxiety may be associated with the opposite pattern of RH activation when compared to depression, in fact, patients with an early-onset atypical depression (Stewart et al., 2003) or suffering from social phobia with or without a comorbid depressive disorder (Bruder et al., 2004) have shown a diminished REA in verbal DL tests. It is difficult to know whether the present mood induction resulted in increased sadness or anxiety (note that a high NA score for the PANAS subsumes different aversive mood states including disgust and also nervousness). Second, our data hint at individual differences in hemispheric asymmetry during negative affect. It is possible that negative affect may be associated with increased activation of right parietotemporal regions in some individuals, but decreased activity of this region in other individuals, and this could be related to individual differences in which hemisphere is dominant for language function or affective processing. Finally, and turning to Kinsbourne's model, a secondary task may result in activation of a hemisphere, but also in interference, depending on the amount of processing load that is imposed on that hemisphere (low versus high, respectively; Kinsbourne, 1982). If one assumes the negative affect experience as an RH function it would be interesting to consider the degree or intensity of that negative affect. Thus, mild to moderate negative experiences (such as a experimentally INA or even a more clinical anxious state) might result in RH processing activation (and an attentional bias to the LE), but an intense experience (such as a real, pure major depression) might interfere with RH processing, with eventual damage if some critical point is reached, thus resulting in less LE items reported. We would like to point out that this is not meant to be a response for conflictive findings, but a heuristic suggestion to encourage more research in the field of laterality and affect.

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