

An ERP study of vocal emotion processing in asymmetric Parkinson's disease

Running title: Vocal emotion in Parkinson's disease

Authors:

Patricia Garrido-Vásquez^{1*}, Marc D. Pell², Silke Paulmann³, Karl Strecker⁴, Johannes Schwarz⁵, and Sonja A. Kotz⁶

Author affiliations:

1 Department of General and Biological Psychology, University of Marburg, Germany

2 School of Communication Sciences and Disorders, McGill University, Montreal, Canada

3 Department of Psychology, University of Essex, Colchester, UK

4 Center for Neurological Rehabilitation (NRZ Leipzig), Bennewitz, Germany

5 Department of Neurology, University of Leipzig, Germany

6 Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

*Correspondence to:

Patricia Garrido-Vásquez, University of Marburg, Department of General and Biological Psychology, Gutenbergstrasse 18, 35032 Marburg, Germany

E-Mail: pgarrido@uni-marburg.de

Abstract

Parkinson's disease (PD) has been related to impaired processing of emotional speech intonation (emotional prosody). One distinctive feature of idiopathic PD is motor symptom asymmetry, with striatal dysfunction being strongest in the hemisphere contralateral to the most affected body side. It is still unclear whether this asymmetry may affect vocal emotion perception. Here, we tested 22 PD patients (10 with predominantly left-sided [LPD] and 12 with predominantly right-sided [RPD] motor symptoms) and 22 healthy controls in an event-related potential study. Sentences conveying different emotional intonations were presented in lexical and pseudo-speech versions. Task varied between an explicit and an implicit instruction. Of specific interest was emotional salience detection from prosody, reflected in the P200 component. We predicted that patients with predominantly right-striatal dysfunction (LPD) would exhibit P200 alterations. Our results support this assumption. LPD patients showed enhanced P200 amplitudes, and specific deficits were observed for disgust prosody, explicit anger processing, and implicit processing of happy prosody. Lexical speech was predominantly affected while the processing of pseudo-speech was largely intact. P200 amplitude in patients correlated significantly with left motor scores and asymmetry indices. The data suggest that emotional salience detection from prosody is affected by asymmetric neuronal degeneration in PD.

Keywords: Parkinson's disease; vocal emotion perception; asymmetry; striatum, event-related potentials

Abbreviations: EEG = electroencephalogram; ERP = event-related potential; BG = basal ganglia; PD = Parkinson's disease; LPD/RPD = Parkinson's disease with predominantly left/right-sided motor symptoms; HC = healthy controls; IT = implicit task; ET = explicit task

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Introduction

Emotional prosody (speech melody) is an important social signal, which needs to be processed quickly and accurately to allow successful interpersonal interactions. “Prosody” refers to pitch and intensity variations and also temporal aspects (speech rate) of spoken language (Grandjean, Bänziger, & Scherer, 2006; Pell *et al.*, 2006). The basal ganglia (BG), more specifically the striatum (caudate and putamen), have been implicated in vocal emotion processing (Phillips *et al.*, 1998; Morris *et al.*, 1999; Kotz *et al.*, 2003; Grandjean *et al.*, 2005; Beaucousin *et al.*, 2007; Bach *et al.*, 2008; Quadflieg *et al.*, 2008; Leitman *et al.*, 2010; Wittfoth *et al.*, 2010). This raises the question of how this process is affected by neurodegenerative changes of the BG in Parkinson’s disease (PD).

A core feature of idiopathic PD is the unilateral onset of motor symptoms, with more pronounced neurodegeneration in the BG contralateral to the most affected body side (Nahmias *et al.*, 1985; Morrish *et al.*, 1995; Tatsch *et al.*, 1997). This leads to two PD subgroups with predominantly left-sided (LPD) versus right-sided (RPD) motor symptoms, respectively. Distinguishing between subgroups may provide new insight into a possible functional lateralization of the striatum and cortico-striatal circuits in vocal emotion perception.

To date, a possible functional lateralization of the striatum in emotion perception remains largely unexplored. However, at the cortical level hemispheric asymmetry in auditory emotion perception has been documented (e.g., Kotz *et al.*, 2006; Wildgruber *et al.*, 2006, 2009; Kotz and Paulmann, 2011). In particular, emotional salience detection from speech may be predominantly mediated by right superior temporal cortex due to its underlying time scales (Boemio *et al.*, 2005; Schirmer and Kotz, 2006). Derivation of emotional significance from speech is linked to the P200 component of the event-related brain potential (ERP). This

positivity, which peaks around 200 milliseconds after a prosodic stimulus onset, responds differently to emotional and neutral intonations (Paulmann and Kotz, 2008).

Schirmer and Kotz (2006) speculated about early bottom-up influences of subcortical structures, e.g., the striatum, on cortical responses during vocal emotion perception. In fact, one recent study reports increased effective connectivity of superior temporal areas related to emotional speech perception with the right putamen during listening to affective prosody (Ethofer *et al.*, 2011). However, fMRI does not provide sufficient temporal resolution to determine at which point in time a potential right-striatal – superior temporal interaction may take place, and the role of the BG during early stages of vocal emotion perception is still under debate (Kotz *et al.*, in press). There is sparse ERP evidence that early processing of emotional prosody (mismatch negativity; Schröder *et al.*, 2006) and faces (early posterior negativity; Wieser *et al.*, 2011) may be affected in PD. However, damage to the left striatum may not affect the P200 during emotional prosody processing (Paulmann *et al.*, 2011), while the role of the right striatum still warrants investigation.

Very few studies on emotional prosody processing in PD have considered asymmetric degeneration. Blonder *et al.* (1989) and also Clark *et al.* (2008) reported no asymmetry effects on explicit emotion categorization. Ariatti *et al.* (2008) reported problems in categorizing disgust prosody in RPD patients, which is in line with Yip *et al.* (2003). LPD patients showed recognition deficits for happy prosody (Ariatti *et al.*, 2008). Recently Ventura *et al.* (in press) reported that LPD patients exhibit problems in sad prosody recognition.

Thus, results regarding the influence of asymmetric PD on vocal emotion processing remain inconclusive. Furthermore, lesion evidence suggests that impairments in explicit emotional prosody categorization are not indicative of early stage processing deficits (Paulmann *et al.*, 2010, 2011). Likewise, dissociations between early, intact ERP responses and later, altered

explicit ratings have previously been observed in emotional picture perception in PD (Wieser *et al.*, 2006). Lastly, categorization performance in PD may be confounded with cognitive deficits (Benke *et al.*, 1998; Breitenstein *et al.*, 2001; Pell and Leonard, 2003).

We were therefore interested in three different aspects of vocal emotion processing in PD, i) the impact of asymmetry, ii) early versus late processing stages, and iii) explicit versus implicit task settings. We conducted an ERP study in which participants listened to sentences conveying different emotional intonations under explicit and implicit task instructions. We also manipulated lexicality to test emotional prosody processing independent of semantics.

Greater right- than left-striatal dopamine depletion (LPD) was expected to lead to alterations during emotional salience detection (P200). We additionally conducted a behavioral emotion categorization experiment and predicted that impaired categorization performance would affect both patient groups, which would be in line with a great deal of behavioral studies (for reviews see Gray and Tickle-Degnen, 2010; Péron *et al.*, 2011). Comprehensive testing of cognitive functions was performed to assess whether cognitive impairments may influence vocal emotion perception.

Methods

Participants

The sample consisted of 22 patients (11 female) with idiopathic PD. Ten exhibited rather left-lateralized (LPD) and twelve rather right-lateralized (RPD) motor symptoms according to the motor subscale (part III) of the Unified Parkinson's Disease Rating Scale (UPDRS; Fahn *et al.*, 1987), with a difference of at least two points between left and right motor scores and an asymmetry index (AI) of $|0.2|$ to $|1|$ [$AI = (\text{left} - \text{right motor score}) / (\text{left} + \text{right motor score})$]. Exclusion criteria were Beck Depression Inventory scores ≥ 18 (BDI; Beck *et al.*, 1961), task

performance at chance level, signs of dementia indicated by the Mini-Mental State Examination (MMSE; Folstein *et al.*, 1975), and hearing aid use. The UPDRS motor score (part III) and the Hoehn and Yahr stage (Hoehn and Yahr, 1967) were assessed by a movement disorder specialist (KS) during the on state. Patients reported no history of neurological or psychiatric illness except PD. For details on the patient history, please refer to Table 1.

-----Table 1 about here-----

We additionally assessed 22 (11 female) healthy controls (HC) who matched the patients for age, sex, and education. All scored 27 points or higher on the MMSE and below 18 points in the BDI. None reported any history of neurological or psychiatric illness.

All participants were native speakers of German and right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) or self-report (in the case of seven patients). The three groups did not differ significantly in terms of age, education, BDI, or MMSE scores. The patient groups were comparable for Hoehn and Yahr stage, total motor score, and disease duration (see Table 2). Prior to testing, we obtained informed consent from each participant, and the study was approved by the Ethics Committee at the University of Leipzig. Experimental procedures were in accord with the Declaration of Helsinki.

-----Table 2 about here-----

Stimulus material

The stimulus material consisted of auditorily presented sentences. Half were presented in lexical German speech and half in unintelligible pseudo-speech matching German phonotactic rules. All sentences had the same syntactic structure and corresponded to one of four emotional intonations (angry, disgusted, fearful, happy) or a neutral baseline. For lexical sentences, semantics matched emotional prosody. Sentences were spoken by a trained male

or female speaker, were of approximately three seconds duration, normalized, and digitized at a 16-bit/44.1 kHz sampling rate. The material has been successfully used in prior studies (Paulmann *et al.*, 2010, 2011). For the stimuli used in this experiment, previous rating studies reported the following recognition rates (in percent, standard deviations in brackets): anger 99.69 (1.40), disgust 100 (0), fear 86.11 (9.34), happiness 86.63 (7.51), neutral 91.48 (7.57) for lexical sentences; anger 95.40 (5.05), disgust 82.92 (17.01), fear 77.90 (17.47), happiness 73.52 (6.91), neutral 90.10 (15.42) for pseudo-sentences. For each of the four emotions, 20 lexical and 20 pseudo-sentences were presented, adding up to 160 emotional sentences. Additionally, 160 neutral (80 lexical, 80 pseudo) sentences were included. Thus, the material consisted of 320 sentences. For examples, see Table 3.

-----Table 3 about here-----

To ensure intact allocation of attention, an auditory oddball experiment was conducted with 600 Hz tones as standards and 660 Hz tones as deviants (225 standards, 75 deviants; probability: 0.25). Each tone lasted 200 ms, and the inter-stimulus interval was 1000 ms.

Participants completed a comprehensive test battery, comprising the following procedures: MMSE, Benton Facial Recognition Test (Benton *et al.*, 1983), forward and backward digit span (Wechsler, 1997), Trail-Making Test A/B (Reitan, 1992), a listening span test (auditory version of the reading span by Daneman and Carpenter, 1980, translated into German), Token Test (De Renzi and Vignolo, 1962), an in-house phoneme discrimination (audiotaped syllable pairs, each syllable consisting of a phoneme and the vowel “a”) and a word fluency measure (phonemic fluency, semantic fluency, alternating phonemic fluency, alternating semantic fluency), Spielberger State-Trait Anxiety Inventory (STAI; Spielberger, 1983), Depression Anxiety Stress Scales (DASS; Lovibond and Lovibond, 2004), BDI, and Freiburg Personality Inventory (FPI; Fahrenberg *et al.*, 1994), a comprehensive questionnaire that assesses various personality traits.

Procedure

The study consisted of three sessions in which patients were on their normal medication. In session one, the test battery was applied. The EEG was acquired in sessions two and three. The EEG sessions were separated by one week except in the case of one patient. Application of the test battery preceded the first EEG session by maximally two months. In both EEG sessions, participants heard all 320 sentences in a pseudo-randomized order. The task either involved an implicit task (IT) or an explicit task (ET) (see below). The task changed after the first half of a session; 50% of the participants started with the IT, the other 50% with the ET. In the second EEG session, this sequence was reversed.

Half of the participants pressed the “yes” button with their right and the “no” button with their left hand and vice versa. EEG sessions took place in an electrically shielded, sound-attenuated room. Trials started with a fixation cross for 1000 ms, followed by a sentence presentation via loudspeakers while the cross remained on the screen. Subsequently, the question (“emotional or not emotional?”[ET]/ “German or not German?”[IT]) appeared on the screen for 300 ms. Response time via button press was set at a maximum of 1500 ms. A blank screen was presented for 1500 ms before the next trial started.

Trials were divided into eight blocks of 40 stimuli each. The experiment lasted about 40 minutes. At the beginning of each EEG session, the oddball experiment was performed. Participants were instructed to silently count the deviant tones. This procedure took approximately six minutes. After the second EEG session, a selection of 100 (20 per emotion, 50% pseudo) sentences was presented again to the participants. These had the highest recognition rates in prior rating studies. Participants were asked to categorize each sentence as one of five emotional categories within eight seconds after sentence offset.

Data acquisition and analysis

The EEG was recorded from 25 Ag/AgCl electrodes mounted in an elastic cap according to the extended 10-20 system (Sharbrough *et al.*, 1991). Signals were recorded from FP1, FP2, F7, F3, FZ, F4, F8, FT7, FC3, FC4, FT8, T7, C3, CZ, C4, T8, CP5, CP6, P7, P3, PZ, P4, P8, O1, and O2 with a bandpass between DC and 250 Hz and digitized at a sampling rate of 500 Hz. Additional electrodes were placed on the sternum (ground electrode) and bilateral mastoid bones. The left mastoid served as online reference, and electrodes were re-referenced to linked mastoids offline. The electrooculogram (EOG) was recorded from bilateral outer canthi and from one site below and above the right eye, respectively, for subsequent artifact correction purposes. Electrode resistance was kept below five k Ω . The EEG was filtered offline with a bandpass (0.5 – 30 Hz, 3571 points, Blackman window). A 10 Hz lowpass filter (101 points, Hamming window) was additionally applied to the data for graphical display only. An EOG correction was performed using EEP software (Pfeifer *et al.*, 1995).

Seven topographical regions were defined: left-frontal (LF: FT7, F3, FC3), right-frontal (RF: FT8, F4, FC4), left-central (LC: T7, C3, CP5), right-central (RC: T8, C4, CP6), left-posterior (LP: P7, P3, O1), right-posterior (RP: P8, P4, O2), and midline (ML: FZ, CZ, PZ). Normality tests indicated that the data did not follow the assumptions of a normal distribution. Therefore, all data were Box-Cox transformed (Box and Cox, 1964). The most suitable lambda for the transformation was estimated using a transform regression. A constant was added to all data beforehand so that the smallest value equaled one (LaLonde, 2005). Due to the unbalanced design involving different group sizes, type II sums of squares were requested in the ANOVA (Langsrud, 2003). The Huynh-Feldt method was applied to correct for possible violations of the sphericity assumption. Statistical analyses were performed using SAS 8.02.

This paper only reports main effects of group or interactions involving this factor. Significant effects not involving group can be found in the supplementary materials.

Only correctly responded trials were analyzed. There was no significant difference between groups regarding the number of trials per condition that entered the analysis ($p > 0.36$). Data were averaged in an epoch of 1800 ms time-locked to sentence onset, with a 200 ms pre-stimulus baseline. P200 was analyzed from 200 – 380 ms post sentence onset based on previous evidence (Paulmann and Kotz, 2008) and visual inspection. A 5 (emotion) x 2 (lexicality) x 2 (task) x 7 (region) x 3 (group) repeated-measures general linear model analysis was conducted with group as a between-subjects factor and the remaining variables as within-subjects factors. Note that because of many underlying questions to the present study and its rather exploratory nature, the design is quite complex. Therefore, we refrained from analyzing significant interactions with step-down ANOVAs. Instead, Scheffé tests ($\alpha: p < 0.05$) were performed to compare the groups in case of significant interactions and main effects. Thereby, subjectivity in the step-down ANOVAs of manifold interactions and the cumulation of type I errors are avoided. Effect sizes were computed using ω^2 (Olejnik and Algina, 2003). For the behavioral data acquired in the EEG, only percent-correct rates but not reaction times were analyzed, as responses were given in a fixed and delayed time window. The oddball P300 was analyzed from 250 – 600 ms after tone onset (100 ms within-stimulus baseline) using a 2 (condition) x 7 (region) x 3 (group) analysis. The data from the behavioral study were analyzed in a 5 (emotion) x 2 (lexicality) x 3 (group) ANOVA with number of correct answers as a dependent variable.

Test scores and correlative analyses

Group differences for each test score were assessed via nonparametric Kruskal-Wallis tests with Monte Carlo exact estimates. Significant group effects were followed up with Mann-Whitney tests adopting a critical alpha level of $p < 0.017$ due to multiple comparisons.

In order to correlate the test results with the ERP data, three composite scores were built (working memory, frontal functions, psychopathology) based on intercorrelations and theoretical considerations. Therefore, single test scores were first z-standardized with respect to the whole sample (N = 44). The composite scores consisted of the following subtest z-scores: frontal measures – word fluency, Trail-Making Test A/B; working memory – forward and backward digit spans, listening span; psychopathology – STAI (trait scale), BDI, DASS (depression scale), FPI (neuroticism and satisfaction with life scales). Z-scores of test results negatively related to a factor (e.g., satisfaction with life as negatively related to psychopathology) were multiplied by -1 before calculating the composite scores. We did not include the MMSE (lowest score: 25/30), Facial Recognition Test (lowest: 17/27), Token Test (maximum errors: 2), and phoneme discrimination (lowest: 19/25) measures here as they were only applied to ensure intact basic perceptual and cognitive functions and to exclude basic deficits for social stimuli (assessed with the Benton test). As the composite scores showed a normal distribution, group differences were assessed with a MANOVA. Pearson correlations were applied to assess possible relationships of the P200 amplitude with these composite scores as well as age, education, and the oddball P300 amplitude. These analyses were conducted on the whole sample (N = 44), and the alpha level was set to $p < 0.0083$ due to multiple comparisons. P200 amplitudes that were altered in the patients were correlated with motor sidedness scores and asymmetry indices of the patients (N = 22).

Results

Cognitive tests and psychopathology

A significant group effect emerged for the following test scores: backward digit span [$H(2) = 6.86, p < 0.05$], STAI trait scale [$H(2) = 7.77, p < 0.05$], DASS anxiety scale [$H(2) = 9.48, p < 0.01$], and DASS depression scale [$H(2) = 10.49, p < 0.01$].

At $p < 0.017$, LPDs outperformed RPDs in the backward digit span [$U(1) = 149.0, z = 2.24, p < 0.01$]. Both LPD and RPD patients had significantly higher STAI scores than HC (LPD: $U = 273.5, z = 2.28, p = 0.017$; RPD: $U = 276.5, z = 2.38, p < 0.01$). Depression and anxiety scores measured by the DASS were higher for RPD than HC [anxiety: $U(1) = 294.0, z = 3.02$; depression: $U = 300.0, z = 3.24$, both $ps < 0.01$].

The MANOVA did not return any significant group differences in the composite scores working memory, frontal measures, or psychopathology ($ps > 0.07$).

Oddball P300

There were no significant effects involving group ($ps > 0.35$), indicating intact allocation of attention in patients.

Main EEG experiment

Behavioral data

Overall percent-correct rates (standard deviations) were: LPD 82.42 (20.07), RPD 86.18 (19.78), and HC 92.46 (13.04); thus, all groups performed well above chance level (50%). The ANOVA yielded a significant main effect of group [$F(2,41) = 5.88, p < 0.01, \omega^2 = 0.18$]. Scheffé tests indicated that LPD patients' performance was significantly below that of HC

while the other group comparisons were not significant. There were no significant interactions involving group ($p>0.16$).

Emotional salience detection (P200)

A global enhancement of P200 amplitude in LPD patients compared to HC and RPD was found, reflected in a main effect of group [$F(2,41) = 4.39, p<0.05, \omega^2 = 0.13$]. This effect is depicted in Figure 1.

-----Figure 1 about here-----

Furthermore, there were two significant interactions involving group: emotion x task x lexicality x group [$F(8,164) = 2.18, p<0.05, \omega^2 = 0.01$] and emotion x task x lexicality x region x group [$F(48,984) = 1.72, p<0.05, \omega^2 = 0.002$]. Scheffé tests of the first interaction revealed an enhanced P200 amplitude in LPD compared to HC and RPD during the explicit processing of lexical anger. This enhancement was especially pronounced at midline and right-central electrodes, as informed by Scheffé tests of the five-way interaction. Furthermore, the P200 was enhanced during implicit processing of lexical disgust in LPD compared to HC and RPD. The five-way interaction confirmed this effect at all but the two posterior regions. Here, the LPD-RPD difference was significant only for midline electrodes. Finally, the five-way interaction also indicated enhanced P200 amplitudes during the implicit processing of disgust expressions in pseudo-speech in LPD compared to HC and RPD in the right-posterior region. Furthermore, the LPD group showed enhanced P200 amplitudes to lexical sentences in happy intonation during the explicit task at midline electrodes. This was significant in comparison to HC, but not RPD. Please refer to Figure 2 for a graphical display of condition-specific P200 effects.

-----Figure 2 about here-----

As emotional salience detection was of specific interest to the present study, we analyzed the P200 emotion main effect separately for each group and planned contrasts between emotional and neutral prosody were calculated (Paulmann and Kotz, 2008). A highly significant main effect of emotion was observed in all groups [LPD: $F(4,36) = 23.94$, RPD: $F(4,44) = 14.46$, HC: $F(4,84) = 20.43$, all $ps < 0.0001$]. All groups showed lower amplitudes for fear versus neutral [LPD: $F(1,9) = 32.39$, $p < 0.001$, RPD: $F(1,11) = 74.76$, $p < 0.0001$, HC: $F(1,21) = 33.19$, $p < 0.0001$]. Furthermore, the HC group exhibited a reduced P200 amplitude for disgust compared to neutral [$F(1,21) = 6.91$, $p < 0.02$]. This was also the case in RPD [$F(1,11) = 6.19$, $p < 0.04$]. All remaining contrasts were not significant ($ps > 0.12$), which implies that the LPD group did not show a differentiation between disgust and neutral. Please refer to Figure 3 for a graphical illustration of the emotion effect in each group.

-----Figure 3 about here-----

To sum up, the LPD group showed generalized and condition-specific P200 amplitude enhancements during the perception of disgust, anger, and happiness, while the RPD group did not significantly differ from HC in any condition.

Behavioral emotion categorization results

Overall percent-correct rates (standard deviations) were: LPD 78.10 (21.35), RPD 80.25 (22.36), and HC 85.73 (18.63), and thus highly above chance (20%). The main effect of group did not reach significance ($p > 0.05$).

Correlative analyses

There was a positive correlation of the working memory composite score with P200 amplitude for lexical happy sentences during the IT at midline electrodes [$r = 0.40$, $p < 0.01$]. Significant correlations of left motor scores and asymmetry indices with P200 amplitude were observed in several conditions, as displayed in Table 4.

-----Table 4 about here-----

Discussion

The present study investigated vocal emotion perception in PD, with special emphasis on asymmetric patterns of neuronal degeneration. We report altered emotional salience detection from prosody in patients primarily suffering from right-hemispheric dysfunction (LPD). Complementing previous evidence of a role for the striatum in emotional prosody perception (Phillips *et al.*, 1998; Morris *et al.*, 1999; Kotz *et al.*, 2003; Grandjean *et al.*, 2005; Beaucousin *et al.*, 2007; Bach *et al.*, 2008; Quadflieg *et al.*, 2008; Leitman *et al.*, 2010; Wittfoth *et al.*, 2010), the current ERP data raise the possibility that the right striatum influences early emotional prosodic processing. This influence probably consists of a bottom-up mechanism modulating the superior temporal response to emotional prosody (Schirmer and Kotz, 2006). Thus, the interaction between the right striatum and superior temporal areas which respond to emotional speech intonation (Ethofer *et al.*, 2011) may occur early in time. The P200 alteration fits with evidence reported by Schröder *et al.* (2006), who observed alterations in receptive emotional prosody in PD in a comparable time window. The RPD results are in line with previous evidence from patients with left-striatal lesions, who show an intact P200 response to emotional prosody (Paulmann *et al.*, 2011). Thus, the left striatum may not play an essential role in early emotional salience detection, while the right striatum may be involved in this process.

Condition-specific P200 effects

Our findings indicate that stronger right than left-hemispheric degeneration in PD may lead to impairments in emotional salience detection as a function of experimental condition. Thus, it is unlikely that rather unspecific changes of auditory processing in LPD may have caused the

results. For instance, disgust perception was altered during the implicit task. Furthermore, LPD patients generally failed to exhibit a P200 reduction for disgust relative to neutral. Importantly, the P200 amplitude to disgust was positively correlated with left motor score and motor symptom asymmetry, supporting an impact of right-striatal dysfunction. Currently not much is known about a possible striatal involvement in disgust detection from prosody; however, Pell and Leonard (2003) have previously assumed a role for the BG in vocal disgust perception based on their PD data. Furthermore, the right striatum has been implicated in processing disgust from faces (Phillips *et al.*, 1998; Sprengelmeyer *et al.*, 1998). Conversely, a recent meta-analysis primarily involving visual presentation and mood induction studies reports the greatest activation foci for disgust compared to anger, fear, and happiness separately in the right striatum (Vytal and Hamann, 2010). Moreover, individual disgust sensitivity scores are positively correlated with the magnitude of right-striatal activations to disgust-inducing pictures (Mataix-Cols *et al.*, 2008). However, Phillips *et al.* (1998) reported heightened striatum activations only to facial, but not vocal disgust. Several aspects could have contributed to this discrepancy, e.g., stimulus characteristics (vocalizations instead of sentences), comparison condition (mildly happy instead of neutral), or low temporal resolution of fMRI, which may not necessarily cover early emotional salience detection. Further investigation is necessary to clarify the role of the right striatum for processing disgust prosody. Our results suggest that early vocal disgust perception may involve the right striatum, confirming the view of an important role for the BG in disgust processing (Calder *et al.*, 2001).

The P200 was also altered when LPD patients explicitly judged anger expressed in lexical speech. Furthermore, the P200 amplitude at the affected electrode sites (midline/right-central) was positively correlated with left motor score and the asymmetry index. This result fits well with previous research indicating that the striatum is involved in processing anger from

prosody (Kotz *et al.*, 2003; Grandjean *et al.*, 2005; Bach *et al.*, 2008; Quadflieg *et al.*, 2008; Wittfoth *et al.*, 2010). Our results extend these findings by showing that the right striatum could be involved in early emotional salience detection from angry prosody when attention is allocated to its emotional content. The finding is in line with Bach *et al.* (2008), who reported right putamen activation in response to angry prosody especially under explicit task instructions.

LPD patients also showed an enhanced P200 response while implicitly processing lexical happy stimuli. This supports the previously reported role of the striatum in perceiving happy speech intonation (Kotz *et al.*, 2003, 2006). In the visual domain, a meta-analysis identified the right striatum as one of the most consistently activated regions during the processing of happy facial expressions (Vytal and Hamann, 2010). Thus, it may be cross-modally involved in processing happy stimuli. The present results are in line with Ariatti *et al.* (2008), who reported deficits in the explicit categorization of happy prosody in LPD, which – according to our results – may be a consequence of early neural alterations during vocal emotion processing. The fact that happiness was affected calls into question earlier accounts associating PD primarily with impairments for negative emotions (Pell and Leonard, 2003; Dara *et al.*, 2008; Gray and Tickle-Degnen, 2010). In this context, it is also important to consider that the processing of fear was not affected in the present study while impairments for fearful prosody in PD have been reported in several behavioral studies (Breitenstein *et al.*, 1998; Yip *et al.*, 2003; Dara *et al.*, 2008). Moreover, the striatum has been involved in vocal fear processing (Phillips *et al.*, 1998). Early processing of vocally conveyed fear is probably relatively spared in PD, and deficits become apparent at later, more cognitive processing stages, as observed in patients with left-striatal lesions (Paulmann *et al.*, 2009).

Regarding task effects, the current results suggest task-independent P200 alterations in LPD for disgust prosody, although greater during implicit processing. Furthermore, angry prosody

was affected during explicit and happy prosody during implicit processing. Thus, the result pattern seems to depend on the specific emotional category rather than task per se. In the behavioral study, recognition rates for angry prosody were very high while they were lowest for disgust and happiness (see supplementary material). There is also evidence from a gating experiment (Pell and Kotz, 2011) that disgust and happiness are recognized from prosody much later than anger. Thus, it may be easier to derive emotional significance from angry prosody than from happy or disgust prosody. Task instructions, which exert an influence on the attention paid to a prosodic stimulus, may interact with the recognition difficulty of specific emotional intonations. Future investigations will have to consider how these different prosodic characteristics interact with attention.

Regarding lexicality, pseudo-speech was unaffected in LPD, with the exception of disgust, which revealed more wide spread impairments. This fits well with the observation that the putamen is more involved in intelligible than unintelligible speech processing (Kotz *et al.*, 2003, 2006). The role of the BG in speech perception may lie in tracking its temporal structure (Kotz and Schwartz, 2010). More specifically, the BG may integrate dynamically changing speech information such as speech rate, pitch, or intensity variations into a coherent emotional percept (Paulmann and Pell, 2010; Kotz *et al.*, in press). Previous evidence has indicated that PD patients have problems using speech rate information from emotionally inflected speech (Breitenstein *et al.*, 2001). Difficulties with speech rate information have also recently been reported specifically for a group of LPD patients (Flaskamp *et al.*, 2012). Thus, the fact that enhanced P200 responses in the LPD group were mainly limited to lexical speech could indicate that unknown speech patterns do not, or only to a very small extent, rely on BG functions, while these are necessary to derive emotional significance from natural speech.

Behavioral emotion categorization results

Explicit emotion recognition in PD was intact in the present study. Accordingly, some previous studies have also reported an intact categorization performance in PD (Blonder *et al.*, 1989; Kan *et al.*, 2002; Clark *et al.*, 2008; Mitchell and Bouças, 2009). Note, however, that patients may have habituated to the stimuli as the behavioral study was conducted after the EEG sessions. Furthermore, cognitive decline, which may influence categorization performance (Benke *et al.*, 1998; Breitenstein *et al.*, 2001; Pell and Leonard, 2003), was not strong in the present patient sample. LPD patients even outperformed RPD patients in the backward digit span and were numerically also better than HC. This finding weakens the possibility that the P200 effects reported here result from more generalized cognitive deficits.

Limitations of the present results

Although the BG of one hemisphere are predominantly affected in PD, both sides are already involved during early disease progression (Schwarz *et al.*, 2000). Thus, asymmetry of degeneration is only relative, but not absolute. Moreover, the detrimental effects of PD are not confined to the BG. Rather, the disease leads to more wide spread changes in the brain (Braak *et al.*, 2003; Tinaz *et al.*, 2011). For example, according to the model by Braak *et al.* (2003, 2006), the disease proceeds in six stages, starting in the dorsal motor nucleus of the vagal nerve and anterior olfactory structures. Recently in the third stage, the BG are affected and the more advanced the disease, the more wide spread is the pattern of neuronal degeneration. This may also lead to damage in cortical regions at later disease stages. Hence, it should be pointed out that our patients were quite heterogeneous with respect to disease duration and severity of motor symptoms, and thus advancement of degenerative processes in the brain. Furthermore, all were under different regimens of medication and the two patient

groups differed with respect to the distribution of motor subtypes. Therefore, the interpretation of our findings should be rather cautious and warrants further investigation.

Summary and conclusion

In sum, our data show that the asymmetry of neuronal degeneration in PD may affect early emotional salience detection from prosody, indicating that PD is not a uniform disorder. The differential impact of a predominant right- versus left-hemispheric dysfunction on the P200 in the present study is strengthened by correlations with motor variables. This pattern should be replicated and elaborated by future studies.

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Table 1. Characteristics of the patient sample

N°	Age	Sex	Dur	Type	Medication	HY	MS	LMS	RMS	MMSE	BDI
Left-dominant motor symptoms group (LPD)											
01	44	F	13	EQ	LD ^{1,3} , DA, GA	3	10	3	1	28	11
02	64	M	6	AR	LD ¹ , DA	2	19	9	1	28	1
03	77	M	3	TD	DA	2	21	9	6	27	8
04	67	F	15	EQ	LD ³ , DA	3	13	7	0	27	17
05	64	F	7	EQ	LD ¹ , DA	2	10	5	0	30	3
06	69	M	1	EQ	DA	1.5	17	6	0	27	17
07	58	F	3	EQ	DA	1.5	9	5	0	29	11
08	72	M	3	EQ	DA	2	19	8	4	30	10
09	51	F	1	EQ	DA, MI	2	18	13	1	30	17
10	73	F	8	EQ	LD ¹ , DA	2	21	11	6	26	7
Right-dominant motor symptoms group (RPD)											
11	72	M	5	TD	LD ² , DA	2	12	0	4	29	9
12	72	M	3	TD	DA	2	11	2	5	30	5
13	69	F	1	AR	--	1	9	1	7	30	11
14	80	M	6	EQ	LD ¹ , GA	2.5	17	2	7	27	9

15	70	F	12	AR	LD ¹ , DA, MI, CI	4	17	4	6	30	17
16	66	M	3	TD	DA	1.5	10	0	7	28	9
17	55	M	1.5	TD	DA, MI	2	6	1	3	29	3
18	67	M	11	AR	LD ¹ , DA, MI	3	14	1	5	29	7
19	74	F	11	EQ	LD ^{1,3}	3	20	3	7	25	5
20	71	F	5	EQ	LD ^{1,3} , DA	2	8	0	6	29	6
21	62	F	3	EQ	LD ³ , DA	2.5	19	1	14	28	1
22	65	M	5	EQ	LD ² , DA	2.5	21	0	10	29	17

Note. Dur = disease duration (years), HY = Hoehn & Yahr stage (modified; Goetz *et al.*, 2004), (L/R)MS = (left/right) motor score (UPDRS). Sex: M = male, F = female; Type: TD = tremor dominant, AR = akineto-rigid, EQ = equivalent; Medication: LD = levodopa (¹ + benserazide, ² + carbidopa, ³ + carbidopa and COMT inhibitor), DA = dopamine agonist, GA = glutamate antagonist, MI = MAO inhibitor, CI = COMT inhibitor.

Table 2. Summary of group characteristics and test results with means, standard deviations, and statistics

Variable	HC	LPD	RPD	Group effect
Age	65.91 (8.20)	63.90 (10.29)	68.58 (6.33)	p > .41
Education (median) ¹	6	4.5	7	p > .42
Hoehn & Yahr (median)	--	2	2.25	p > .34
UPDRS motor score	--	15.70 (4.50)	13.67 (4.84)	p > .35
Disease duration in years	--	6.00 (4.60)	5.54 (3.64)	p > .90
MMSE	29.01 (0.75)	28.20 (1.48)	28.58 (1.44)	p > .25
Forward digit span	9.27 (1.72)	10.40 (1.51)	9.33 (2.02)	p > .23
Backward digit span	6.64 (1.36)	7.70 (1.49)	6.00 (2.76)	p < .05
Trail-Making Test A completion time (seconds)	40.18 (15.13)	40.80 (14.77)	53.92 (29.13)	p > .34
Trail-Making Test B completion time (seconds)	80.59 (25.67)	82.00 (27.11)	123.08 (90.06)	p > .23
Listening span	3.82 (0.73)	3.60 (0.46)	3.50 (0.64)	p > .30
Word fluency (mean)	27.76 (5.56)	25.58 (7.27)	24.04 (5.47)	p > .29

over four subtests)				
BDI	6.41 (4.35)	10.20 (5.69)	8.25 (4.96)	p > .12
STAI trait scale	33.68 (7.17)	38.80 (5.63)	38.67 (5.19)	p < .05
DASS				
Depression scale	3.32 (4.03)	5.20 (4.13)	7.50 (3.03)	p < .01
Anxiety scale	4.23 (3.57)	7.40 (5.54)	8.33 (3.65)	p < .01
Stress scale	10.77 (7.49)	9.80 (3.29)	11.67 (5.19)	p > .68
FPI				
Satisfaction with life	8.77 (2.29)	8.30 (2.36)	8.58 (2.97)	p > .84
Neuroticism	3.73 (2.95)	5.60 (3.72)	6.00 (3.64)	p > .10

Note. ¹Educational attainment was scored on a scale from 1 to 9, with higher numbers indicating higher education.

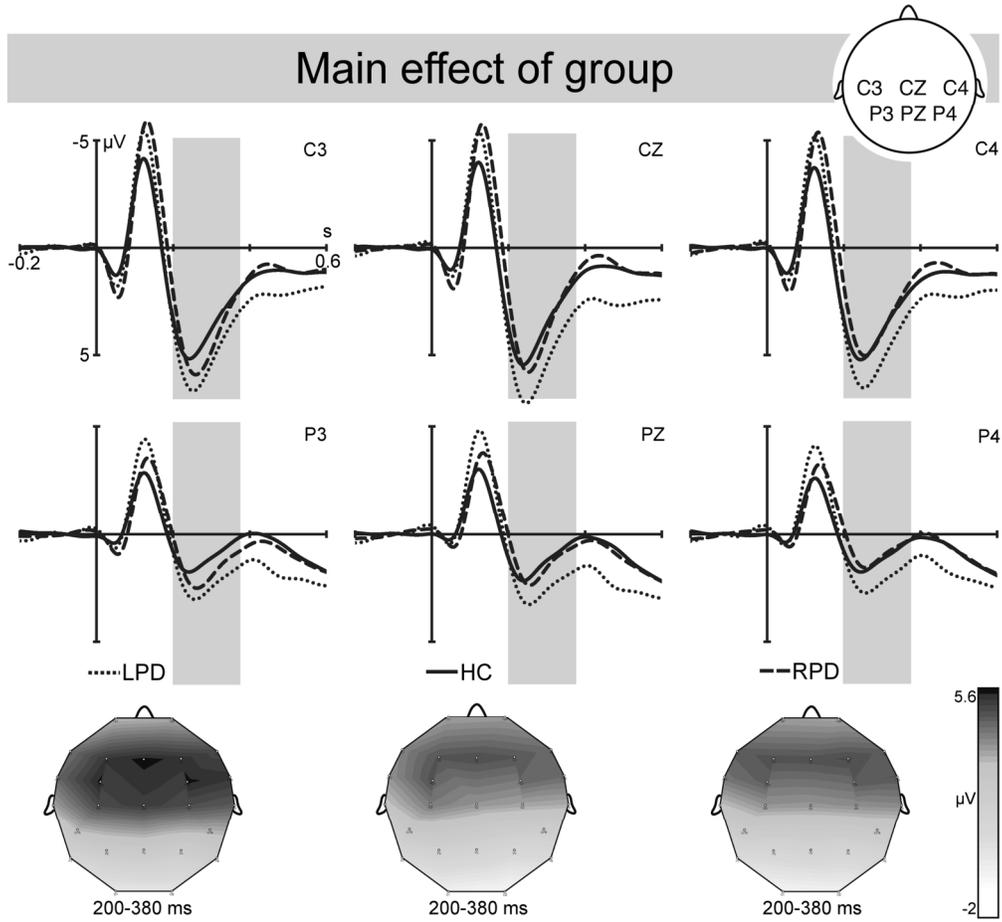
Table 3. Example sentences, with translation for lexical sentences in cursive

Category		Sentences
anger	intelligible	Er hat das Paar gereizt und aufgebracht. <i>He has teased and upset the couple.</i>
	unintelligible	Hung set das Raap geleift ind nagebrucht.
disgust	intelligible	Er hat die Hygiene vernachlässigt und gestunken. <i>He has ignored the hygiene and smelled.</i>
	unintelligible	Hung set die Quadrul verinlussigt ind gepfunken.
fear	intelligible	Sie hat das Messer geschliffen und gezogen. <i>She has sharpened and whipped out the knife.</i>
	unintelligible	Mon set das Bakobi gedellen ind gezagen.
happiness	intelligible	Er hat die Prüfung bestanden und gejubelt. <i>He has passed the exam and cheered.</i>
	unintelligible	Hung set die Pillant gestöngen ind gekobelt.
neutral	intelligible	Sie hat die Speisen erhitzt und angeboten. <i>She has heated and offered the meals.</i>
	unintelligible	Mon set die Galuppe itzmitzt ind ingebaten.

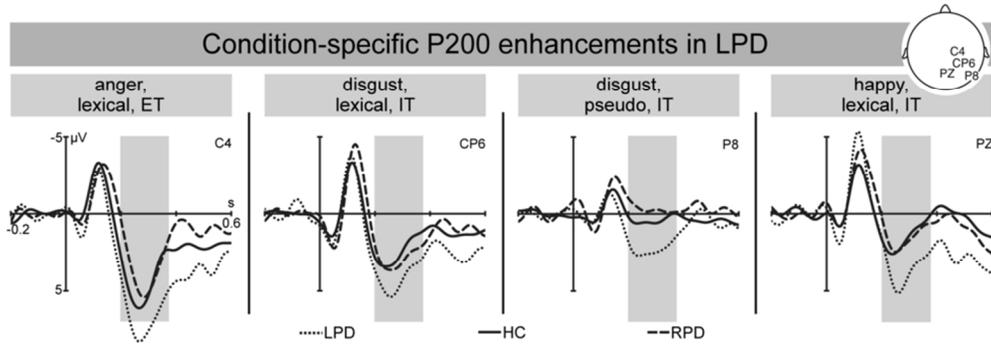
Table 4. Correlation of motor variables with P200 amplitudes in conditions altered in LPD

Emotion	Lexicality	Task	Region	LMS	AI
overall				0.39	0.52*
anger	lexical	ET	overall	0.46°	0.59**
			ML, RC	0.50*	0.65**
disgust	overall			0.50*	0.63**
disgust	lexical	IT	All except LP & RP	0.33	0.43°
disgust	pseudo	IT	RP	0.30	0.52*
happy	pseudo	IT	ML	0.16	0.30

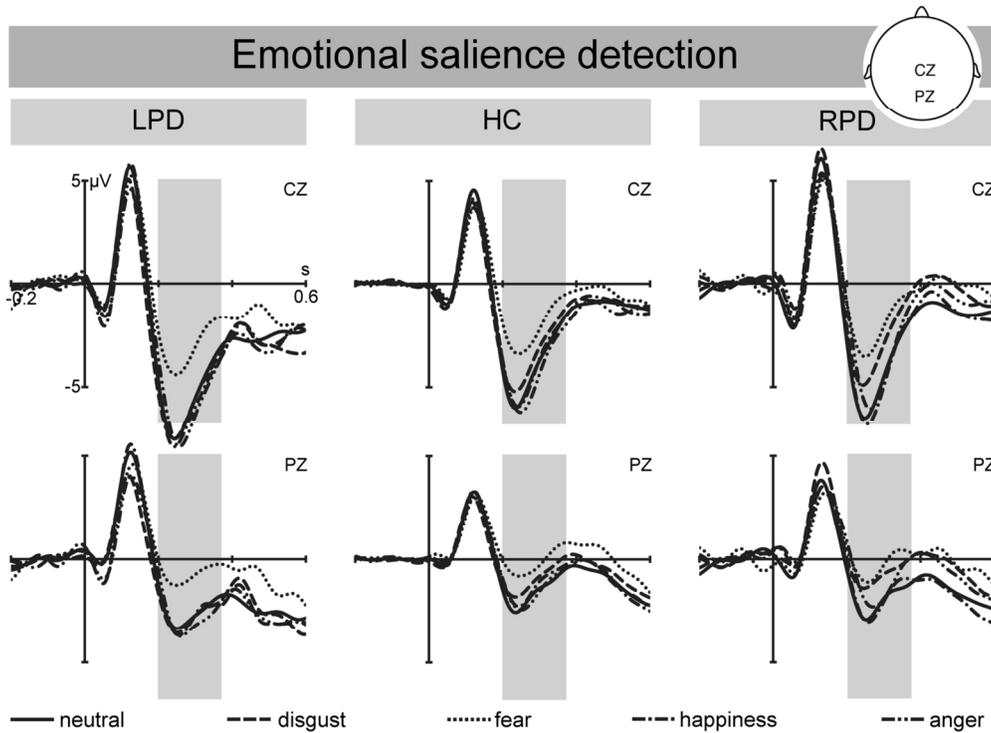
Note. LMS = left motor score, AI = asymmetry index (see participants section), ML = midline, RC = right-central, LP = left-posterior, RP = right-posterior. Significance level was set to $p < 0.025$. ° $p < 0.05$, * $p < 0.025$, ** $p < 0.01$.



Main effect of group: globally enhanced P200 in LPD patients (dotted line). Displayed are the ERPs at six centro-posterior electrodes. Group-specific potential maps for the P200 time window are presented below. 80x73mm (600 x 600 DPI)



Condition-specific P200 enhancements in the LPD group (dotted line). One representative electrode is shown for each of the four affected conditions.
41x14mm (600 x 600 DPI)



Emotional salience detection (P200) separately for each group at two midline electrodes (CZ and PZ). LPD patients do not show an amplitude reduction for disgust sentences (dashed line) relative to the neutral intonation (solid line).
 66x48mm (600 x 600 DPI)

Appendix: Significant effects not involving the factor group

Abbreviations: IT = implicit task; ET = explicit task; LF = left-frontal; RF = right-frontal; LC = left-central; RC = right-central; LP = left-posterior; RP = right-posterior; ML = midline.

Oddball P300

The main effect of condition was significant [$F(1,41) = 52.10, p < 0.0001$], indicating a more positive-going wave for deviants than for standards. We also found a significant interaction of condition x region [$F(6,246) = 6.26, p < 0.001$]. The condition effect was significant at all regions [$F(1,41) = 23.05$ (LF), $F = 32.48$ (RF), $F = 43.79$ (LC), $F = 60.20$ (RC), $F = 80.30$ (LP), $F = 56.86$ (RP), and $F = 27.66$ (ML), all $ps < 0.0001$].

Main EEG experiment

Behavioral data

There was a significant main effect of emotion [$F(4,164) = 17.77, p < 0.0001$]. Percent-correct rates for the neutral condition differed significantly from anger, the category with the highest percent-correct rates [$F(1,41) = 23.49, p < 0.0001$], and from happy, the condition with the lowest percent-correct rates [$F(1,41) = 7.21, p < 0.0125$]. The difference between neutral and fear and neutral and disgust was not significant ($ps > 0.06$).

The main effect of task was significant [$F(1,41) = 160.35, p < 0.0001$], as percent-correct rates were higher for the IT than the ET.

There was a significant interaction of emotion x task [$F(4,164) = 17.08, p < 0.0001$]. No significant main effect of emotion was evident in the IT ($p > 0.84$), while there was an effect of emotion in the ET [$F(4,164) = 20.47, p < 0.0001$]. Percent-correct rates for anger were

significantly higher than for neutral [$F(1,41) = 26.82, p < 0.0001$] while they were lower for happy sentences compared to neutral [$F(1,41) = 7.63, p < 0.01$]. No differences emerged with the other emotions at the $p < 0.0125$ level ($ps > 0.04$).

The interaction between emotion and lexicality was also significant [$F(4,164) = 13.15, p < 0.0001$]. The emotion main effect was significant for both lexical [$F(4,164) = 21.67, p < 0.0001$] and pseudo-sentences [$F(4,164) = 11.85, p < 0.0001$]. In lexical sentences, percent-correct rates were significantly reduced for disgust versus neutral [$F(1,41) = 25.40, p < 0.0001$] and for happy versus neutral [$F(1,41) = 22.84, p < 0.0001$], while the other categories did not differ from neutral ($ps > 0.06$). In pseudo-sentences, percent-correct rates were higher for anger than for neutral [$F(1,41) = 36.58, p < 0.0001$] while no differences emerged between neutral and the other emotion categories ($ps > 0.1$).

The task x lexicality interaction [$F(1,41) = 12.08, p < 0.01$] was characterized by no effect of lexicality on percent-correct rates in the IT ($p > 0.58$), but there was an effect in the ET [$F(1,41) = 10.43, p < 0.01$], reflecting better performance in response to pseudo-sentences than lexical sentences.

Lastly, a three-way interaction of emotion x task x lexicality was also significant [$F(4,164) = 15.22, p < 0.0001$]. The step-down analysis by task yielded significant emotion x lexicality interactions for both the ET [$F(4,164) = 19.58, p < 0.0001$] and the IT [$F(4,164) = 3.37, p < 0.05$]. For the ET, the emotion main effect was significant for lexical [$F(4,164) = 30.99, p < 0.0001$] and pseudo-sentences [$F(4,164) = 10.17, p < 0.0001$]. In response to lexical sentences, percent-correct rates were significantly reduced for disgust [$F(1,41) = 33.75, p < 0.0001$] and happy sentences [$F(1,41) = 27.67, p < 0.0001$] compared to neutral, and enhanced for anger compared to neutral [$F(1,41) = 7.05, p < 0.05$]. In pseudo-sentences only neutral and anger sentences [$F(1,41) = 32.49, p < 0.0001$] differed, with better performance for

anger. The remaining contrasts were not significant ($p > 0.06$). No significant effect of emotion emerged in either of the two lexicality conditions in the IT ($p > 0.07$).

Emotional salience detection (P200)

We observed significant main effects for the factors emotion [$F(4,164) = 51.85$, $p < 0.0001$] and lexicality [$F(1,41) = 30.62$, $p < 0.0001$] with higher P200 amplitudes in response to lexical compared to pseudo-sentences.

The emotion main effect was manifested in reduced amplitudes for fearful [$F(1,41) = 110.65$, $p < 0.0001$] and disgust sentences [$F(1,41) = 10.99$, $p < 0.01$], compared to neutral.

Significant interactions were found for emotion x lexicality [$F(4,164) = 5.29$, $p < 0.01$], emotion x region [$F(24,984) = 6.73$, $p < 0.0001$, $\omega^2 = 0.$], lexicality x region [$F(6,246) = 3.88$, $p < 0.05$], and task x region [$F(6,246) = 4.62$, $p < 0.01$].

The analysis of the emotion x lexicality interaction indicated a significant lexicality effect on P200 amplitude for the categories of disgust [$F(1,41) = 34.17$, $p < 0.0001$], fear [$F(1,41) = 6.91$, $p < 0.05$], happiness [$F(1,41) = 5.51$, $p < 0.05$], and neutral [$F(1,41) = 23.91$, $p < 0.0001$], with smaller amplitudes in response to pseudo- than lexical sentences, respectively.

Next, the emotion x region interaction was analyzed. In all regions, the main effect of emotion was highly significant [$F(4,164) = 55.93$ (LF), $F(4,164) = 64.49$ (RF), $F(4,164) = 49.29$ (LC), $F(4,164) = 61.59$ (RC), $F(4,164) = 8.92$ (LP), $F(4,164) = 12.86$ (RP), $F(4,164) = 39.63$ (ML), all $p < 0.0001$]. Fearful sentences exhibited significantly reduced P200 amplitudes compared to neutral sentences in all regions [$F(1,41) = 93.42$ (LF), $F(1,41) = 129.46$ (RF), $F(1,41) = 87.05$ (LC), $F(1,41) = 118.46$ (RC), $F(1,41) = 30.38$ (LP), $F(1,41) = 42.94$ (RP), $F(1,41) = 105.28$ (ML), all $p < 0.0001$]. The same applied for difference between disgust and neutral, which was at least marginally significant in all regions at an alpha level

of $p < 0.0125$ [$F(1,41) = 6.51$ (LF), $F(1,41) = 5.97$ (RF), $F(1,41) = 10.89$ (LC), $F(1,41) = 11.20$ (RC), $F(1,41) = 8.39$ (LP), $F(1,41) = 6.29$ (RP), $F(1,41) = 9.51$ (ML), all $ps < 0.019$].

The lexicality x region interaction was also analyzed region-wise. There was a significant main effect of lexicality in all regions [$F(1,41) = 25.96$ (LF), $F(1,41) = 58.84$ (LC), $F(1,41) = 17.38$ (RC), $F(1,41) = 25.79$ (LP), $F(1,41) = 23.60$ (ML), all $ps < 0.0001$; $F(1,41) = 10.20$, $p < 0.01$ (RF), $F(1,41) = 7.15$, $p < 0.05$ (RP)], with higher amplitudes in response to lexical than pseudo-sentences, respectively.

Finally, the task x region interaction was manifested in a significant task effect in the two frontal regions [$F(1,41) = 11.55$ (LF), $F(1,41) = 11.07$ (RF), both $ps < 0.01$], each showing higher amplitudes for the ET than for the IT.

Behavioral emotion categorization results

We observed significant main effects of emotion [$F(4,164) = 21.42$, $p < 0.0001$] and lexicality [$F(1,41) = 38.71$, $p < 0.0001$]. The latter effect was explained by higher percent-correct rates for lexical than pseudo-sentences (87.45 vs. 77.55).

For the emotion main effect, performance for the neutral category was contrasted against the other emotional categories. Percent-correct rates were significantly lower in the categories of disgust [$F(1,41) = 57.53$, $p < 0.0001$], happiness [$F = 32.75$, $p < 0.0001$], and fear [$F = 9.44$, $p < 0.01$].

The omnibus analysis yielded a significant interaction of emotion x lexicality [$F(4,164) = 3.12$, $p < 0.05$]. Lexicality affected categorization performance in the case of anger [$F(1,41) = 29.59$, $p < 0.0001$], disgust [$F(1,41) = 16.01$, $p < 0.001$], fear [$F(1,41) = 10.51$, $p < 0.01$], and neutral [$F(1,41) = 5.86$, $p < 0.05$], with lower accuracy scores for pseudo- than lexical speech.