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Yuvaraj, Rajamanickam and Murugappan, Murugappan and Palaniappan, Ramaswamy (2016) The Effect of Lateralization of Motor Onset and Emotional Recognition in PD Patients Using EEG. Brain Topography . pp. 1-10. ISSN 0896-0267.

DOI

https://doi.org/10.1007/s10548-016-0524-0

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The Effect of Lateralization of Motor Onset and Emotional Recognition in PD Patients Using EEG

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Abstract

The objective of this research was to investigate the relationship between emotion recognition and lateralization of motor onset in Parkinson's disease (PD) patients using electroencephalogram (EEG) signals. The subject pool consisted of twenty PD patients [ten with predominantly left-sided (LPD) and ten with predominantly right-sided (RPD) motor symptoms] and 20 healthy controls (HC) that were matched for age and gender. Multimodal stimuli were used to evoke simple emotions, such as happiness, sadness, fear, anger, surprise, and disgust. Artifact-free emotion EEG signals were processed using the auto regressive spectral method and then subjected to repeated ANOVA measures. No group differences were observed across behavioral measures; however, a significant

reduction in EEG spectral power was observed at alpha, beta and gamma frequency oscillations in LPD, compared to RPD and HC participants, suggesting that LPD patients (inferred right-hemisphere pathology) are impaired compared to RPD patients in emotional processing. We also found that PD-related emotional processing deficits may be selective to the perception of negative emotions. Previous findings have suggested a hemispheric effect on emotion processing that could be related to emotional response impairment in a subgroup of PD patients. This study may help in clinical practice to uncover potential neurophysiologic abnormalities of emotional changes with respect to PD patient's motor onset.

Keywords

FEG

Emotion

Parkinson's disease

Body side of motor onset

Electronic supplementary material

The online version of this article (doi:10.1007/s10548-016-0524-0) contains supplementary material, which is available to authorized users.

Background

Emotions are defined as a mental and physiological state characterized by feelings, thoughts, and behavior. They are considered a basic component of intelligence and have been proposed as a better predictor for measuring the aspects of success in life. Several studies have reported emotional recognition impairments in Parkinson's disease (PD) patients (Gray and Tickle-Degnen 2010; Péron et al. 2012). More recently, there has been a discussion on the role of lateralization (left versus right hemisphere) in emotional processing in PD patients. Some studies have reported an absence of asymmetry effects on explicit emotional categorization (Blonder et al. 1989; Clark et al. 2008), while others have found impairments in recognising disgust prosody in patients with predominantly right-sided (RPD) motor symptoms (Ariatti et al. 2008; Yip et al. 2003). Ventura et al. (2012) reported that predominantly left-sided (LPD) patients show impairments in the identification of sadness (Ventura et al. 2012). Recently, Garrido-Våsquez et al. (2013) reported alterations in emotional salience detection from prosody using

event related measures (ERP) measures in patients primarily suffering from RPD (Garrido-Vásquez et al. 2013). Other studies have shown that patients with left- or right-sided damage perform poorly in emotional prosodic identification tasks compared to healthy controls (HC) (Pell and Baum 1997; VanLancker and Sidtis 1992). Thus, findings on the effect of lateralization in PD patients on emotion processing remain inconclusive.

Studies in healthy individuals have shown that EEG signals may reflect the underlying true emotional state of an individual (Petrantonakis and Hadjileontiadis 2010; Wang et al. 2013); evidence of such connection has been found in several EEG frequency bands, including theta, alpha, beta and gamma (Aftanas et al. 2004; Balconi and Lucchiari 2008; Mikutta et al. 2012; Sammler et al. 2007; Sarlo et al. 2005; Yuvaraj et al. 2014a; Yuvaraj et al. 2014c). Especially, spectral power changes in these bands have been implicated in studies of emotional response (Lin et al. 2014; Yuvaraj et al. 2013b). In order to calculate spectral power, several methods are possible for EEG signal processing. The auto-regressive (AR) method, which is based on Burg's algorithm, is a recently developed technique to estimate power spectrum, which has been widely used to estimate EEG signals of epilepsy, migraine, and alcoholic patients (Akben et al. 2011). Compared to classical spectrum estimation methods (e.g., the Fast Fourier Transform method), the AR Burg method can reduce spectral leakage effects due to windowing and provides better frequency resolution (Akben et al. 2011).

The present study examined the relationship between emotional processing and lateralization of motor onset in PD patients. We conducted an EEG spectral power study using the AR Burg method in which PD patients and HC participants viewed multimodal emotional stimuli in order to elicit the six basic emotions (happiness, sadness, fear, anger, surprise, and disgust). As far as we are aware, there has not been any study conducted to explore the relationship between emotional states and lateralization in PD patients using EEG frequency bands and we set out with this aim.

Participants and Methods

Participants

For this study, we recruited 20 right-handed individuals (10 females, 10 males) with PD including 10 predominantly left-sided (LPD) and 10 right-affected (RPD) motor symptoms and 20 healthy right-handed participants, who were matched for age (range between 45 and 65 years), gender, and education level (Table 1). The

patients' side of symptom onset was determined from self-report and symptoms were matched by an experienced neurologists using 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 = (left-right motor score)/(left/right motor score)] (Garrido-Vásquez et al. 2013). The severity of Parkinsonian symptoms ranged from I to III on the Hoehn and Yahr stage scale [H & Y; (Hoehn and Yahr 1967]. All PD patients were optimally medicated during experiment session (ON state) with d2-agonist (n = 10); carbidopa/L-dopa (n = 8), monoamine oxidase B (MAO-B) inhibitor (n = 8), catechol-O-methyltransferase (COMT) inhibitor (n = 7), amantadine (n = 5), or anticholinergics (n = 2). They were recruited through the Neurology Unit outpatient service at the Department of Medicine at the Hospital University Kebangsaan Malaysia (HUKM) medical center in Kuala Lumpur, Malaysia. None of the patients had coexisting neurological (e.g., epilepsy, stoke) or psychiatric disturbance (e.g., major depression or anxiety, psychotic symptoms, etc.) that might independently influence their cognitive functioning. The HC participants were recruited through hospital's medical unit community and/or the patients' relatives. Exclusion criteria for HC participants included any current psychiatric or neurological disorder. Participants' handedness was decided through self-report and confirmed by the Edinburgh handedness inventory (EHS); this test consisted of 10 questions that assessed preference of handedness for a several activities (e.g., writing, throwing, and using scissors).

Table 1
Summary of demographic and clinical data

Characteristics	LPD (n = 10)	RPD (n = 10)	HC (n = 20)	Test's value	p value*
Age (45– 65 years)	57.60 ± 5.32	59.10 ± 3.75	58.10 ± 2.95	F(2,37) = 0.365	p = 0.697
Gender	F = 5, M = 5	F = 5, M = 5	F = 11, M = 9	$\chi^2 = 0.066$	p = 0.796
Education (years)	11.30 ± 4.27	11.20 ± 3.49	11.05 ± 3.34	F(2,37) = 0.005	p = 0.995
MMSE (25-30)	27.50 ± 1.35	26.40 ± 1.26	27.15 ± 1.63	F(2,37) = 2.181	p = 0.127
H & Y (I/II/III)	2.30 ± 0.67	2.50 ± 0.53	NA	F(1,18) = 0.545	p = 0.470
Motor UPDRS	16.70 ± 1.70	18.30 ± 4.60	NA	F(1,18) = 1.066	p = 0.470
Left motor score	9.54 ± 3.74	3.80 ± 2.92	NA	F(1,18) = 3.285	p = 0.021

Right motor score	4.92 ± 3.29	8.75 ± 3.47	NA	F(1.18) = 3.015	P = 0.018
Disease severity	6.25 ± 3.26 (range 1- (n° 10)	RPD ± 3.95 (frangfo) -6)	M& (n = 20)	म्(देत्18)ः जात्तवः ०१५	P ₹alul03
BDI (0-18)	6.30 ± 3.13	6.60 ± 3.89	5.45 ± 2.18	F(2,37) = 0.016	p = 0.984
EHS (1-10)	9.90 ± 0.32	9.60 ± 0.70	9.84 ± 0.72	F(2,37) = 0.429	p = 0.655

Mean ± standard deviation scores are reported. One-way ANOVA was used to test the group effect

LPD left-affected PD patients, RPD right-affected PD patients, HC healthy controls, F female, M male, MMSE mini-mental state exam, H & T Hoehn & Yahr, UPDRS unified Parkinson's' disease rating scale, BDI beck depression inventory, NA not applicable

The participants with normal or corrected vision and normal hearing capabilities (minimum 30 dB HL at 0.5, 1, 2, and 4 kHz, of the better ear) were included in the study. Participants with depression severity [Beck depression inventory (BDI) score ≥ 18; (Schröder et al. 2006)], and global cognitive deterioration [mini mental sate examination (MMSE) score ≤ 24; (Wieser et al. 2006)) were excluded from this study. The HUKM Faculty of Medicine Institutional Review Board (Ref. Number: UKM1.5.3.5/244/FF-354-2012) approved this study. Informed written consent was obtained from each participant or caretaker prior to data collection. All participants were native speakers of Malaysia.

Experiment Design

Emotional stimuli were obtained from a variety of sources, including the international affective picture system (IAPS) database, international affective digitized sounds (IADS) database, and from video clips (collected from internet resources). In order to elicit sadness, fear, and disgust, stimuli were taken from the IAPS and IADS databases; to elicit happiness, surprise, and anger, video clips (after successful pilot studies) were used. Self-assessment questionnaires were also administered in order to gain feedback on subjective responses to the stimuli. A comprehensive description of the stimulus materials, experimental protocols, and procedures followed for the data collection can be found in (Yuvaraj et al. 2014b, c) or refer the supplementary file (S1).

^{*} Group effect is significant at $p \le 0.05$ level. χ^2 Chi square test. One patient in the LPD group had disease duration of 12 years, while among the other LPD patients maximum disease duration was 7 years

EEG Recordings and Data Analysis

An Emotive EPOC (San Francisco, USA) 14-channel wireless (2.4 GHz band) neuroheadset was used to collect the EEG data with a sampling rate of 128 Hz. Brain activity was recorded from AF3, AF4, F7, F8, F3, F4, FC5, FC6, T7, T8, P7, P8, O1, and O2 sites of the 10-20 international system and linked ears were used as reference.

The recorded emotional EEG signals were pre-processed using a 6th order Butterworth bandpass with cut-off frequencies at 4–49 Hz. The frequency bands of interest included theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and gamma (30–49 Hz). The signals were segmented into 6 s epochs (768 samples) (Yuvaraj et al. 2014c). A thresholding method was then used to remove artifacts such as eye blinks, muscle tension, and tremors. Epochs with amplitudes exceeding ± 80 μV were discarded from the study (Gotlib et al. 1998; Yuvaraj et al. 2014b, c). Finally, 120 epochs of artifact-free EEG signals of each emotional state were selected from LPD, RPD, and HC participants for further analysis (Yuvaraj et al. 2014b). A power spectral density (PSD) estimate was computed from each of the selected epochs using the auto-regressive (AR) Burg method (Akben et al. 2011). Then, the relative power of each frequency sub-band (theta, alpha, beta, and gamma) was obtained by dividing the power of each sub-band by the total power estimated by the AR Burg method (Yuvaraj et al. 2013b). MATLAB software was used to compute AR PSDs with window length of emotional EEG signals.

The first step in data analysis was calculation of analysis of variance (ANOVA) with GROUP (3 groups: LPD, RPD, and HC) as the between-group factor and EMOTION (six emotions: happiness, sadness, fear, anger, surprise, and disgust) and LOCATION (14 electrodes: AF3, AF4, F7, F8, F3, F4, FC5, FC6, T7, T8, P7, P8, O1, and O2) as the within-group factors, for each frequency band. If a significant main effect or interactions with EMOTION were found in a frequency band, a post hoc analysis was conducted using ANOVA with GROUP as the between-group factor and LOCATION as the within-group factor. For the post hoc two-way ANOVA, a Tukey honest significant difference (HSD) test was performed to compare the relative power spectra of each emotion across the three groups. The Greenhouse–Geisser correction was used to adjust for violations of sphericity. When a significant GROUP X LOCATION interaction was detected by ANOVA, a separate ANOVA with the single factor LOCATION was performed. The behavioral measures (recognition rate and subjective ratings) were analyzed by another ANOVA with GROUPS as the between-group factor and EMOTIONS as the

within-group factor. Significance was established using a p value less than 0.05 in all cases.

Results

Participant Characteristics

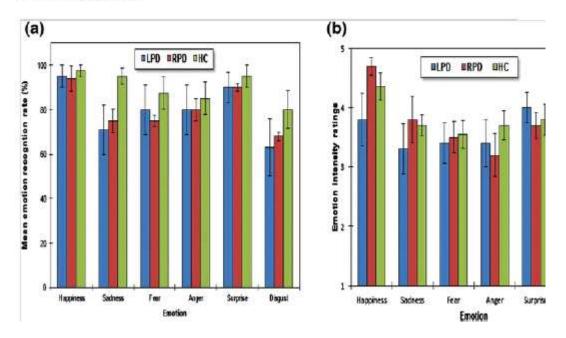
ANOVA was conducted to establish homogeneity between the groups (LPD, RPD, and HC participants) with regards to demographic and clinical variables. As shown in Table 1, the three groups did not differ across demographic variables, such as age, gender, and years of education. The analysis did not indicate any significant differences between the groups across MMSE, BDI, and EHI scores (p > 0.05). The scores on the measures of H & Y, disease severity, and motor performance also did not across PD groups. These results indicate that the PD and HC participants were homogenous with respect to demographic and clinical characteristics. An expected significant group difference emerged for both left and right motor scores.

Behavioral Measures

Figure 1 shows the results of the behavioral data obtained from the self-assessment questionnaire. Figure 1a shows the mean recognition rates of six emotional stimuli presented to LPD, RPD, and HC participants. The ANOVA did not yield a significant main effect between Group [F(2,37) = 0.769; p = 0.802]. Overall, the happiness stimuli was most easily recognized (average recognition rate (%) = LPD 95.42; RPD 94.14, HC 97.50), whereas stimuli related to disgust was least easily recognized (average recognition rate (%) = LPD 65.26 %, RPD 68.21, HC 80.16). Therefore, the recognition performance by all three group levels was well above chance level of 50 % i.e. most of the participants were induced by the expected emotion through the stimuli. The mean subjective ratings of LPD, RPD, and HC participants are shown in Fig. 1b. The ratings were higher for happiness (ratings [1-5] = LPD 3.8, RPD 4.7, HC 4.35) and lower for disgust (ratings = LPD 2.5, RPD 3.4, HC 2.85) in both groups. There was no significant difference between Group [F(2,37) = 1.746; p = 0.189] and Group X Emotion interaction [F(10,185) = 0.762; p = 0.646] was not observed. These behavioral measures ensures the validity of the stimuli used to elicit the targeted emotions and to investigate the correspondence with EEG responses. Moreover, behavioral responses were given at a fixed point in time (15 s). Therefore, behavioral data were not further analysed.

Fig. 1

Behavioral measures results. a Mean (±standard error) percentage of correct response for each of the six emotions to emotional stimuli across the three experimental groups and b Mean (±standard error) subjective ratings of emotion intensity across the three experimental groups



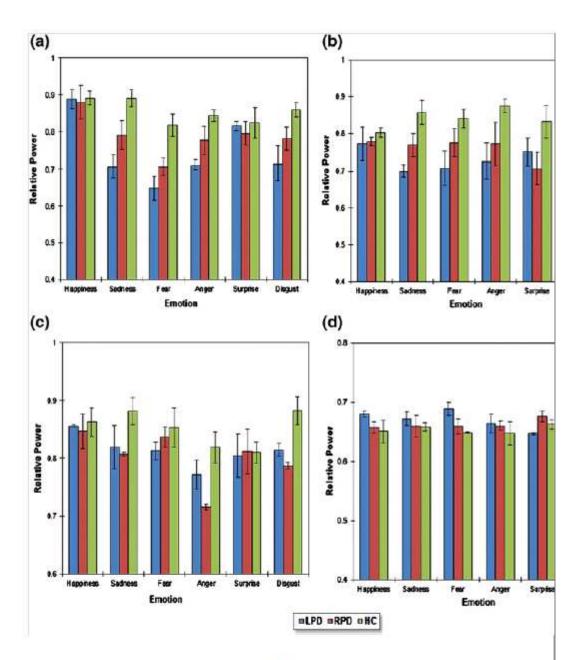
Emotion EEG Analysis

For the gamma band, significant differences between the factor Group [F(2,357)=67.70; p<0.0001], Emotion [F(5,1785)=16.209; p=0.0284], and Location [F(13,4641)=174.347; p<0.0001] were identified. We also noticed a significant Group X Emotion [F(10,1785)=18.838; p<0.0001], Emotion X Location [F(26,4641)=5.616, p<0.0001], and Group X Emotion X Location interaction [F(130,23205)=6.411; p<0.0001] on the gamma band. The second ANOVA, on the gamma band, separately confirmed the significant effect of Group X Location interaction with happiness [F(26,4641)=27.219; p<0.0001], sadness [F(26,4641)=34.508; p<0.0001], fear [F(26,4641)=30.539; p<0.0001], anger [F(26,4641)=40.393; p<0.0001], surprise [F(26,4641)=40.128; p<0.0001], and disgust [F(26,4641)=31.475; p<0.0001]. The Tukey HSD post hoc test found that LPD patients (right hemisphere pathology) had less gamma activity compared to RPD patients HC participants (Fig. 2a). In particular, both PD groups had lower spectra values for negative emotions (sadness, fear, anger, and disgust) than positive emotions (happiness and surprise). The significant emotion difference in

gamma band activity was from the electrodes located over the anterior part of the scalp (AF3, AF4, F7, and F4), as revealed by one-way ANOVA test.

Fig. 2

Relative powers of EEG signals across a gamma b beta c alpha and d theta frequency bands for LPD, RPD, and HC participants averaged over the 14 electrodes. *Standard errors* are represented with *vertical lines*



A significant difference between the LPD, RPD, and HC participants was identified [F(2,357)=26.148; p<0.0001] on the beta band. Significant differences were also found for Emotion [F(5,1785)=15.035; p<0.0001] and Location [F(13,4641)=101.266; p<0.0001]. We also detected a significant interaction between Group X Emotion [F(10,1785)=20.975; p<0.0001] and Emotion X Location [F(26,4641)=5.394; p<0.0001] on the beta band. Second ANOVA on

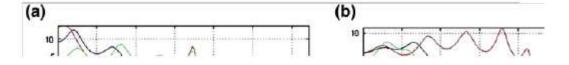
the beta power spectra separately confirmed a significant effect of Group X Location interaction with happiness [F(26,4641)=21.978; p<0.0001], sadness [F(26,4641)=25.799; p<0.0001], fear [F(26,4641)=25.532; p<0.0001], anger [F(26,4641)=31.563; p<0.0001], surprise [F(26,4641)=33.880; p<0.0001], and disgust [F(26,4641)=23.102; p<0.0001]. A post hoc Tukey HSD test indicated that LPD patients showed less emotional activity in the beta band compared to RPD and HC participants (Fig. 2b). The difference in beta band emotional activity was distributed over frontal and temporal regions (F8, T8, and F4).

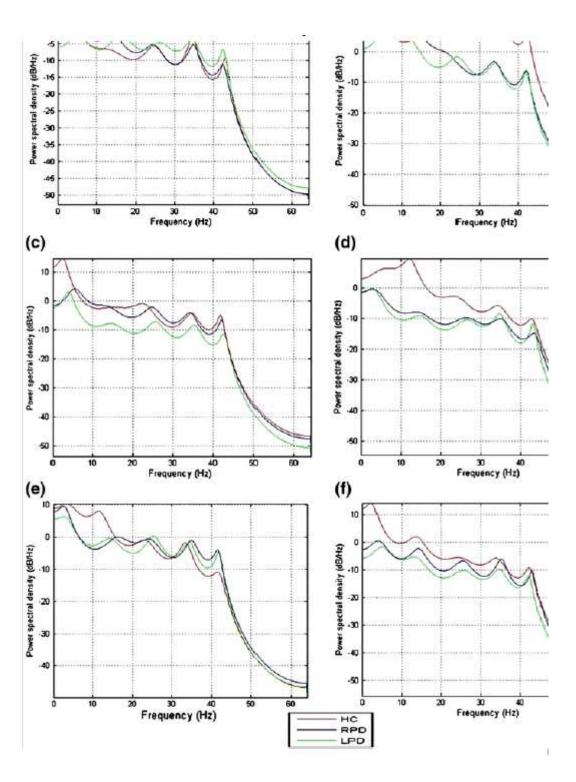
There was no significant group difference found for the alpha band (p=0.369); however, we found a significant main effect for Emotion [F(5,1785) = 3.330; p=0.005] and Location [F(13,4641) = 189.354; p<0.0001]; additionally, we detected a significant interaction between Group X Emotion [F(10,1785) = 9.612; p<0.0001] and Group X Location [F(65,23205) = 10.754; p<0.0001]. In order explain this interaction, a post hoc 2-way ANOVA separately confirmed significant the effect of the Group X Location interaction with happiness [F(26,4641) = 6.836; p<0.0001], sadness [F(26,4641) = 5.187; p<0.0001], fear [F(26,4641) = 4.805; p<0.0001], anger [F(26,4641) = 5.760; p<0.0001], surprise [F(26,4641) = 5.420; p<0.0001], and disgust [F(26,4641) = 5.275; p<0.001]. LPD patients showed significantly less alpha activity during emotional processing compared to RPD and HC participants, notably for negative emotions, as revealed by Tukey HSD test (Fig. 2c). Differences in alpha band power spectra were mostly distributed over anterior regions (AF4, F8, F4, and FC6).

There was no difference found for the theta band in the LPD, RPD, and HC participants (p > 0.375) during emotional processing (Fig. 2d). Figure 3 shows the average power spectra of the EEG using AR Burg of LPD, RPD, and HC participants. The power spectra across different emotional states of LPD patients were lower compared to RPD and HC participants, suggesting a pattern of underconnectivity in PD patients primarily suffering from right hemisphere dysfunction (LPD) during emotional processing.

Fig. 3

Power spectral density (1-49 Hz) of EEG using AR Burg method across different emotional states taken from HC participants, RPD and LPD patients. a Happiness b Sadness c Fear d Anger e Surprise and f Disgust





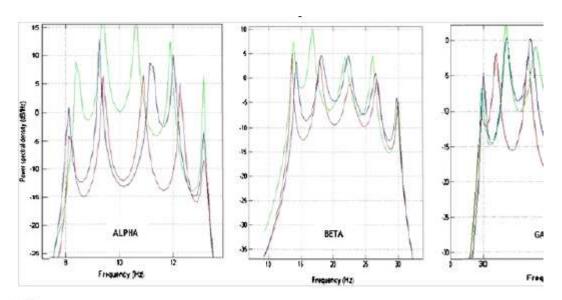
Discussion

The current study evaluated the effect of lateralization of motor onset on emotional recognition in PD patients using EEG. We did not find any differences across behavioral measures. Intact behavioral performance was reported in previous studies (Clark et al. 2008; Garrido-Vásquez et al. 2013; Kan et al. 2004) This may due to the levels of cognitive decline (MMSE score: LPD-27.50 \pm 1.35; RPD-26.40 \pm 1.26), which may influence emotion recognition performance (Garrido-Vásquez et al. 2013; Pell and Leonard 2003), were low in the current study. LPD patients outperformed RPD patients in recognizing the emotional stimuli for happiness, fear, anger, and surprise and performed numerically better than HC participants (see Fig. 1).

Regarding emotional EEG signals, the spectral powers at alpha, beta and gamma frequency oscillations were significantly different between LPD, RPD, and HC participants during emotional processing. Especially, the LPD patients showed decreased spectral power at these frequency bands compared to RPD and HC (Fig. 4). This difference can be attributed to neuropathological evidence that PD is associated with the slowing of oscillatory brain activity (Neufeld et al. 1988). Distributed neural processes are integrated to allow highly ordered cognitive functions through high frequency oscillations and such oscillations are considered critical for cognitive, perceptual, attention, and emotional processes (Luo et al. 2007; Sammler et al. 2007). The distribution of these frequency oscillations recorded from the scalp surface can help identify links between emotional experiences in PD patients with respect to EEG recordings.

Fig. 4

Spectral power at alpha (8-13 Hz), beta (13-30 Hz) and gamma (30-49 Hz) frequency oscillations of emotional EEG signals



AQ1

We found that PD patients who exhibited worse symptom on the left side of the body (inferred right-hemisphere pathology) were specifically impaired in emotional recognition, as indicated by reduced relative power values compared to RPD patients. This finding suggests that stronger right- versus left-hemispheric degeneration in PD may cause emotional recognition impairments. These results are concordant with Garrido-Vásquez et al. (2013) and Ventura et al. (2012) who reported that LPD patients had greater difficulty with emotional processing (Garrido-Vásquez et al. 2013; Ventura et al. 2012), as the processing of emotional information is right hemisphere-dominant (Yuvaraj et al. 2013a). Furthermore, the right hemisphere is also believed to play a role in social awareness and in the recognition of salient social cues (Ventura et al. 2012); however, studies have also shown that emotional processing is disrupted in both left- and right-affected PD patients regardless of emotional valence (Dara et al. 2008; Schröder et al. 2006). Methodological differences, such as in the individual characteristics of the participant's characteristics and in the emotional stimuli used (Gray and Tickle-Degner 2010) may be the cause of these conflicting results. We separated our PD patients based on pre-dominantly affected side whereas Schröder et al. (2006) and Dara et al. (2008) grouped all PD participants together (Dara et al. 2008; Schröder et al. 2006). It has also been shown that difficulties in emotion recognition in PD patients may vary as a function of stimulus modality, either visual or auditory (Lima et al. 2013) however, this study contributes to new findings on neurophysiological disassociations using the multimodal stimuli approach.

Selective impairments in emotional processing suggest hemispheric effects, which may contribute to the impairment of emotional communication in a subset of PD patients. In the present study, LPD patients showed a reduced EEG response of alpha, beta and gamma frequency oscillation while processing negative emotions compared to positive emotional stimuli. These results conform well with previous research which showed that the right hemisphere may be specialized to process negative emotions whereas the left hemisphere may be specialized to process positive emotions. Adolphs et al. (2001) found that patients with right hemisphere damage were impaired in recognizing sad emotional faces when presented to the participant's left visual field (Adolphs et al. 2001). Garrido-Vasquez and colleagues found diminished event-related potentials to anger emotional speech in patients with right hemisphere damage (Garrido-Vásquez et al. 2013). Additional studies have shown that emotion recognition deficits in PD patients may selectively impair negative emotion processing which is likely due to damage of specific emotion-related brain structures (Dara et al. 2008; Péron et al. 2012; Tessitore et al. 2002), including centrally located limbic structures within the basal ganglia's limbic loop such as the amygdala and ventral striatum. There is also a large body of evidence pointing towards the involvement of dopamine in emotional processing (Salgado-Pineda et al. 2005); however, both LPD and RPD patients were taking dopamine medication during the experiment and still showed signs of dopamine deficiency as indicated by their mean value of motor UPDRS scores (LPD 16.70 ± 1.70 ; RPD 18.30 ± 4.60) (see Table 1). This finding is in line with previous studies demonstrating that the difficulties that PD patients processing emotional information's are only partly improved by dopaminergic therapy (Tessitore et al. 2002). Thus, impairments in processing emotional information could be attributed to dopamine depletion, although involvement of other transmitter systems, such as the serotoninergic or noradrenergic systems, cannot be excluded.

Limitations

This study is limited by the fact that the recruited PD population consisted of PD patients in H & Y 1-3 stages only (see Table 1). Thus, our findings are limited by the fact that patients with severe PD were not included in the study (H & Y 4-5 stages). Moreover, the differences in spectral powers may have been impacted by other variables such as variability in daily doses of medication, differences in the treatment and disease duration, medication usage, etc. These variables should be controlled in future studies to minimize its impact on lateralization of motor onset and emotional recognition. Furthermore, it is essential to apply machine learning algorithms to extract more typical features and further make classification analysis.

Summary and Conclusion

In sum, this is the first study to investigate the varying influence of a predominant right- versus left-hemisphere dysfunction on PD patients using EEG signals during emotional processing. No significant group differences were observed based on behavioral measures; however, a significant decrease at alpha, beta and gamma frequency EEG oscillation was found in LPD and RPD compared to HC participants. These findings could complement the differential diagnosis of emotional disorders in Parkinsonian syndrome.

Acknowledgments

This research was financially supported by Fundamental Research Grant Scheme (FRGS), Ministry of Higher Education, Malaysia, Grant No: 9003-00507.

Compliance of Ethical Standards

Conflict of interest The Author(s) declare(s) that there is no conflict of interest.

Electronic supplementary material

Below is the link to the electronic supplementary material.

Supplementary material 1 (DOCX 409 kb)

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