Matemática: Una publicación de FCNM – ESPOL
2015, Vol. 13, No.2

HEMI-PARKINSON'S DISEASE: DIFFERENTIAL ALTERATIONS DURING TACTILE PERCEPTION

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Resumen. *La manifestación inicial del mal de Parkinson (PD) es frecuentemente unilateral, con síntomas que afectan predominantemente el lado izquierdo (LPD) o el lado derecho (RPD) del cuerpo. Aunque la afectación asimétrica es característica de esta enfermedad, pocos estudios han investigado sus efectos sobre el sistema no-motor. En el presente estudio mediante fMRI, se examinan dos tareas de discriminación táctiles en 24 pacientes del mal de Parkinson y 18 individuos sanos (controles). La mitad de los pacientes tiene LPD y la otra mitad RPD. La tarea realizada consiste en aplicar de forma separada pares de vibraciones sinusoidales en cuatro puntos del dedo índice de ambas manos. Se solicitó a los sujetos identificar la cercanía de la localización de los estímulos, la presentación simultánea o sucesiva o simplemente responder a la detección del estímulo. La investigación resultante reveló que el LPD difiere del comportamiento de los controles al exhibir un desenvolvimiento pobre. En contraste, pacientes con RPD se comportan de igual forma que los controles. Estos hallazgos sugieren que los pacientes de LPD exhiben una leve y generalizada desatención en la percepción. Nuestros resultados muestran que la actividad cerebral anormal durante el proceso táctil en pacientes de Parkinson depende de la aparición de los síntomas clínicos de la enfermedad.*
Palabras clave: fMRI, Mal de Parkinson, percepción táctil

Abstract: *The initial clinical manifestation of Parkinson's disease (PD) is frequently unilateral, with symptoms predominantly affecting the left (LPD) or right-side of the body (RPD). Although asymmetric affectation is characteristic of this disease, few studies have investigated its effects on non-motor systems. In the current fMRI study, we examined two tactile discrimination tasks in 24 PD patients ('ON') and 18 healthy-controls (HCs). Half of the patients were LPD and half RPD. The task consisted of separately applying pairs of sinusoidal vibratory stimuli at four locations on the index finger of both hands. Subjects were required to identify either the proximal or distal stimulus location, the simultaneous or successive presentation or simply respond to stimulus detection. Behavioural results revealed that the LPD differed from the HCs by exhibiting poorer performance. In contrast, RPD patients behaved in similar manner to the HCs. Image data analysis revealed decreased cortical activity in the right intraparietal sulcus which was associated to lower performance in the LPD patients. These findings suggest that the LPD patients exhibited mild generalized perceptual inattention. Our results demonstrate abnormal brain activity during tactile processing in PD patients depending upon clinical initiation onset.*
Keywords: fMRI, Parkinson's disease, tactile perception.

Recibido: Agosto 2015.
Aceptado: Agosto 2015.

1. INTRODUCTION

Parkinson's disease (PD) has been classically considered a motor disorder, with most PD patients (85%) clinically presenting an asymmetrical involvement with the unilateral initiation of tremors, bradykinesia and rigidity. In the first stages of the disease, patients present progressive asymmetric degeneration of nigral dopaminergic neurons, which primarily project to the left basal ganglia in RPD patients Although several aspects of brain function are lateralised to the right or left hemisphere [1], little is known about the relationship between disease.

However, it has not been clearly established whether LPD and RPD patients exhibit different disease courses. Furthermore, it is unclear whether lateralised somatosensory processing may be affected differently in LPD and RPD patients and how the asymmetric dopamine and to the right basal ganglia in LPD patients. motor asymmetry in PD and the lateralisation of spatial brain functions[2]–[4]. Following this line of thought, it is possible that the natural brain asymmetry may cause different alterations in the pathophysiology of hemi-Parkinson's depletion affects the spatial and temporal processing of tactile stimuli in PD patients

The objective of the current study was to identify the dysfunctional brain regions related to the inattention phenomenon in tactile processing of PD patients

2. MATERIALS AND METHODS

Participants

For this study, we recruited 24 PD patients and 18 healthy control (HCs). Twelve patients had predominantly right-sided symptoms, and twelve

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showed left-sided symptoms. All patients were taking their normal dosage of medication at the time of MRI examination. All participants were right-handed, as assessed by the Edinburgh Handedness Inventory [5]. The demographic data of the PD patients and HCs are summarised in Table 1. Prior to scanning, all subjects gave written informed consent, and the study was approved by the local ethics committee.

Vibratory stimulation

For this study, we developed two computer-controlled MRI-compatible vibratory devices. Each vibratory stimulus was composed of two pulses of sinusoidal vibration with 100 ms duration at 197 Hz, separated by an inter-stimulus interval (ISI), and pulses were delivered at one of the four stimulation shafts.

fMRI study

During the fMRI experiment, we delivered to the subject's index phalanx two vibratory stimuli, requesting that subjects determine the Spatial Location Discrimination (SLD), Simultaneity Succession Discrimination (SSD) and a simple detection as control task for base line. Subjects completed the tasks in two scan sessions in which the left index finger and the right index finger were separately stimulated. Answers were given with the middle and ring finger of the opposite hand on a response box.

Scanningprotocol

Imaging was performed using a 3-Tesla scanner (Siemens Trio TIM) equipped with a 12-channel head array coil. The presentation of the stimuli was designed using Matlab v6.5 A T2*-weighted echo planar imaging sequence sensitive to BOLD contrast was used to acquire 298 volumes per session over 15.0 min. Each volume comprised 45 transverse slices with a 15% gap, covering the entire brain. Anatomical images were also acquired with an MPRAGE sequence.

Data Analysis

Performance data analysis

For each subject, task (SLD and SSD) and hand, we evaluated the performance using a consistency index (CI), calculated using the equation $CI = abs(r1-r2)/(r1+r2)$, where *r1* and *r2* correspond to the number of the two types of possible responses given by the subject.

Image data analysis

We used Statistical Parametric Mapping (SPM8) software for image processing and analysis. For each subject, the 596 volumes of the two sessions were brain-extracted using the BET tool[6], realigned to the first volume, sinc-interpolated over time, coregistered to the anatomical image, normalised to the MNI305 template brain, spatially smoothed with an 8 mm^3 isotropic Gaussian filter and filtered over time using a high-pass filter of 128 s.

Subsequent analyses were performed using a general linear model to estimate the effects at each voxel[7]. At the first level, the tasks were modelled as Dirac delta function [8] and convolved with a canonical double gamma as a hemodynamic response function (HRF). We estimated the following contrasts of interest for each subject: SLD vs. detection and SSD vs. detection.

At the second level, we used a random effects analysis [9]. Given that we were interested in evaluating the hypothesis that LPD and RPD patients would show differential hemispheric dysfunction during tactile processing, the individual contrast images (SLD vs. detection and SSD vs. detection) were separately assessed using a one-way ANOVA for each contrast with the group as a factor (LPD, RPD or HC). Subsequently, post-hoc pairwise comparisons were computed to assess group differences. In all cases, the areas of significant activation were identified at a significance of $P<0.05$ and corrected for multiple comparisons using the false discovery rate (FDR)[10].

3. RESULTS

Demographic data and clinical profiles

The demographic data revealed no significant differences between groups (Table 1). Additionally, the between-group comparisons of the clinical features of the PD patients showed no significant differences between the LPD and RPD groups.

Performance data

Behavioural analysis revealed that the LPD group performance during the SLD task was poorer than that of the RPD and HC groups, but there were no significant differences between the RPD and HC groups.

	Healthy Controls	LPD	RPD	Statistical P Value
Age (SD), y.	58.3 (9.0)	60.7 (8.2)	59.1 (9.1)	0.69
Sex (male/female)	42167	42102	42045	--
MMSE ON (SD)	30.0 (0.7)	29.4 (2.2)	28.3 (0.5)	0.48
Handedness/50 (SD)	49.4 (1.4)	49.5 (1.7)	47.2 (4.8)	0.13
Disease duration (SD) y.	N/A	6.8 (6.9)	4.4 (3.4)	0.14
Hoehn & Yahr	N/A	1.75 (0.45)	1.67 (0.49)	0.67
UPDRS ON (SD)	N/A	15,0(6,9)	11,55(5,5)	0.31
L-Dopa (mg/day)	N/A	427.0 (131.3)	310.0 (299.0)	0.28

Fmri results

LPD vs. HC

For the SLD vs. detection comparison, the LPD group, when compared to healthy controls, had significant hyperactivity in the right inferior frontal gyrus (p. triangularis), the right angular gyrus (Pgp and Pga)[11], the preSMA, the right middle frontal gyrus and the right superior frontal gyrus. The hypoactivity of LPD patients compared to the HCs was found in the bilateral visual and cerebellar regions (Fig. 2A). We did not find any significantly hyperactive regions in the LPD group when compared to the HCs in the SSD vs. detection comparison. We found hypoactivity in the left cuneus (BA18) and the right calcarine and right lingual gyri, as shown in Fig. 2B.

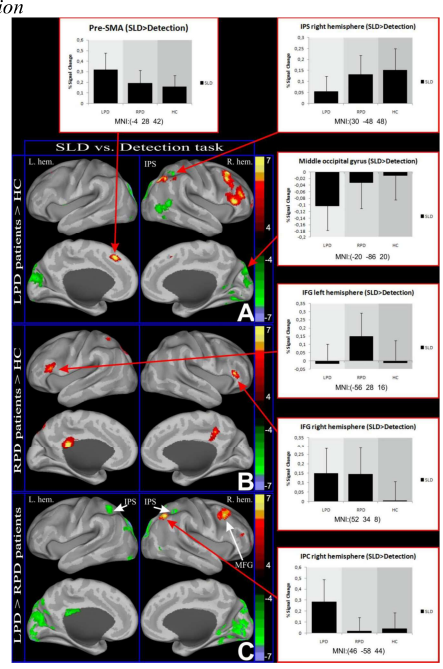
RPD vs. HC

The RPD group compared with healthy controls for the SLD vs. detection task exhibited hyperactive regions in the left superior parietal lobule (7P and 7A), the bilateral inferior frontal gyrus (p. triangularis) and the left posterior cingulate and right middle cingulate cortices (Fig. 2C).

In the SSD vs. detection comparison, the only significantly hyperactive region was located in the left calcarine gyrus (BA17), as shown in Fig. 2D. We did not find any significantly hypoactive regions for this comparison.

FIGURE 1:

T-contrasts showing brain activity differences between LPD, RPD and the HC groups during SLD vs. detection contrast*. Warm colors represent hyperactivity, and cold colors represent hypoactivity of PD patients with respect to the HC group. P-value <0.05, FDR correction*



LPDvs.RPD

Direct comparisons between both groups of patients revealed that the LPD group had increased activity compared to the RPD group in the SLD vs. detection comparison solely in the following right hemisphere regions: the middle frontal gyrus, the angular gyrus, the inferior parietal cortex (PGa and PGp)[11] and the middle frontal and superior frontal gyri. For the same comparison, the LPD group showed decreased activity in the bilateral structures of the superior occipital gyrus, the lingual gyrus, the intraparietal sulcus, the right cuneus, the left calcarine gyrus and the left posterior cingulate cortex (Fig. 3A).

4. DISCUSSION AND CONCLUSION

The results of both the SLD and SSD tasks provided evidence of distinct brain activity patterns in PD patients that are associated with the initially affected side of the body. In conclusion, we have found evidence for differential cognitive impairments in PD patients based on the initially affected side of the body. This finding may be a consequence of functional lateralisation of the brain. Our behavioural results point to mild tactile inattention in LPD patients that was associated with a predominantly right hemisphere dysfunction. This behaviour may be a result of the decreased cortical activity in the right intraparietal sulcus observed in the LPD patients. In contrast, the hyperactivity found in other parietal regions could be related to a cortico-cortical cognitive tactile processing compensatory mechanism. Additionally, hyperactivity in the inferior frontal Gyrus pars triangularis, which is common for LPD and RPD patients and predominantly occurring in the affected hemisphere, may be induced by excitatory mechanisms of the cortico-subthalamic pathway.

5. ACKNOWLEDGEMENTS

This study was supported by the Spanish Government: grant saf2004-07813 and the Senescyt (Secretaría Nacional de Ciencia, Tecnología e Innovación) through the Prometheus Program 2013 of the Ecuadorian Government.

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