LBA 01

Progressive Relaxation Trainning in Parkinson's Patients as a Way to Manage Levodopa Induced Dyskinesia*A. Aguilar, J. Herruzo (Cordoba, Spain)*

Objective: The aim of this work is to determine the efficacy of progressive relaxation training for reduction of the dyskinesia in Parkinson's patients.

Background: Long-term levodopa treatment in Parkinson's disease (PD) induces the appearance of dyskinesia. Its appearance is a problem for the wellbeing in the patient's life, and it is an obstacle for the future treatment of the disease because lowering the dose of levodopa to reduce the dyskinesia implies a reduction on the movements capability.

Methods: Participants were 20 people with PD who presented dyskinesia related to levodopa treatment (n = 10 experimental group and n =10 control) measured with PDYS-26 (Parkinson Disease Dyskinesia Scale), matching both groups in gender, age, time since the diagnosis and score in the UPDRS. The experimental group received a relaxation training (independent variable).

Results: The progressive relaxation training resulted in a reduction of dyskinesias severity in the experimental group before and after the treatment in the summation of the PDYS-26 scores (t= 4.6; 18df; p=0.000) and in relation to the control group ((t=2.79; 18df; p=0.012). See Fig 1.

Conclusion: The training in relaxation results in a reduction of dyskinesias severity, reflected in an improvement in the development of the daily life activities and an improvement in the patient's well being with Parkinson's disease.

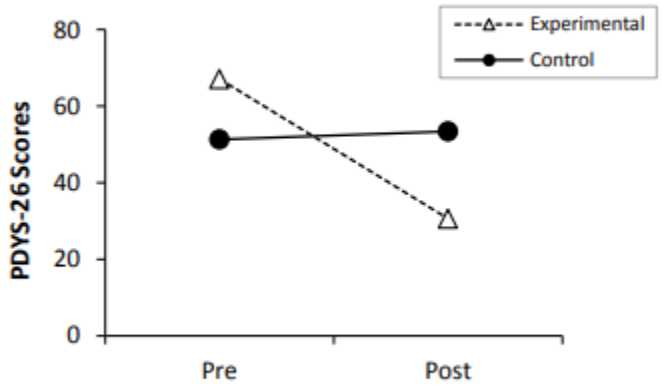

Figure 1

LBA 02

Cognitive Changes in DBS-STN Implant in Parkinson Disease: Analysis of Neuroimaging and Clinical Variables

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Objectives: To investigate the association of post-operative cognitive impairment with neuroimaging findings and clinical variables in Parkinsonian patients submitted to DBS-STN.

Background: Deep brain stimulation (DBS) surgery is an effective procedure in the control of motor complications of selected cases of Parkinson's disease (PD). Although relatively safe, it has been associated with some cognitive and neuropsychiatric complications. Transfixation of the electrode through the ventricles may occur in some patients. The same is not associated with major complications, however, as far as we know the same has never been studied in regard to cognitive changes. Also little is known about the association between preoperative MRI findings of the preoperative brain and the risks of developing postoperative cognitive complications in patients undergoing surgery.

Methods: It is a retrospective historical cohort, including 25 patients with PD underwent DBS-STN surgical procedure at Hospital de Clínicas de Porto Alegre (HCPA) from 2012 to 2015 (80% were men, mean age of 55.8 ± 8.5 years, mean age of onset of the disease 43.1 ± 6.9 years, mean duration of the disease 13.0 ± 2.9 years, mean educational level 7.8 ± 5.0 years). Magnetic resonance imaging (MRI) and computed tomography (CT) performed in the pre-operative period were evaluated. Cognitive assessments were performed in the pre-operative period and 6 months after surgery. Follow-up assessment included the following neuropsychological testes: Mini Mental State Examination (MMSE), Verbal Fluency with phonological restriction (FAS), Semantic Fluency (animal category), Rey Auditory Verbal Learning Test (RAVLT), Montreal Cognitive Assessment (MoCA), Frontal Evaluation Battery (FAB) and Scopa-cog.

Results: Patients presented a statistically significant difference between the pre and post-operative periods in phonemic verbal fluency ($p=0.003$). The transfixation of the ventricles by cable with electrodes was associated with impairment in post-operative memory ($p=0.016$) and semantic fluency ($p=0.009$). The lesion on the white matter was associated to a decrease regarding to memory ($p=0.050$), semantic fluency ($p=0.039$) and executive function ($p=0.017$) in the post-operative.Impairment of the semantic fluency, memory and executive function in the post-operative period in relation to the pre-operative scores is associated with the presence of lesion in the white matter and transfixation of the ventricles. Although the patients demonstrate loss in phonemic verbal fluency after DBS surgery this decrease was not associated with findings in MRI.

Conclusion: It is important to emphasise that our sample was composed of relatively young patients (less than 60 years old) and the majority with onset disease before the age of 50 years. Cognitive assessments were performed at 6-month intervals. It is, therefore, likely that the cognitive changes do not stem from the natural history of the disease but they are related to the surgical procedure (non-elderly patients with short time between evaluations). Ventricular transfixation and white matter lesion were found to be associated with post-operative outcome of memory, executive function, and semantic fluency decreasing. Thus, it is proposed that greater attention is given to neuropsychological assessments, especially in the tests of verbal fluency, memory and executive function of patients presenting alterations in the pre-operative imaging tests, once there is an increased risk of cognitive loss of these functions in the post-operative. This study has some limitations such as the small sample size and the fact that it is not controlled. However, even with these limitations, a study that sought to verify whether volumetric measurements could have any influence on the post-operative outcome has not yet been seen in the literature.

LBA 03

Efficacy and Safety of Sublingual Apomorphine film (APL-130277) for the Treatment of OFF Episodes in Patients with Parkinson's disease: Results from a Double-Blind, Placebo-Controlled Trial

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Objective: To evaluate the efficacy and safety of APL-130277 (APL) as an acute therapy for OFF episodes in a double-blind, placebo-controlled trial in patients with Parkinson's disease (PD).

Background: OFF episodes are a common, disabling complication of PD. APL is a sublingual formulation of apomorphine.

Method: The APL dose (10-35mg) to produce a FULL ON was determined in the Titration Phase. During the Maintenance Phase (MP), patients were randomized to receive the titrated dose of APL or placebo, up to 5x/d for 12 wks. MDS-UPDRS-III scores were determined monthly at pre-dose and at 15, 30, 45, 60 and 90 mins post-dose. The primary endpoint was the change in MDS-UPDRS-III score at 30 mins post-dose after 12 wks. The key secondary endpoint was the % of patients with a patient-determined FULL ON response within 30 mins at 12 wks. Safety assessments were performed.

Results: 141 patients were enrolled who experienced a mean of 3.9 OFF episodes/d. 109 patients were randomized. Discontinuation was higher with APL (27.8%) than placebo (9.1%), most commonly due to AEs. 80 patients completed the study. The LS Mean (SE) change from pre-dose to 30 min post-dose for the MDS-UPDRS-III score at 12 wks was -11.1 (1.5) and -3.5 (1.3) for the APL and placebo groups, respectively (mean difference = -7.6; p=0.0002). Similar results were observed at day 1, and wks 4 and 8. Separation from placebo was observed at 15 mins and persisted up to 90 mins. There was a significant difference favoring APL over placebo in the % of patients who rated themselves as FULL ON at 30 mins at 12 wks (p=0.04), % of patients ON within 30 mins who remained ON for at least 30 mins, CGI, and PGI. Home dosing diary showed a larger % of APL patients turned ON within 30 mins post-dose (LS mean 78.70%) compared to placebo (LS mean 31.10%). The most frequent AEs during the MP for APL were nausea (27.8%), somnolence (13%) and dizziness (9.3%). Most TEAEs were mild to moderate in severity. There were only 6 SAEs and 1 death (placebo). Oral AEs occurred in 31.5%/7.3% of APL/placebo-treated patients, respectively. These were generally mild and reversible.

Conclusion: The results of this trial demonstrate that APL offers an effective and well-tolerated treatment for the acute management of OFF episodes in patients with PD.

LBA 04

Microsurgical Anatomy of the Thalamus

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Objective: In the present study, we aimed to delineate the 3D anatomy of the thalamic nuclei and unveil the complex relationship between the anatomical structures within the thalamic region.

Background: Deep brain stimulation is a common treatment for medication refractory essential tremor. Despite the extensive practice of the ventral intermedius (VIM) thalamus as a deep brain stimulation (DBS) target, unveiling the extensive functional connectivity of the nucleus, relating its structural connectivity to the stimulation-induced adverse effects, still remains challenging. Mastering the three-dimensional (3D) anatomy of the thalamic nuclei should be the fundamental goal in order to achieve the best surgical results, due to the deep-seated position of these nuclei, its variable shape and relatively small size and extensive structural connectivity.

Method: Fiber dissection were performed in 20 hemispheres and one cadaveric head in accordance with the Klingler method. All around fiber dissections from all aspects of the brain were performed in a stepwise manner to reveal the 3D anatomy of the thalamus. The thalamic nuclei were segmented in the serial 400µm thick histological sections according to cytoarchitectonic criteria and projected into MRI space.

Results: Our study correlated the results of thalamic fiber dissection with those of 3D MRI reconstruction and tractography. A 3D terrain model of the thalamic area have been built in order to clarify its anatomical relations with the putamen, GPi, GPe, internal capsule, caudate nucleus laterally, subthalamic nucleus and zona incerta inferiorly. We also described the relationship of the medial lemniscus and dentatorubrothalamic tract by using tractography with 3D thalamic model.

Conclusion: This study revealed the complex 3-D anatomy of the thalamic area. In comparison with previous clinical data on thalamic targeting, the results of this study promises further understanding on the structural connections of the thalamus, and the clinical applications such as stimulation induced adverse effects during DBS targeting.

LBA 05

Mastering the Substantia Nigra: Microsurgical anatomy to MRI signal loss in Parkinson's Disease

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Objectives: The aim of this study is to delineate the anatomy of the SN and unveil its complex relationship between the anatomical structures within the subthalamic area and demonstrate the signal changes in the early disease stage.

Background: Parkinson's disease (PD) is a neurodegenerative disorder characterized by progressive loss of neuromelanin of the substantia nigra (SN). A specific T1-weighted magnetic resonance imaging (MRI) sequence has been shown to detect neuromelanin (NM) signal changes that discriminate PD patients from controls. It is not clear, however, if this decreased signal can be a marker of disease progression.

Methods: Fiber dissection were performed in 20 hemispheres in accordance with the Klingler method. All around fiber dissections from all aspects of the brain were performed in a stepwise manner to reveal the three-dimensional (3D) anatomy of the SN. After multidisciplinary clinical evaluation, T1-weighted magnetic resonance imaging was performed in one PD patient and compared to the findings in the human cadaveric brain in a 11.7T MRI in axial, coronal and sagittal cuts.

Results: Our study correlated the results of SN fiber dissection with those of 3D MRI reconstruction and T1-weighted magnetic resonance imaging. A 3D model of the SN have been built in order to clarify its anatomical relationships with the GPi lateral and superiorly, the posterior limb of the internal capsule anterior and laterally, the medial lemniscus posteriorly, the subthalamic nucleus superiorly, and the nucleus medially. The clinical findings of mild tremor and no significant alteration in balance tests were minor when compared to the severe reduction of NM signal in the T1-weighted MRI.

Conclusion: This study revealed the complex 3D neuroanatomy of the SN are peri-subthalamic area. SN area evaluated by NM-sensitive MRI may be a promising biomarker of nigral degeneration, but not disease progression in PD patients. Further studies may help to elucidate these findings.

LBA 06

Examining Parkinson's Disease Psychosis Treatment Outcomes in the Real World: The Insyte Observational Study

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Objectives: The goal of the INSYTE Study – Management of Parkinson's Disease Psychosis in Actual Practice – is to gain a better understanding of the real-world management of Parkinson's disease psychosis (PDP) and treatment outcomes.

Background: Minimal data is available on anti-psychotic (AP) therapy in PDP treatment, and in mitigating the burden of PDP by reducing falls, hospitalizations and placement of PDP patients in long-term care facilities.

Methods: INSYTE is an ongoing observational study expected to enroll up to 750 PDP patients and their caregivers from approximately 100 sites; patients are followed for up to 36 months. INSYTE employs validated assessment instruments, although as an observational study, it does not impose a pre-defined visit schedule, medical tests, laboratory tests, procedures, or interventions.

Results: Baseline data for first 90 patients enrolled found that majority are male (63%), white (96%), and live in a private residence (93%). Average age is 75.7 years. At baseline, 22% had mild/mild to moderate Parkinson's disease (PD), 58% had moderate/moderate to advanced PD, and 20% had advanced PD. 39% of patients were borderline to mildly mentally ill and 46% were moderately to markedly mentally ill. Most patients, 63%, were diagnosed with PDP about a year prior to study enrollment. AP use was reported in 36 patients, of which 26 used pimavanserin either as monotherapy (n=21) or in combination with other atypical AP (n=5). The second most common AP was quetiapine, followed by olanzapine, clozapine and aripiprazole.

Conclusion: INSYTE is the first observational study to evaluate how patients with PDP are treated in the real-world setting, and how treatments affect patients and outcomes. Initial results indicate that only 40% of PDP patients reported AP use at baseline despite their diagnosis. Results from this study will inform the scientific community on best practices and potentially inform PDP treatment guidelines and standards of care.

LBA 07

Understanding the Treatment of Parkinson's Disease Psychosis and Physician-Reported Control of Symptoms Across Treatment Options

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Objectives: Understand current treatment and management of Parkinson's Disease Psychosis (PDP) and compare physician-reported outcomes of pimavanserin and other pharmacological agents commonly used to treat this condition.

Background: PDP is a common and debilitating condition associated with Parkinson's Disease (PD). More than 50% of PD patients develop PDP over the course of their disease. Understanding treatment outcomes for PDP patients can improve disease management.

Methods: 1800 anonymized patient charts were collected from 200 physicians who personally managed a minimum of 8 pharmacologically treated PDP patients in the last 6 months. Each physician provided abbreviated charts for their 6 most recently treated PDP patients (1200 total), with select information collected pertaining to demographics, symptoms, and current treatment. Physicians additionally provided 3 detailed charts (600 total), which included more detailed demographic information, full treatment history, and physician-rated control of symptoms. Data was weighted to account for physician specialty distribution and PDP patient volume and then analyzed in aggregate, with Z test used to identify any statistically significant differences.

Results: 90% of treated PDP patients received an anti-psychotic (AP) agent first line. More than 50% receive quetiapine, 18% pimavanserin (PIM), and the remainder other AP or other treatments (e.g., anti-dementia agents, anti-depressants). Among those who receive quetiapine, 68% are treated with a low dose 100 mg/day (HDQ). Patients treated with 34mg PIM achieve significantly better symptom control (60% 'Adequately Controlled') within 6 months compared to patients treated with LDQ (39% 'Adequately Controlled') (p

Conclusion: Despite the widespread use of quetiapine as a first line treatment of PDP, we find that patients treated with 34mg PIM achieve significantly better physician-reported control of PDP symptoms, especially compared to those treated with LDQ. The data suggest that use of PIM is associated with significantly improved treatment outcomes, both within and beyond 6 months of treatment. Therefore, increased use of 34mg PIM as a first line pharmacological treatment for PDP is suggested to maximize control of symptoms of psychosis associated with PD.