Parkinsonism and Related Disorders 33 (2016) 84–89

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Body fat distribution in Parkinson's disease: An MRI-based body fat quantification study

Denise Bernhardt [a, b, c], Hans-Peter Müller [a], Albert C. Ludolph [a], Luc Dupuis [d, e], Jan Kassubek [a, *]

[a] Department of Neurology, University of Ulm, Germany
[b] Department of Radiation Oncology, University Hospital of Heidelberg, Heidelberg, Germany
[c] Heidelberg Institute of Radiation Oncology (HIRO), Heidelberg, Germany
[d] Inserm U1118, Mécanismes centraux et périphériques de la neurodegenerescence, Strasbourg, France
[e] Université de Strasbourg, Faculté de Médecine, UMR_S1118, Strasbourg, France

ARTICLE INFO

Article history:
Received 8 May 2016
Received in revised form
22 August 2016
Accepted 15 September 2016

Keywords:
Parkinson's disease
Magnetic resonance imaging
Metabolism
Body fat distribution
Weight loss

ABSTRACT

Introduction: There is some evidence that Parkinson's Disease (PD) patients have lower body weight and lower fat mass when compared to healthy subjects and that lower body weight and fat mass influence disease risk and progression. It remains unclear, however, if weight loss of fat mass loss occurs only in a subgroup of patients and whether fat distribution is altered during PD. The aim of this study was to prospectively investigate adipose tissue content and distribution in PD patients.
Methods: The body fat composition of PD patients (N = 54) was compared with age matched healthy controls (N = 55) using a magnetic resonance imaging (MRI)-based method. A longitudinal MRI scan was acquired in 25 PD patients after a mean follow up period of 12 months.
Results: The volume of total body fat as well as of visceral fat showed no difference between PD patients and healthy controls at baseline or at follow up. However, PD patients displayed decreased subcutaneous fat tissue ($p = 0.01$) and a higher visceral to subcutaneous fat ratio as compared to controls ($p = 0.004$). After follow up, 16 PD patients did not lose weight, while 9 PD patients lost between 0.5 and 10 kg.
Conclusion: Fat distribution is altered in PD patients, with an increased ratio of visceral to subcutaneous fat.

1. Introduction

Multiple studies have shown that Parkinson's Disease (PD) patients have lower body weight as compared to healthy subjects [1–3]. The impact of body composition on metabolism in PD has already been investigated by dual-energy X-ray absorptiometry [4]. The reasons for weight loss in PD may be multifactorial since both motor and non-motor symptoms, i.e. dysphagia [5], depression [6], levo-dopa medication [7], motor symptoms [8], gastrointestinal dysfunction [6,9] may contribute to weight loss. On the contrary, weight gain is observed in PD patients after deep brain stimulation [10]. Importantly, weight loss appears, at least in a subset of studies, to be mostly caused by loss of fat tissue [2]. Despite important differences in physiological properties among fat pads, few studies investigated fat distribution in PD patients [11], and, to our knowledge, a precise quantification of visceral vs. subcutaneous fat volumes is lacking in PD patients.

Magnetic resonance imaging (MRI) techniques offer a powerful tool to differentiate distinct fat compartments [12,13] and have already been successfully applied to other neurodegenerative disorders [14,15]. The present longitudinal study uses this MRI-based method together with anthropometry and bioelectrical impedance analysis (BIA) measurements in order to quantitatively study the fat distribution in PD. The intention was to identify factors that correlate with increased or decreased body weight in PD patients.

* Corresponding author. Department of Neurology, University of Ulm, Oberer Eselsberg 45, 89081, Ulm, Germany.
E-mail addresses: denise.bernhardt@med.uni-heidelberg.de (D. Bernhardt), hans-peter.mueller@uni-ulm.de (H.-P. Müller), albert.ludolph@rku.de (A.C. Ludolph), ldupuis@unistra.fr (L. Dupuis), jan.kassubek@uni-ulm.de (J. Kassubek).

http://dx.doi.org/10.1016/j.parkreldis.2016.09.016
1353-8020/

2. Methods

2.1. Patients

Fifty-four patients with PD and 55 age matched healthy volunteers were included in the study and underwent the MRI scanning protocol (Supplementary Table 1). Twenty-five PD patients underwent a follow-up scan after an average time interval of 12 months (Fig. 1A). The patients were recruited in the Department of Neurology, University of Ulm, Germany, a tertial referral center for movement disorders. All patients had been diagnosed with PD according to the UK brain bank criteria by a movement disorders specialist and had a disease duration of 8 ± 5 years. None of the patients had clinically relevant edema at the time of the investigations; and none of the patients had the diagnosis of diabetes; however, the patients were not specifically investigated for the presence of diabetes so that it was possible that diabetes might have been underdiagnosed in the study sample. The PD patients were rated by use of the Unified Parkinson's Disease Rating Scale (UPDRS) [16]. The protocol for the calculation of a total daily levodopa equivalent dose (TLED) was used for the individual PD medications [17]. The dopaminergic medication in the patients consisted of levo-dopa, sometimes in combination with a catechol-O-methyltransferase-inhibitor (entacapone), and/or dopamine agonists, sometimes combined with amantadine or rasagiline. In detail, twelve patients had a dopamine agonist monotherapy (ropinirole, N = 5, one of them in combination with the monoamine oxidase-B inhibitor rasagiline; pramipexole, N = 3; rotigotine, N = 3; piribedil, N = 1), six patients had levo-dopa and entacapone, three patients had levo-dopa and amantadine, twenty-three patients had a combination therapy of levo-dopa and dopaminine agonists (levodopa and ropinirole, N = 6; levo-dopa and pramipexole, N = 3; levo-dopa and entacapone and ropinirole, N = 8; levo-dopa and entacapone and pramipexole, N = 3; levo-dopa and entacapone and rotigotine, N = 2; levo-dopa and entacapone and piribedil, N = 1), the remaining patients had levo-dopa monotherapy. At follow-up, dosages might have been modified, but none of the patients had a fundamentally changed medication regimen. At follow-up, dosages might have been modified, but none of the patients had a fundamentally changed medication regimen.

The control group without any neurological/psychiatric disease or other medical condition was recruited through a volunteer panel (University for the Aged, volunteer work exhibition) or spouses of patients.

Height and weight were measured in order to calculate the BMI, and BIA was performed in order to assess the body composition. A written informed consent was obtained from all participants after the Ethical Review Committee of the University of Ulm had approved this study (#138/09).

2.2. MRI measurements

MRI data were acquired on a 1.5 T scanner (Symphony, Siemens Medical, Erlangen, Germany), with a quantum gradient system with gradient field strength up to 30 mT/m (52 mT/m effective) and a slew rate up to 125 T/m/s (216 T/m/s effective). The whole body MRI scan was recorded by acquisition of 6–8 T1-weighted volumes (standard T1 weighted spin-echo sequence), each consisting of 36 2-D slices of 6 mm thickness. In-plane resolution was 1.25 mm × 1.25 mm (294 × 384 voxels), phase encoding direction was right to left, 206 phase encoding steps were used, zero-filling for image reconstruction. Flip angle was 20°, repetition time (TR) was 476 ms, and time to echo (TE) was 12 ms, the total acquisition time for one volume was 4:30 min. Slices were recorded with no gap; to confirm that no gap was left between the consecutive volumes, an overlap of about 6–18 mm was chosen between the volumes so that a total area of at least 120 cm was scanned.

2.3. Data analysis

For the measurement of adipose tissue volume and distribution, the in-house developed software package *Automatic Tissue Labeling*

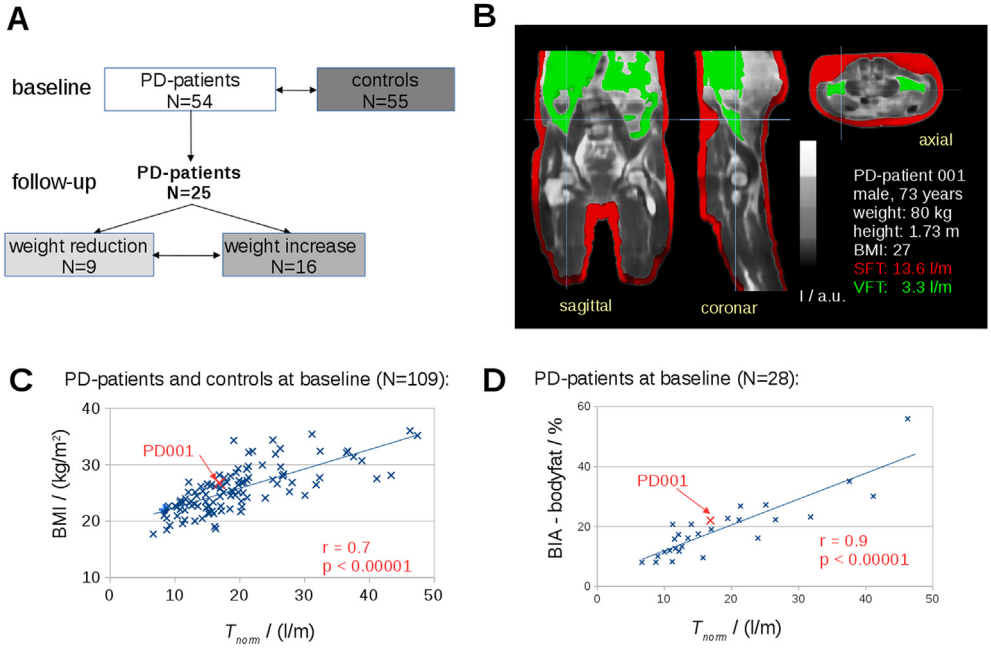

Fig. 1. MRI-based body fat determination. **(A)** Schematic overview of participating subjects. **(B)** Example of MRI-based fat pads determination: 73 year old male PD-patient – coronar, sagittal, axial slice representation. **(C)** Correlations of MRI-based normalized body fat T_{norm} to body mass index (BMI) (PD-patients and controls – N = 109) and bioimpedance analysis (BIA) (PD-patients – N = 28).