LATE-BREAKING ABSTRACTS

International Parkinson and
Movement Disorder Society
Pan American Section

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4TH PAN AMERICAN PARKINSON'S DISEASE AND MOVEMENT DISORDERS CONGRESS

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LBA 1

Ocular screening as a diagnostic tool for Parkinson's Disease - a pilot study

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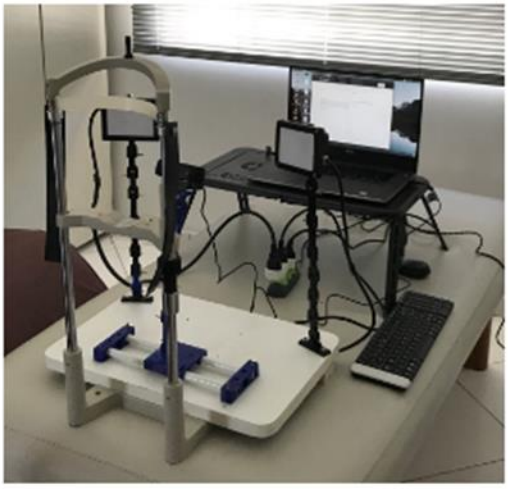
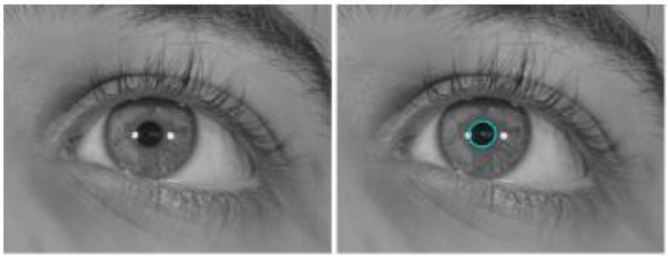
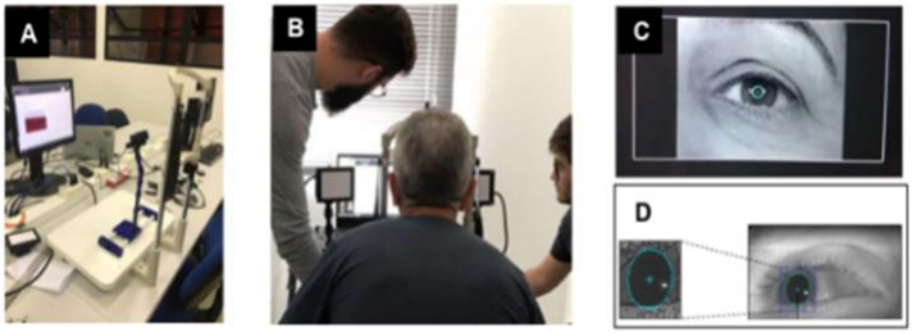
Objective: To investigate the possible relationships between eye movement and Parkinson's disease (PD) by establishing a new oculomotor activity recording tool, for early diagnosis and prognosis of PD.

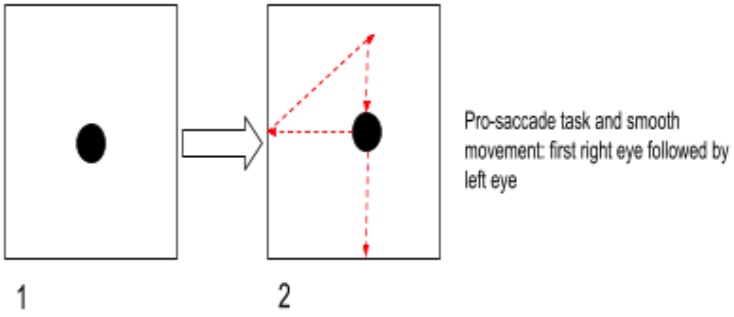
Background: Early diagnosis of PD is challenging. Our study aim was the standardization and establishment of a non-invasive diagnostic tool based on the development of a software/application that evaluates saccades and smooth pursuit movements by eye tracking in patients with PD at different stages of the disease.

Methods: The study included 32 patients with PD and 9 age-matched controls. The control arm with > 42 years old (G42+) was paired by age with the Parkinson's Group. The control arm with < 42 years old (G42-) had a highly homogeneous performance in the task, allowing the validation of the task allowing a comparison parameter closer to an ideal performance. The prototype to perform the visual test is composed of a notebook and a platform that contains a face support, two led reflectors and a digital camera (Figure 1 and 2). The exercise had a duration of 30 seconds for each eye, consisting of a path in the form of a number four, in order to assess the range of movements of the gaze and stimulate the saccades (Figure 3 and 4). The system registered the participant's data, performed the visual test to stimulate saccadic movements, computed an oculomotor change score and displayed results and graphics of the patient's performance.

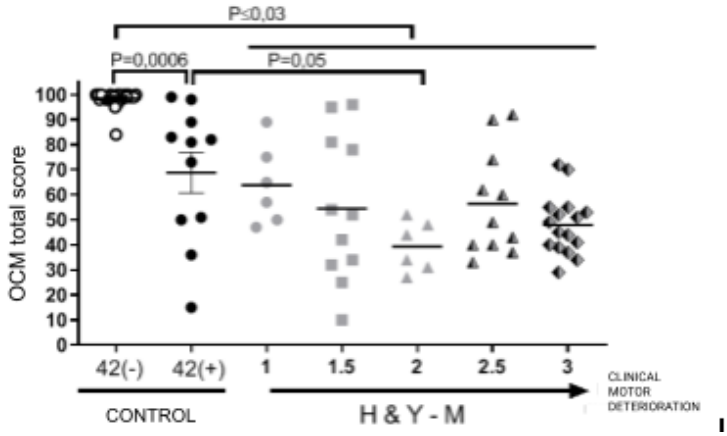


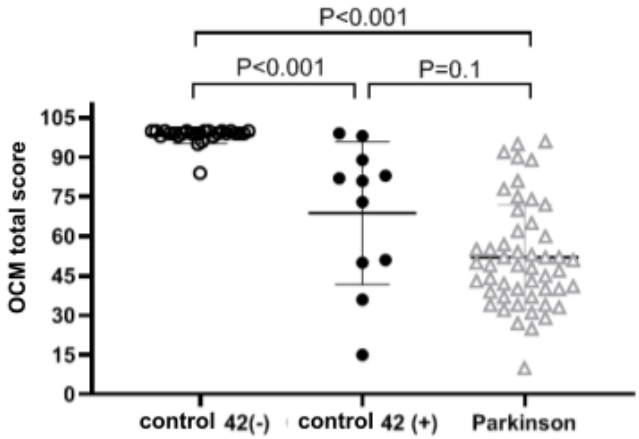






Results: The Parkinson's group with Hoehn and Yahr 2 staging showed a significant reduction in the OCM score when compared to the control group 42(+) (Graph 1 and 2), which probably represents evolution of the disease in this phase. Another relevant finding is the significant reduction in performance this task observed in the control group (G42+), when compared to the control group (G42-), suggesting an aging effect on the performance of the tasks as well.





Conclusions: The proposed ocular screening can be a non-invasive and low-cost biomarker to assess the severity and progression of the PD, especially when cognitive impairment is present, since the tool can assess motor and cognitive demands. The assessment is simple and can be reproduced without fatigue.

Future studies need to evaluate a larger number of patients in order to confirm the benefit of this screening in clinical practice.

LBA 2

Early biochemical changes in colonic α-synuclein in Parkinson's disease

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Objective: The goal is to understand whether early biochemical changes in α-Synuclein (αSyn) can be detected in the enteric nervous system in Parkinson's disease (PD) using a novel mouse model and human tissue.

Background: αSyn aggregates are the main components of Lewy bodies found in both the brain and in the enteric nervous system of PD patients. Pathological changes and accompanying neurodegeneration precede diagnosis by years, with non-speci_c, gastrointestinal symptoms among the earliest prodromal symptoms of PD, pointing to the gut as a potential starting point for pathology.

Method: We hypothesize that biochemical changes in αSyn occur first in the gut, and are a marker of early pathology. We first characterized motor and gastrointestinal function in a mouse model expressing human αSyn under all its regulatory elements, thus enabling human-like spatiotemporal expression of αSyn that does not rely on overexpression, allowing for detection of early, disease-causing changes. We also examined expression of αSyn in the brain and gut in these mice, as well as in post-mortem brain tissue and colon tissue collected during routine screening colonoscopy in subjects with PD.

Results: We showed that our mouse model demonstrates typical motor impairments, as well as impairments of gastrointestinal function (Fig 1). It has previously been shown that membrane-bound αSyn is protected from aggregation, while cytosolic, soluble αSyn has a propensity to aggregate. We show reduced membrane-binding of α-Syn in brain and gut in our mouse model as well as in post-mortem PD cortex (Fig 2). In preliminary results from human PD gut tissue obtained during routine screening colonoscopy, compared to healthy controls, we see a trend towards reduced membrane-binding of αSyn in the colon, as well as trends towards alterations in known pathogenic post-translational modifications of αSyn (Fig 2).

Conclusion: Changes in in αSyn membrane-binding can be detected in mouse and human gut tissue. This study represents the first biochemical assessment of αSyn in the gut, and suggests that biochemical changes in αSyn in the gut can serve as a biomarker of disease.

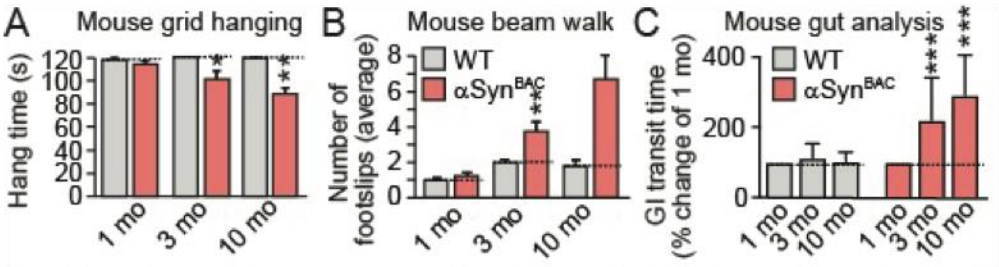

Fig. 1. Impairments in motor and gut function in αSynBAC mice. WT and αSynBAC mice were subjected to grid hanging (A), a beam walk assay (B) and gut transit time (C) analysis at 1, 3 and 10 months of age. Data are means ± SEM (n = x mice; * p<0.05, ** p<0.01, *** p<0.001 using Student's t-test).

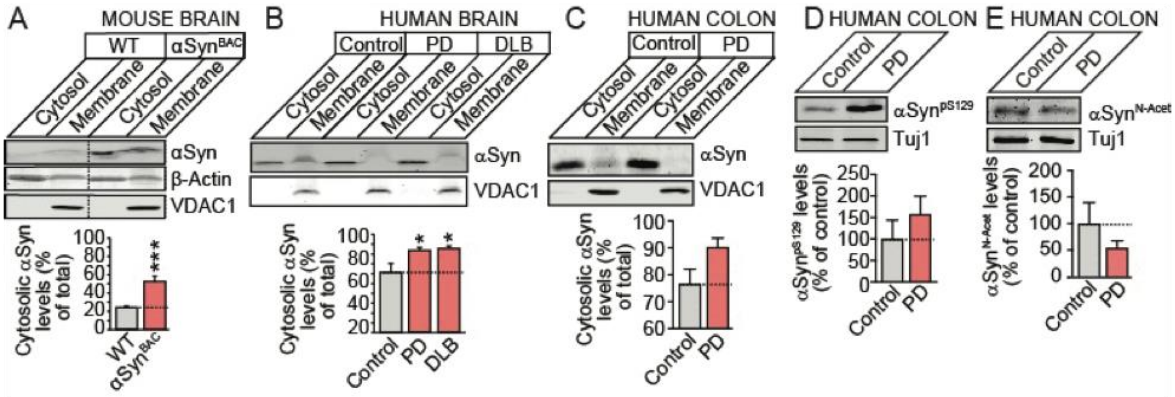

Fig. 2. Biochemical changes in αSynBAC mice. Increased cytosolic levels of αSyn in the brains of αSynBAC mice (A; n = 3 mice each), and (B) PD and DLB patients, but not in healthy controls (frozen cortical sections from the frontal lobe (2nd or 3rd slab), obtained from the Human Brain and Spinal Fluid Resource Center (LA). Control brains were from patients who had died of non-neurological causes and displayed no signs of brain pathol-ogy (Control: n = 5, 78.2 years median age, 40% female, 13.2h postmortem interval (PMI); PD: n = 5, 71.8 years median age, 60% female, 12.4h PMI; DLB: n = 2, 81 years median age, 50% female, 12.8h PMI). (C) Increased cytosolic levels of αSyn in colon tissue from PD patients, and (D & E) changes in pS129 αSyn (D) and N-terminally acety-lated αSyn (E) in human colon tissue (n=3-4 patients each). Data are means ± SEM (* p<0.05, ** p<0.01, *** p<0.001, Student's t-test). Data are means ± SEM (n = x mice; * p<0.05, ** p<0.01, *** p<0.001 using Student's t-test).

LBA 3

Impact of Isolation During the COVID-19 Pandemic on Non-motor Symptoms of Parkinson's Disease: A PMD Alliance Survey

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Objective: This survey aimed to assess the impact of social isolation on self- or proxy-reported Parkinson's disease (PD) symptoms during the COVID-19 pandemic.

Background: Social isolation impairs physical and mental health, particularly among the elderly. As PD usually affects the elderly, we hypothesized that social isolation during the COVID-19 pandemic could exacerbate non-motor symptoms of PD.

Method: The survey was distributed online between 01/06/21 and 02/27/21 among 7,109 subscribers of the Parkinson and Movement Disorders Alliance (PMD Alliance) newsletter. It was open only to people with PD (PwP) and Care Partners (CP, defined as main caregivers of PwP, and serving as proxy respondents). The survey did not identify matched PwP-CP pairs. Respondents were grouped by level of social support from outside of their household during the pandemic (decreased or maintained [i.e., the same as pre-pandemic or increased]). The results were analyzed descriptively, and Wilcoxon signed-rank test was used for pairwise comparisons across groups.

Results: 718 of 7,109 invited participants responded to the survey (response rate 10.1%). PwP (self-reports) accounted for 70.6% of respondents and CP (proxy reports) for 29.4%. Compared with maintained level of social support, decreased social support from outside of the household during the COVID-19 pandemic (58.5% of all responses) was significantly associated with increases in sadness/depression and anxiety ($p<0.0001$ for both comparisons). It was also associated with increased burden of several non-motor PD symptoms (decline in memory, problem solving, or communication, $p=0.0009$; new or worsening confusion, $p<0.0001$; and new or worsening delusions, $p=0.018$).

Conclusion: Decline in social support from outside of the household during the COVID-19 social restrictions was significantly and negatively associated with the burden of mood and non-motor symptoms of PD. These results call for increased vigilance towards non-motor symptoms in PwP experiencing social isolation and highlight the need for stronger provider focus on encouraging PwP and their CPs to build and maintain social connections. Shedding light on the effects of social isolation in general, the results can be generalized to contexts other than the COVID-19 pandemic.

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LBA 4

The effects of short- and long-term dance interventions on motor and non-motor symptoms of Parkinson's disease: A systematic review

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Objective: To examine the effects of short- and long-term dance interventions on the motor and non-motor symptoms of PD.

Background: Dance has emerged as an alternative treatment for people with Parkinson's disease (PD). Despite this, there is still no consensus in the evidence regarding the intervention length and the effects of different dance modalities on motor and non-motor symptoms of PD.

Method: This is a systematic review conducted in accordance with the PRISMA statement. Five databases (Pubmed, LILACS, Scielo, Elsevier, and Cochrane) were electronically searched until November 2021. Search terms were (Dance OR Dancing OR dance therapy) AND (Parkinson's Disease OR Parkinson Disease OR DP). Studies in adults with PD; both sexes; having dance as an intervention for the experimental group and without any exercise for the control group; quasi-experimental, experimental, and pilot studies; published in English were included. Studies were divided into short- (< 11 weeks) and long- (> 12 weeks) term dance intervention. PEDro scale verified the quality of the studies and the level of scientific evidence was measured by GRADE.

Results: The search resulted in 30,014 studies, from which 10 studies were included. Dance modalities included: tango, ballet, contemporary dance, typical cultural dances, and mixed dance styles. A total of 382 participants, 65 years of age and older, Hoehn & Yahr (H&Y) stages I to IV (Table 1) were included. Six studies (60%) had a long-term intervention. Based on Grade, long-term Tango intervention had moderate scientific evidence on motor symptoms of PD (UPDRS III). Typical cultural dances had moderate scientific evidence on PD disease severity, balance, and depression and high scientific evidence on health-related quality of life. The short-term mixed dance styles had moderate scientific evidence over mood.

Conclusion: Motor and non-motor symptoms of PD can be improved after performing short and long-term dance interventions. Future clinical trials should examine the effects of different dance modalities in people with specific levels of PD.

Table 1. Summary of characteristics of included studies.

Dance	Authors (year)	Objectives	Dance intervention length	Participants	Outcomes	Results	PEDro
Typical Cultural Dances	Shanahan et al. (2017)	To examine the feasibility of a randomized controlled study design and to explore the benefits of a set dancing intervention compared with usual care.	90min/week 10 weeks (+20 minutes of a home dance program 3 times/ week).	H&Y = I - II EG: N = 45 Age: 69 ± 10 CG: N = 45 Age: 69 ± 8	- Motor function (UPDRS) - Quality of life (PDQ-39) -Functional endurance (6MWT)) - Balance (mini-BESTest)	No difference between groups	6
Ballet	McGill et al. (2018)	To determine if weekly ballet classes can affect gait variability for a group of people with Parkinson's.	85 - 90 min/day 10 – 12 weeks	H&Y = I - II EG: N = 19 Age: 69.83 ± 4.55 CG: N = 13 Age: 73.25 ± 8,09	-Gait Patterns (Autocorrelation of acceleration signals) - Balance Confidence (ABC) Confidence	No difference between groups	4
Mixed Dance Styles	Ventura, et al. (2016)	To perform a pilot trial to inform selection of primary and secondary outcomes for a larger trial.	85 min/ day 1 time/ week 10 weeks	H&Y = I - II EG: N = 8 Age: 71,8 ± 3,6 CG: N = 5 Age: 70.4 ± 5.5	-Motor function (TUG, timed gait speed test, the standing balance test) -Cognitive function (TEA, Action Fluency, AU, and DSF) -Depressive symptoms (GDS) -Quality of life (FES-I, PDQ-39)	In the intervention group, large (≥0.8) within-group effect sizes were observed for measures of TEA, gait speed, FES-I, GDS and DSF. In the control group, a large positive effect size was observed for balance, and a large negative effect size was observed for gait speed.	5
	Lewis et al. (2014)	To examine the moderating effect of dance on mood in the elderly and more specifically in a group of people with PD across a long cycle of 12 weeks and a short cycle of 1 hour.	50 minutes Once a week 10 weeks	H&Y = I-III EG: N = 18 Age: 65.94 (9.33) CG: N = 10 Age: 64.5 (9.86)	-Mood changes (POMS - Long Cycle Time) (BRUMS - Short Cycle Time)	Improvements in favor to the intervention group	6
Tango	Duncan; Earhart, (2012)	To determine the effects of a 12-month community-based tango program for individuals with	60 min/day 2 times/week 12 months	H&Y = I-IV EG: N = 26	-Disease severity (MDS-UPDRS) -Balance (Mini-BESTest) -Gait (FOG_Q, six-minute walk) -Upper extremity function (9HPT).	Improvements in favor to the intervention group	7

		PD on disease severity and physical function.		Age:69.3 ± 1.9 (48-89) CG: N = 26 Age: 69.0 ± 1.5 (48-81)			
	McKee; Hackney (2013)	To examine the effects of Adapted Tango on spatial cognition as well as disease severity in individuals with PD while controlling for social interaction.	90 min/day 1x/week 12 weeks	H&Y = I - III EG: N = 23 Age: 68.4 ± 7.5 CG: N = 8 Age:74.4 ± 6.5	-Disease severity (UPDRS-III) -Spatial cognition (MOCA, Reverse Corsi Blocks, Brooks Spatial Task) -Balance and fall incidence (FAB, Four-Square Step Test, Single/Dual timed up and go, BBS) -Psychosocial (PDQ-39, FOGQ, SF-12, PCS e MCS)	Improvements in favor to the intervention group on disease severity, spatial cognition, balance and executive There were no main effects on psychosocial questionnaires.	6
Typical Cultural Dances	Tillman et al. (2019)	To investigate the feasibility of a Brazilian samba protocol for patients with Parkinson's disease.	60 min/day 2 times/week 12 weeks	H&Y = I-IV EG: N = 10 Age: 65.30 ± 10.5 CG: N = 10 Age: 67.6 ± 10.9	-Balance (BBS) -Disease severity (UPDRS) -Quality of life (PDQ-39).	Improved in favor to the intervention group	5
	Tillman et al (2020)	To analyze the influence of Brazilian samba on the non-motor symptoms of PD according to TD and PGID subtypes.	60 min/day 2 times/week 12 weeks	H&Y = I-IV EG: N = 23 Age: 67 ± 9.2 CG: N = 24 Age: 69.6 ± 9.5	-Mental health (UPDRS-I) -Health-related Quality of life (PDQ-39) - Sleep quality (PDSS) - Depression (BDI) - Fatigue (FSS)	Improved in the intervention group without significant changes. When compared to the control group, there was a significant difference on the UPDRS I.	5
	Solla et al. (2019)	Evaluate the effects of Sardinian folk dance (Ballu Sardu, BS) on functional performance and motor and nonmotor symptoms in individuals with PD.	90 min/day 2 times/week 12 weeks	H&Y = II EG: N =10 Age:67.8±5.9 CG: N = 10 Age: 67.1 ± 6.3	- Motor function (UPDRS-III, TUG, BBS, FTSST, BST, SRT, and 6MWT) - Non-motor symptoms (PFS-16, BDI-II, SAS, and MOCA)	Improved in the intervention group Non-significant difference between groups on SRT test, PFS-16 and, apathy symptoms	6
Contemporary Dance	Bar; Cohen; Federmn (2021)	To examine the difference in the level of psychological flexibility, creative self-efficacy and quality of life	Once a week 3 months	H&Y = - EG: N = 25 Age: 69.44 ± 7.76 CG: N = 25 Age: 73.24 ± 8.04	- Health-related Quality of life (PDQ-8)	Improved in the intervention group	5

Abbreviations: H&Y (Hoehn and Yahr), UPDRS (Unified Parkinson's Disease Rating Scale), PDQ - 39 (and Parkinson's Disease Questionnaire-39) , 6MWT (6-minute walk test,), TUG(Timed Up-and-Go), AU (The Alternate Uses), TEA (Test of Everyday Attention), GDS (Geriatric Depression Scale), FES-I (Falls Efficacy Scale-International), POMS (Profile of Mood States), BRUMS (Brunel University Mood Scale), FOG_Q (Freezing of Gait Questionnaire), 9HPT(Nine-Hole Peg Test), MOCA (Montreal Cognitive Assessment), FAB (Fullerton Advanced Balance Scale), SF-12 (Short Form health survey-12), PCS (Physical Composite Scale) e MCS (Mental Composite Scale), BBS (Berg Balance Scale), PDSS (Parkinson's Disease Sleep Scale), BDI (Beck Depression Inventory), FSS (Fatigue Severity Scale), FTSST (Five Times Sit-to-Stand Test), BST (Back Scratch Test), SRT (Sit-and-Reach Test), PFS-16 (Parkinson's Disease Fatigue Scale), SAS (Starkstein Apathy Scale), PDQ-8, ABC (Activities-Specific Balance), BDI II (Beck Depression Inventory), UPDRS III (Unified Parkinson's Disease Rating Scale Part-III), MDS-UPDRS (Movement Disorders Society–Unified Parkinson Disease Rating Scale), DSF (Digit Span Forward).

LBA 5

Parkinson's Disease, aplha-Synuclein, melanin and melanoma. Differences and convergences – puzzles to be solved

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Objective: To determine the commonalities and divergences of two diseases: Parkinson's disease (PD) and melanoma, by comparing the expression of phosphorylated alpha-synuclein (p-ASyn) in the skin of affected and healthy subjects.

Background: There is an established relationship between PD and an increased incidence of melanoma, and both disorders coincide with increased presence of alpha-synuclein (p-ASyn) in the skin. While melanoma is the leading aetiology of death from skin cancer worldwide, PD is the second most prevalent neurodegenerative disease. In addition, PD is associated with other skin diseases, like seborrheic dermatitis, sweating disorders, bullous pemphigoid and rosacea.

The unfortunate concurrence of melanoma and PD must involve genetic, epigenetic and environmental factors that favour it, as well as a series of physio-pathogenic modifications. In both cases, cells that synthetize a protective molecule are involved. Melanocytes synthetize melanin, which pigments the skin, eyes and hair; its production is increased in melanoma, along with melanocyte reproduction. In PD, neuromelanin disappears from the substantia nigra and locus coeruleus as monoaminergic neurons die. Both A-Syn and neuro/melanin function as a shields against protectors cellular damage. Phosphorylated ASyn (p-ASyn) binds to DNA and protects the neuronal genome, but its increased cytoplasmic presence contributes to its aggregation and accumulation in Lewy bodies, the characteristic marker of PD. Reduced binding due to aggregation or defective phosphorylation results in transcriptional deregulation, e.g., cell cycle genes. In non-replicative cells (neurons) this would lead to neurodegeneration (PD), while in replicative cells, this would lead to cancer (melanoma). Therefore, we looked for differences and convergences of its expression in the skin.

Method: Hypothesis. The epidermis of patients with melanoma and PD shows a reduced nuclear presence of p-ASyn.
Material and methods.

Using the skin as the study organ, we analyzed the presence of p-ASyn by IHC in biopsies from healthy subjects (17), melanoma (20) and PD patients (18), by immunohistochemistry using an antibody for p-ASyn and by computerized measurement of its expression in the skin using a mathematical algorithm to compare its presence in the three groups.

Results: Using an automated color image segmentation algorithm, we found significantly fewer nuclei harboring p-ASyn in PD epidermal cells (19%); $p<0.05$ than in healthy controls (45%). Melanoma cases had a wider scatter of p-Syn-positive nuclei, ranging from 18 to 41%.

Conclusion: Preliminary results suggest that the decreased nuclear presence of p-ASyn is a common trait of PD and melanoma skin, which would reflect transcription and cell cycle alterations in different cell types. The study is ongoing.