

# LATE BREAKING ABSTRACTS

## LB-01

### Levodopa's effects on anorectal constipation in de novo Parkinson's disease patients: The QL-GAT study

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**Aims:** Gastrointestinal tract (GIT) dysfunction is common in Parkinson's disease (PD) patients. We aimed to perform an open study of levodopa's effects on anorectal constipation in de novo PD patients by the quantitative lower-gastrointestinal autonomic test (QL-GAT).

**Methods:** Nineteen unselected de novo PD patients (10 men, 9 women; mean age, 66 years; mean duration of the disease, 2.2 years) were recruited in the study. All but except for one patient had constipation according to a questionnaire on pelvic organ function. These patients were treated with 200 mg/day of levodopa with 20 mg/day of carbidopa for 3 months. Pre- and post-treatment, objective parameters in the QL-GAT that comprised colonic transit time (CTT) and rectoanal videomanometry were obtained. Statistical analysis was made by Student's t-test.

**Results:** Most patients reported subjective improvements in bowel frequency and difficult defecation after levodopa. Levodopa did not change significantly CTT of the total colon or any segment of the colon. During rectal filling, levodopa significantly lessened the first sensation ( $p < 0.05$ ). It also tended to augment the amplitude in rectal contraction, though these changes did not reach statistical significance. During defecation, levodopa significantly lessened the amplitude in paradoxical sphincter contraction upon defecation (PSD) ( $p < 0.01$ ). It also tended to augment the amplitude in rectal contraction, lessen the amplitude in abdominal strain, though these changes did not reach statistical significance. Overall, levodopa significantly lessened post-defecation residuals ( $p < 0.05$ ).

**Interpretation:** The enteric nervous system (ENS) is regulated by dopamine D2 receptor-mediating inhibition, based on evidences of knock-out mice. However, studies also demonstrated increased motility in the colon (scarce in dopamine receptors) in response to externally-administered dopamine, presumably mediated by other receptor populations such as adrenergic or 5-HT receptors, or by central nervous system (CNS) mechanisms. Under stress conditions, intra-cerebroventricular administration of dopamine facilitates colonic spikes. Therefore, levodopa might act on lower-GIT function by both ENS and CNS mechanisms.

**Conclusion:** The QL-GAT showed for the first time that levodopa augmented rectal contraction, lessened PSD, and thereby ameliorated anorectal constipation in de novo PD patients without serious adverse effects.

## LB-02

### Imaging characteristics of patients with early Parkinson disease: Evaluation with <sup>18</sup>F-FDG SPECT imaging

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**Objective:** To discuss the clinical diagnostic value of <sup>18</sup>F-FDG cerebral glucose metabolism SPECT in patients with early Parkinson disease through semi-quantitative analysis of metabolic function of the striatum structures.

**Methods:** 18 patients with early Parkinson's disease at Hoehn-Yahr grade I were selected from outpatients and inpatients of Parkinson's disease of Department of Neurology of Affiliated Lianyungang Hospital of Xuzhou Medical College from January 2008 to January 2010. After intravenous injection with FDG, SPECT was used to gain the image of bilateral corpus striatum and thalamo-cortical metabolism. It was checked by 3 nuclear medicine physicians on the basis of cross section in accordance with coronal and broken side. The decrease of radioactivity easy to see by naked eye which appeared more than two as fixed index. Describing the double side corpus striatum, thalamo, parietal lobe, temporal lobe, frontal lobe, occipital lobe and other areas attracted cerebellum to gain unit area radioactivity counting. Every lobe of brain was compared with cerebellum radioactivity counting, and its value was considered as semi-ratio index. Cortical metabolism of every part of brain was judged by eyes, and the damage degree of brain metabolism was evaluated with semi-ratio index.

**Results:** According to intention-to-treat analysis, 18 patients were all involved in the analysis of results. The result of screenage expression: The abnormal radioactivity in 16 patients with early primary Parkinson disease detected with FDG SPECT accounted for 88.89% (16/18); Fourteen radioactivity in non-symmetry corpus striatum were reduced (77.78%) in which 5 was double side reduced; According to the semi-quantitative analysis, the semi-quantitative ratios of striatum of opposite side (Disease Side) to movement disorders with PD were lower than the other side (Caudate Nucleus/Cerebellum:  $1.12 \pm 0.31 / 1.38 \pm 0.28$ ,  $t = 2.64$ ,  $P < 0.05$ ; Putamen/Cerebellum:  $1.22 \pm 0.28 / 1.46 \pm 0.22$ ,  $t = 2.86$ ,  $P < 0.01$ ). Their semi-quantitative ratios of caudate nucleus and putamen, which were contralateral to the affected limb (or first affected limb), were lower than those of ipsilateral.

**Conclusion:** The FDG SPECT in 88.89% (16/18) PD patients show the asymmetry changes of corpus striatum or lobe of brain, in which 77.78% (14/18) patients is asymmetry corpus striatum, which indicate that the glucose metabolism pattern of PD changes in the earlier period. The features of glucose metabolism at earlier stages of PD may be useful for the diagnosis of PD.

**Keywords:** <sup>18</sup>F-FDG; Single Photon Emission Computed Tomography (SPECT); Parkinson's disease

## LB-03

### Experimental parkinsonism: Improved trophic efficacy of GDNF after combination with TGF-beta 1

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**Objectives:** i) to analyze the trophic effects of GDNF, TGF-beta 1 and combination of both in a rat model of Parkinson's disease, and ii) to study the protective effects of these treatments on cultured substantia nigra neurons after 6-OHDA treatment.

**Methods:** Hemiparkinsonian rats were implanted with osmotic minipumps two months after striatal degeneration induced by 6-OHDA, pumps liberating GDNF (10ng/day), TGF-beta 1 alone (2.5 ng/day), or a 4:1 combination, during eight days. Cultured dopamine neurons were treated two hours before and after 6-OHDA (0, 40, 60 microM, 15-min exposure) with GDNF, TGF-beta 1 or 4:1 combination, and protective effects were measured through the LDH and MTT tests.

**Results:** The in vivo study indicated that behavioral deficits and the functional dopamine tone in the denervated striatum were enhanced by GDNF and 4:1 combination, but not by TGF-beta1 alone. Dopamine receptor hypersensitivity after lesion was reduced by TGF-beta 1 and 4:1 combination, but not by GDNF. GDNF+TGF-beta1 combination led to further recovery of functional deficits, striatal dopamine tone (TH+) and dopamine receptor hypersensitivity. Importantly, functional recovery and TH+ improvement were sustained and they remained one month after pump cessation. TGF-beta precluded down-regulation of GFR-alpha1 (GDNF receptor), a fact which is usual after chronic GDNF alone. Regarding in vitro studies, cell death after 6-OHDA insult was reduced after incubation with GDNF, TGF-beta 1 and 4:1 combination. Reduced cell death was inhibited after blocking GFR-alpha1 (GDNF receptor) before incubation with GDNF, TGF-beta 1 or 4:1 combination. Hence TGF-beta 1 acts through GFR-alpha1 because TGF-beta 1-induced cell protection was precluded after blocking these receptors.

**Conclusion:** The functional trophic efficacy of GDNF is improved after combination with TGF-beta1 both in vivo and in vitro models of Parkinsonism. GDNF improves TH activity, and TGF-beta 1 reduces upregulation of dopamine receptors. GFR-alpha1 is involved in the protective effects of both trophic factors, and its down-regulation is precluded by TGF-beta1.

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## LB-04

### Effects of Group I and Group II metabotropic receptor ligands in the rat model of L-DOPA induced dyskinesia

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**Objective:** To assess and compare antidyskinetic potential of metabotropic glutamate receptor (mGluR) ligands: MTEP and fenobam (mGluR5 antagonists), EMQMCM and AIDA (mGluR1 antagonists), and LY354740 (mGluR2/3 agonist) in the rat model of L-DOPA induced dyskinesia (LID).

**Background:** Dopamine replacement therapy with L-DOPA initially provides therapeutic benefit in Parkinson's disease patients. However, most patients develop motor complications including L-DOPA induced dyskinesia (LID) within a few years of treatment. It has been hypothesized that enhanced

glutamatergic neurotransmission and changes in the expression of different mGluR in the basal ganglia may contribute to the pathogenesis of LID.

**Methods:** Within 3 weeks of daily L-DOPA treatment, unilaterally 6-OHDA lesioned rats developed stable abnormal involuntary movements (AIMs), a rodent correlate of LID. The animals were allotted to experimental groups expressing similar degree of AIMs. mGluR ligands were tested in the dyskinetic rats using 2-consecutive-day crossover testing design.

**Results:** In unilaterally 6-OHDA-lesioned rats, mGluR5 antagonists MTEP (2.5, 5 mg/kg) and fenobam (30 mg/kg) markedly reduced AIMs when given prior to L-DOPA challenge. Moreover, MTEP was found to be able to acutely interrupt full-blown dyskinetic-like syndrome in rats. Antidyskinetic-like effects of MTEP persisted for at least seven days of daily co-treatment with L-DOPA. Neither of the two mGluR1 antagonists tested (EMQMCM, 5 mg/kg, and AIDA, 1.25 mg/kg) provided any therapeutic benefit in dyskinetic rats. Interestingly enough, the mGluR2/3 agonist LY354740 (5 mg/kg) exacerbated dyskinesia

**Conclusions:** Of the mGluR ligands investigated, only mGluR5 antagonists proved to provide antidyskinetic-like benefit. The data suggest the critical involvement of mGluR5 in the pathogenesis of L-DOPA-induced dyskinesia.

## LB-05

### Effect of selective NR2B antagonists on L-DOPA-induced dyskinesia in hemiparkinsonian rats

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**Objective:** Antidyskinetic potential of NR2B-subunit selective antagonists Ro 25-6891, traxoprodil (CP-101,606); radioprodil (RGH-896) and MK-0657 was assessed in the rat model of L-DOPA-induced dyskinesia (LID). Moreover, the effect of NR2B antagonists on GABA release in the substantia nigra pars reticulata (SNr) was evaluated.

**Background:** Abnormal function of striatal NMDA receptors was implicated in the pathophysiology of LID. However, the therapeutic potential of NR2B selective ligands remains controversial. In fact, NR2B antagonists reduced dyskinesia in MPTP-treated monkeys (Hadj Tahar et al., 2004) and PD patients (Nutt et al., 2008). On the other hand, the compounds failed to reduce LID and concomitant molecular changes (Rylander et al., 2009), or even increased LID severity (Nash et al., 2004) in rodent models of dyskinesia.

**Methods:** Antidyskinetic-like effects of NR2B antagonists were assessed in the unilaterally 6-OHDA-lesioned rat model of dyskinesia. Modulation of GABA release in SNr by NR2B antagonists was evaluated using in vivo microdialysis in dyskinetic rats. Brain pharmacokinetics of the drugs was monitored in naïve animals.

**Results:** Ro 25-6981 significantly reduced abnormal involuntary movements (AIMs) at 2.5 and 5 mg/kg (-14 % and -24 %, respectively), but not at 10 mg/kg. At all doses tested, brain concentrations of Ro 25-6981 were found to exceed its affinity to the target (~10 nM). The most effective dose of Ro 25-6981 (5 mg/kg) reduced GABA release in SNr of dyskinetic rats by ~40%. Conversely, CP-101,606 failed to affect AIMs at any dose tested. Interestingly, while Ro 25-6981 did not affect locomotive AIMs, CP-101,606 (10 mg/kg) increased them by ~50%. At the effective dose, brain levels of CP-101,606 reached ~400 nM. The assessment of behavioural effects and pharmacokinetic profiles of RGH-896 and MK-0567 is still ongoing.

**Conclusions:** NR2B-selective NMDA antagonists may represent a viable approach to manage the development of motor complications following chronic L-DOPA treatment. However, to fully understand the role of different NMDA receptor subtypes in PD and LID it is important to determine pharmacological profiles of different classes of NR2B-selective NMDA antagonists.

## LB-06

### Motor disturbances in neurocysticercosis: clinical and magnetic resonance imaging aspects

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**Background:** Neurocysticercosis (NC) is the most common parasitic infection of the central nervous system. It's endemic in developing countries and is considered an emergent public health problem in the United States of America and in some European countries. Epilepsy and intracranial hypertension are the most frequent manifestations, but few works report motor disturbances in NC.

**Objective:** To report motor abnormalities in a cohort of NC patients and its correlation with magnetic resonance imaging (MRI).

**Methods:** We describe 69 patients with definite diagnosis of NC according to Del Brutto's diagnostic criteria, in which a thorough motor examination was made, and correlated with MRI. The lesions were classified by their location (frontal cortex, centrum semiovale, basal ganglia, brainstem and cerebellum) and their biological evolutive stage.

**Results:** We found 893 lesions in different evolutive stages. The most common location was at the superficial cerebral cortex, 294 of them at the frontal lobe. Fifty-five lesions were observed at the basal ganglia and brainstem motor nucleus (in 24 patients), and 8 at the cerebellum. Despite the great number of cortical frontal and centrum semiovale lesions, only three patients had motor signs suggesting pyramidal dysfunction. Lesions at extrapyramidal structures were not uncommon, but rarely related to extrapyramidal symptoms. Only two patients showed parkinsonian features. One of them showed two cysts at the granulo-nodular stage at basal ganglia, and the other exhibited ventricular dilatation. There was no association between patients with lesions in extrapyramidal structures and symptoms by the Fisher exact test ( $p=1$ ). We observed eight lesions at the cerebellum with no cerebellar symptom associated; two patients with ataxia had their symptoms resolved with antiepileptic drug change.

**Conclusion:** Motor disturbances in NC are not frequent. Pyramidal dysfunction was found in patients with large cortical cysts or with vascular involvement. Parkinsonian features were found in two patients; one with degenerating cysts at basal ganglia and another with non-treated hydrocephalus. Cerebellar lesions were neither frequent or symptomatic. Viable cysts often remain asymptomatic probably due to immunological evasion mechanisms inherent to the parasite.

## LB-07

### Gait analysis in patients with movement disorders before and after DBS

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Human gait consists in a series of alternating and rhythmic movements of trunk and limbs. Alterations of the normal gait are frequent and normally reflect a neurological dysfunction. Approximately 15 % of the adults between 65 and 74 years old have problems in walking or require another person help or a walking stick, ratio that rises to 29% of the population between 75 and 84 years old. A systematic analysis of walking would be an advantage regarding the classification and evolution of the pathologies involving the locomotor system. Results from patients exposed to deep brain stimulation (DBS) demonstrated significant changes in motor symptoms but walking

has not been well described yet. Our group studied patients with Parkinson before and after DBS and a patient with orthostatic tremor during OFF and ON stimulation, one year after surgery. Gait analysis was studied with the STEP 32, an automatic movement analysis system (Demitalia, Torino Italy). The system allows up to 16 simultaneous EMG recordings. A set of sensors includes foot-switches, accelerometers and goniometers. The signals are displayed in a screen computer simultaneously with the image of the patient captured by a video camera. The muscles studied were the tibialis anterior, gastroniimius, rectus femoris, biceps femoris and paraspinal of the right and left side. The patients walked several times along a corridor 15 meters long. The gait cycle was measured during at least 100 steps. In patients with Parkinson, electrodes were implanted at the subthalamic nucleus and in the patient with orthostatic tremor at the ventral intermedium of the thalamus. The surgical procedures and neurological results have been previously described (Figueiras-Méndez y col. Rev Neurol 2009; 49:511-516; Magariños-Ascone et al., Eur J Neurosci 2000; 12:2597-2607). Patients with Parkinson demonstrated a better cadence and normality of the step cycle after DBS. Both single and double support and foot contact and swing phases were close to normality implying a self-sufficient walking. Gait cycle in the patient with orthostatic tremor was normal with the stimulator OFF and ON. The amplitude of the tremor showed a significant decrement but the frequency persisted during standing. This amplitude was greater in close-eyed than in open-eyed patients in both situations, OFF and ON stimulation, implying an important contribution of the visual afferents to the tremor genesis.

## LB-08

### Comparing exercise in Parkinson's disease - The Berlin BIG study

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Physiotherapy is widely used in Parkinson's disease (PD) but there are only few controlled studies comparing active interventions. Recently, a technique named "Training BIG" has been introduced. Training BIG is derived from the Lee Silverman Voice Treatment and focuses on intensive exercising of high-amplitude movements. In the present comparative study, 60 patients with mild to moderate PD were randomly assigned to receive either one-to-one training of BIG, group training of Nordic Walking (WALK), or domestic non-supervised exercises (HOME). Patients in BIG and WALK received 16 hours of supervised training within 4 (BIG) or 8 (WALK) weeks. The primary efficacy measure was difference in change in UPDRS motor score from baseline to follow-up at 16 weeks between groups. UPDRS scores were obtained by blinded video rating. ANCOVA showed significant group differences for UPDRS-motor score at final assessment ( $p < 0.001$ ). Mean improvement of UPDRS in BIG was -5.05 (SD 3.91) whereas there was a mild deterioration in WALK (0.58, SD 3.17) and HOME (1.68, SD 5.95). BIG was also superior to WALK and HOME in timed-up-and-go and timed 10m walking. There were no significant group differences for quality of life (PDQ39). These results provide evidence that BIG is an effective approach to achieve sustained improvement of motor performance in patients with PD.

## LB-09

### Somatosensory Processing in Parkinson's disease

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Arm and hand movements are frequently affected in Parkinson's disease (PD). Given the remarkable connectivity between somatosensory and motor networks and the dependence on sensory feedback to guide movements, maladaptive changes in sensory regions may contribute to the motor impairments in PD.

The goal of the present research is to characterize somatosensory representation of the digits of the hands in patients with PD. Based on previous studies in patients with focal hand dystonia, we hypothesize that cortical representations of digits are abnormal in PD patients.

We studied 10 PD patients 10 healthy age-matched controls. Functional magnetic resonance imaging (fMRI) was used to quantify the representation of digits in the brain. Digits 2 and 5 and the median nerve on each hand were stimulated. fMRI activation was examined in the primary and secondary somatosensory cortices (S1 & S2), and in the insula. In addition, sensory acuity was measured using techniques of psychophysics and intracortical inhibition was studied with transcranial magnetic stimulation (TMS).

In healthy subjects, vibrotactile stimulation of digits 2 and 5 elicited activation in contralateral S1, bilateral S2 and contralateral insular cortex. In contrast, smaller and inconsistent activations were observed in the S1 area for PD patients, which may be due to dysfunction of the basal ganglia. In some patients, activity also occurred in the ipsilateral S1 area, which could represent compensatory recruitment. PD patients had lower spatial acuity and TMS studies suggest that they had reduced long-latency afferent inhibition.

These results suggest cortical sensory system in PD patients has reduced activation with vibrotactile stimuli, which may partially account for their sensory deficits.

## LB-10

### Effect of long-term levodopa treatment on striatal dopa decarboxylase activity assessed *in vivo* by <sup>18</sup>F-DOPA PET in MPTP-monkeys

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**Background and objective:** Much controversy exists about the interpretation of neuroimaging findings of trials and the potential neuroprotective effect of the different drugs. Nevertheless, changes observed with neuroimaging techniques may represent a modulator effect induced by treatment on radiotracer uptake.

**The objective of this study was:** 1. To assess the long-term effect of chronic levodopa administration on the striatal <sup>18</sup>F-DOPA uptake (Ki) in MPTP treated monkeys and 2. To confirm if the interruption of the drug may reverse the possible pharmacological effect of levodopa on striatal <sup>18</sup>F-DOPA uptake.

**Animals and methods:** Eight monkeys (*Macaca fascicularis*) were included in the study. They were treated with intravenous administration of MPTP (0.25 mg/kg/weekly) for 7 weeks. After Animals were divided in two groups.

Group I received levodopa (30 mg/kg tid) for 12 months and group II was treated with placebo. <sup>18</sup>F-DOPA PET scans were performed in all animals in the following conditions: at baseline, after MPTP administration, after 12 months of treatment and after a washout period of 1, 3 and 6 months. MRI examinations also were performed for adequate PET imaging analysis. Nigral cell counting was performed in the substantia nigra of all animals using the optical fractionator principle.

**Results:** After MPTP injections there was a significant reduction on striatal Ki compared to baseline PET (p=0.004). The percentage of striatal Ki reduction was 29.8 (standard deviation [SD] 20.31). The caudate Ki reduction was 28.05% (SD 20.31), while in the anterior and posterior putamen were 26.38 (SD 24.31) and 37.04% (SD 26.95)

As compared to placebo group, PET studies performed at 3 and 6 month after concluding levodopa administration showed a significant increase (p=0.027) in anterior putamen Ki (% of Ki variation in control animals; -10.03 and -16.56%, vs % of Ki variation in levodopa treated animals 28.39 and 2.66%, respectively). No differences were observed within-group analysis. No significant differences were observed within or between groups when applying statistical parametric mapping analysis.

Control and levodopa treated animals showed a similar cell loss in the substantia nigra pars compacta (42% vs 45%).

**Conclusions:** Chronic levodopa treatment induces a long-term increase on dopa decarboxylase activity in MPTP monkeys. This finding suggests caution in interpretation of functional neuroimaging studies to assess PD progression.

## LB-11

### Iris pigmentation in tourette, transient tic, focal dystonia, essential tremor and Parkinson's disease

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**Introduction:** Overrepresentation of light iris pigmentation in focal Dystonia has been debated between U.S. vs. U.K. populations (light (LE) – gray, blue, green, hazel vs. dark (DE) – brown) (Korein J, Ann Neurol 1982;10:53-55, Lang AE et al, Ann Neurol 1982, 12:585-586, Duane DD, Adv Neurol 1988;50:473-492). Nonetheless differential iris pigment frequency may reflect dopaminergic or genetic differences between specific movement disorder populations.

**Methods:** Retrospective case analysis of five referred populations – Tourette Syndrome (TS), Transient Tic (TT), Focal Dystonia (FD), Essential Tremor (ET), Parkinson's Disease (PD).

#### Results:

TS N = 62 Male 46 (74%) LE – 44 (71%) [1 LE-Mulatto]  
TT N = 49 Male 36 (73%) LE – 29 (59%)  
FD N = 245 Male 58 (24%) LE – 173 (71%) [2 DE-AfrAm, 1 LE-AsAm]  
ET N = 111 Male 42 (38%) LE – 79 (71%)  
PD N = 42 Male 23 (55%) LE – 16 (38%)

#### Fisher's Exact Test

TS vs. PD p = 0.001  
TS vs. TT p = 0.23  
FD & ET vs. PD each p = 0.0001

**Conclusion:** LE predominate in ET, FD and TS at virtually identical frequencies and do not differ statistically from TT. All four however differ from PD in which DE predominate. Whether linked to dopaminergic and/or genetic differences warrants investigation.

## LB-12

### A voxel based morphometry (VBM) study in multiple system atrophy (MSA) and progressive nuclear palsy (PSP)

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**Aim:** We used VBM analysis in a cohort of MSA and PSP subjects recruited to the NNIPPS study (Bensimon et al., Brain 2009) to identify functional correlates of pathology in life, relying on: a) prospective and parallel collection of clinical data and MRI scans using a standardised protocol, b) scores that reflect specific sites of neuronal damage as opposed to global scores of disease severity, c) interpretation of results at stringent p values and, d) the largest number of these patients studied using VBM.

**Methodology:** Patients are part of the UK sub-cohort of NNIPPS. Thirty-two patients diagnosed with MSA and 28 with PSP (NNIPPS criteria) underwent MRI at King's College Hospital. VBM was implemented using SPM5 and BAMB (<http://www-bmu.psychiatry.cam.ac.uk/software/docs/xbamm/index.html>). Grey matter (GM) and white matter (WM) were mapped for regional differences across the whole brain. Disease duration, UPDRS and NNIPPS Parkinson Plus Scales, Frontal Assessment Battery (FAB) and Dementia Rating Score (DRS) were used as independent variables.

**Results:** Differences in regional atrophy between PSP and MSA. In PSP, GM and WM reductions were seen in frontal cortices and midbrain. PSP showed less GM than MSA-P in the thalamus. Motor correlates of VBM: In PSP, oculomotor function correlated with atrophy centrally located in the midbrain. In MSA, cerebellar function correlated with widespread reduction of GM in the cerebellum. Cognitive changes: In PSP, FAB correlated with WM loss in cingulate gyrus (BA 24), putamen and globus pallidus. In MSA, FAB correlated with GM loss in the cerebellum and frontal gyri. In PSP, DRS II correlated with GM loss in the midbrain, parahippocampal and cingulate gyri. WM reduction was seen in the midbrain, pons and middle and precentral gyri (BA 9 and 4). In MSA, DRS II correlated with GM loss in parahippocampal, superior temporal gyri and caudate nucleus and WM loss was seen in cingulate and precentral gyri. Disease duration and global scores of disease severity did not correlate with any volume reduction in either disease.

**Discussion:** The characteristic motor abnormalities in PSP and MSA correlated well with VBM changes. The cognitive abnormalities in PSP and MSA, although similar in nature, may have different pathological substrates judged by these VBM analyses.

## LB-13

### Rasagiline effect over depression disorder symptoms of Parkinson's disease

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**Background:** Parkinson's disease (PD) is a neurodegenerative chronic disorder characterized for motor and non motor symptoms (sleep dysfunction, sensory symptoms, autonomic dysfunction, mood disorders and cognitive abnormalities). Depression occurs in 30-40% of the patients with PD, but only 20% of them are treated. Improvements of dopaminergic tone over ganglion basal circuits results in a major stimulation of cerebral cortex. The limbic circuit mechanism of ganglion basals might be explaining improvements over non motor symptoms after tri-cyclical anti-depressive

administration. Rasagiline is a MAO-B inhibitor effective over motor and nonmotor symptoms of PD. It is possible that Rasagiline administration causes an improvement of dopaminergic tone over limbic circuits of ganglion basals, enhancing positive retro alimentionation to cerebral cortex, hence diminishing depressive effects.

**Objective:** Evaluate depression symptoms evolution over patients with Parkinson disease with Rasagiline as a side therapy.

**Methodology:** We realized a prospective clinical essay with patients with idiopathic Parkinson disease. Patients were in a Levodopa treatment with clinical DSM IV criteria of non treated depression for two months prior the essay. Rasagiline administration of 1 mg/day was initiated. Evacuaciones were realized every three weeks including physical exploration. We measured response applying Hoehn and Jahr stage scale, UPDRS, daily life activities of Schwab and England, and Hamilton's depression scale.

**Results:** We studied 15 patients, 10 males (66.7%) and 5 females (33.3%). Medium age of the group is 61 years (SD  $\pm 8.1$  years) and medium disease time of evolution is 5 years (SD  $\pm 2.87$  years). Depression evolution time is 18 months (SD  $\pm 6$  months).

Disease intensity measured with Hoehn and Jahr scale over the third, sixth and ninth week showed an improvement over 20%, 24% and 27% respectively.

Measurement with UPDRS scale showed a decrease in medium punctuation over the time of essay. Punctuation as followed: third week medium of 78 ( $\pm 30.62$  points), sixth week medium of 75 ( $\pm 32.09$  points) and ninth week medium of 70 ( $\pm 30.49$  points).

Applying Hamilton's depression scale, a medium punctuation of: 18 ( $\pm 6.82$ ), 15 ( $\pm 6.16$ ) and 10 ( $\pm 5.28$ ) over the third, sixth, and ninth week respectively.

We observed adverse effects such as cephalaea and dry mouth only in two patients.

Se observó como efecto adverso cefalea y boca seca solo en dos pacientes.

**Conclusion:** Functional improvement of patients with Rasagiline side therapy is associated with an improvement over depression symptoms on studied patients.

## LB-14

### PYM50028, an orally active neurotrophic factor modulator with disease-modifying potential, enhances the effect of L-DOPA in MPTP-lesioned macaques

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**Objective:** This study investigated the effects of PYM50028 on L-DOPA-induced activity in MPTP-lesioned macaques.

**Background:** PYM50028 restores dopaminergic loss in MPTP-lesioned mice (Visanji et al. 2008) and, as a monotherapy, significantly reduces parkinsonian disability in MPTP-lesioned macaques. However, it remains unknown as to whether the restorative effects of PYM50028 are beneficial in MPTP-lesioned macaques already receiving L-DOPA. Answering this question will define whether PYM50028 has potential not only as a monotherapy but also as an adjunct therapy in Parkinson's disease.

**Methods:** 10 female macaques received MPTP (0.2 mg/kg/day, s.c.) until stable parkinsonian symptoms developed. Macaques received L-DOPA (Madopar, 20 mg/kg/day) twice daily for 19 weeks before commencing

treatment with either L-DOPA+PYM50028 (20 mg/kg/day) or L-DOPA+vehicle (HPMC, 0.5% w/v containing Tween 80, 0.2% v/v) for a further 18 weeks (N=5 macaques/group). Spontaneous activity of each animal over a 24h period was obtained in its home cage by the use of Actical™ passive activity monitors. Measurements of activity were taken pre-MPTP, post-MPTP, from the 1st to 18th week of L-DOPA administration (W1 and W18) and from the 1st to 18th week of L-DOPA+PYM50028 or vehicle administration (W20 to W37).

**Results:** Pre-MPTP, “normal” macaques displayed high activity during waking hours (7 am-7 pm). MPTP administration significantly reduced the level of activity by ~80%. L-DOPA, given twice daily, partially restored activity to ~50-60% of “normal”, though this was still significantly lower than pre-MPTP levels. In macaques receiving L-DOPA+vehicle the level of activity at W20 and W37 was similar to L-DOPA alone (W18). In macaques receiving L-DOPA+PYM50028 the level of activity at W20 was similar to L-DOPA alone (W18) but then increased over time and by W37 was increased to ~80% of pre-MPTP levels and was not significantly different from pre-MPTP “normal” activity levels. The plasma  $C_{max}$  level of PYM50028 at week 18 was  $566 \pm 67$  ng/ml.

**Conclusion:** PYM50028 improved the animal’s activity response to L-DOPA. This effect developed over 18 weeks and was not present during the first week of co-administration.

Ref: Visanji et al. (2008). *FASEB J.* 22(7): 2488-97

## LB-15

### Assessing normative EMG values to increase diagnostic accuracy for REM sleep behavior disorder (RBD)

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**Objectives:** In a recent study, we showed that simultaneous EMG recording of the mentalis, flexor digitorum superficialis and extensor digitorum brevis (SINBAR EMG montage) provided the highest rates of REM sleep phasic EMG activity in subjects with RBD (Frauscher B et al. *Sleep* 2008). The aim of the present study was to assess normative phasic EMG values for the SINBAR EMG montage and to perform a direct comparison with RBD patients.

**Methods:** We analyzed polysomnographic registrations of 15 RBD patients (mean age,  $65.9 \pm 5.9$  years; 8 idiopathic, 7 due to Parkinson’s disease) and 15 age-matched controls. Phasic EMG activity was defined as duration between 0.1 and 5 sec. and an amplitude exceeding twice the REM sleep background EMG activity. Phasic EMG activity was scored and quantified in 3-second mini-epochs. The percentage of phasic EMG activity represents the number of mini-epochs with phasic EMG activity divided by the total number of mini-epochs.

**Results:** Overall, 39.826 mini-epochs (mean,  $1327.5 \pm 555.5$  per patient / control) were analyzed. In the RBD group, mean phasic EMG activity was  $60.5 \pm 16.5\%$  compared to  $22.8 \pm 6.4\%$  in the control group ( $p < 0.001$ ). This difference was less pronounced when using a montage consisting of the mentalis muscle alone (patients,  $37.2 \pm 15.8$ ; controls,  $9.9 \pm 3.2$ ) or when using a traditional EMG montage using the mentalis plus both tibialis anterior muscles (patients,  $55.7 \pm 17.6$ ; controls,  $27.6 \pm 11.1$ ). In order to discriminate between RBD and controls, we performed a ROC analysis for phasic EMG activity of the SINBAR EMG montage. When choosing an EMG activity cut-off of 35 %, both sensitivity (0.91, 95% CI, 0.62-0.98) and specificity (1, 95% CI, 0.73-1) were very high.

**Conclusion:** This is the first study to assess normative values of EMG activity in both the chin and extremity muscles. Our data showed that the SINBAR EMG montage clearly differentiates between RBD and controls. This is of utmost importance since RBD often precedes neurodegenerative disease for years.

## LB-16

### Pridopidine improves voluntary motor function in patients with Huntington’s disease – results from the phase 3 study MermaiHD

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**Objective:** To investigate the efficacy and safety of pridopidine, the first dopaminergic stabilizer, in patients with Huntington’s disease (HD).

**Methods:** MermaiHD was a 6-month randomized, double-blind, placebo-controlled phase III study in eight European countries. Eligible patients were aged  $\geq 30$  years and had a sum score of  $\geq 10$  points in the modified motor score (mMS) at screening. The mMS is a validated subscale of the total motor score (TMS) of the Unified Huntington’s Disease Rating Scale. Patients were randomized equally to receive pridopidine 45 mg once (q.d.) or twice (b.i.d.) daily, or placebo. During weeks 1–4, the patients received once-daily treatment (morning dose). Thereafter, the patients took two treatment doses (morning and afternoon dose) until the end of treatment. The primary objective was to assess the effects of pridopidine on voluntary motor function (change in mMS from baseline to week 26).

**Results:** In the ITT population ( $n = 437$ ), pridopidine resulted in statistically and clinically significant improvements in voluntary motor function compared with placebo, and showed increasing effect separation over time. After 26 weeks of treatment, mean (SE;  $p$  vs placebo) change from baseline was  $-1.20$  (0.51;  $p < 0.02$ ) for mMS;  $-3.51$  (1.05;  $p < 0.001$ ) for TMS;  $-1.29$  (0.41;  $p < 0.02$ ) for eye movements; and  $-1.12$  (0.32;  $p < 0.001$ ) for dystonia. There was no effect on chorea. Pridopidine was well tolerated, with an adverse event profile similar to placebo and no indication of treatment-associated worsening of symptoms.

**Conclusion:** Pridopidine is the first drug shown to improve voluntary motor function in patients with HD in a phase III study. As it is well tolerated, it is likely to improve a relevant dysfunction of daily living in patients with HD.

## LB-17

### A web application for follow-up of results from a mobile device test battery for Parkinson’s disease patients

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A test battery consisting of self-assessments and motor tests (tapping and spiral drawing) was developed for a hand computer with touch screen in a telemedicine setting. This test battery was used in a clinical trial by sixty-five

patients with advanced Parkinson's disease (PD) on 9991 test occasions (four tests per day during in all 362 week-long test periods) at nine clinics around Sweden. Test results are sent continuously from the hand unit over a mobile net to a central computer and processed with statistical methods. They are summarized into scores for different dimensions of the symptom state and an 'overall test score' reflecting the overall condition of the patient during a test period. There is a web application that presents summaries of these test results graphically to the clinical staff. The information in the web application is organized and presented in a way that the general overview of the patient performance per test period is emphasized. Focus is on the overall test score, symptom dimensions and daily summaries.

In a recent preliminary user evaluation, the web application was demonstrated to fifteen study nurses who had used the test battery in a clinical trial (DAPHNE, EudraCT No. 2005-002654-21). At least one patient per clinic was shown. In general, the responses from nurses were positive. They claimed that the test results shown in the system were consistent with their own clinical observations. They could follow complications, changes and trends within their patients.

In conclusion, the system is able to summarise the various time series of motor test results and self-assessments during test periods and present them in a useful manner. Its main contribution is a novel and reliable way to capture and easily access symptom information from patients' home environment. The convenient access to current symptom profile as well as symptom history provides a basis for individualized evaluation and adjustment of treatments.

## LB-18

### 12-month results from a novel test battery used in a duodenal levodopa infusion trial

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A novel test battery consisting of self-assessments and motor tests (tapping and spiral drawing) for patients with Parkinson's disease (PD) was developed for a hand computer with touch screen in a telemedicine setting. Tests are performed four times per day in the home environment during week-long test periods. Results are processed into scores for different dimensions of the symptom state and an 'overall score' reflecting the global condition of a patient during a test period. The test battery was validated in a separate study recently submitted to Mov Disord.

This test battery is currently being used in an open longitudinal trial (DAPHNE, EudraCT No. 2005-002654-21) by sixty-five patients with advanced PD at nine clinics around Sweden. On inclusion, the patients were either receiving treatment with duodenal levodopa/carbidopa infusion (Duodopa<sup>®</sup>) (n=36), or they were candidates for receiving this treatment (n=29). We now present interim results for the first twelve months.

Test periods were performed in three-month intervals. During most of the periods, UPDRS ratings were performed in afternoons at the start of the week. In twenty of the patients, scores were available during individually optimized oral polypharmacy, before receiving infusion and at least one test period after having started infusion treatment.

Usability and compliance with performing tests, this far are good, both with patients and clinical staff. Correlations between test periods 2 and 3 during infusion treatment (three months apart) are stronger for overall test score than for total UPDRS, indicating good reliability. The correlation between overall test score and UPDRS for all test periods is adequate (r=-0.6).

In an exact Wilcoxon signed rank test, where the endpoint is the change from the first to the twelve month test period (n=25), there was no change in test results in any of the test battery dimensions for the patients already receiving infusion when included. However, in the patients entering the study before receiving infusion, there was a significant change (improvement) from the baseline to the twelve month test period in dimensions; 'off', 'dyskinesia' and 'satisfied' and in the 'overall score' (n=15). The mean improvement in overall score after infusion was 29% (p=0.015). We conclude that the test battery is able to measure a functional improvement with infusion that is sustained over at least twelve months.

## LB-19

### Long-lasting improvement of essential tremor by repetitive transcranial magnetic stimulation of the cerebellum: a pilot study

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**Background:** The activity of the cerebello-thalamo-cortical (CTC) pathway can be modulated by repetitive transcranial magnetic stimulation (rTMS) of the cerebellum (Popa et al, 2010). There is growing evidence for an overactivity of the cerebellum and CTC loops in essential tremor (ET). We thus tested the long-term effect of cerebellar rTMS in ET.

**Methods:** Eleven patients with ET underwent 5 daily consecutive sessions of low frequency cerebellar rTMS. rTMS was delivered via a 70 mm inner diameter figure-of-eight coil connected to a Magstim Rapid<sup>2</sup> (Magstim Co, UK). The optimal position of the coil, targeting the VIII.A cerebellar lobule, was maintained throughout all sessions with the help of a MRI-based neuronavigation system (Nextim, Finland). Each session consisted of two sequences of 900 impulses at 1 Hz (15 minutes), delivered consecutively over both sides. Tremor intensity was measured by clinical scores (Fahn-Tolosa-Marin Tremor Rating Scale) and physiological quantification of tremor, using polymyography (EMG) and tri-axial accelerometer (PCBPiezotronics, NY USA) recording (Acc). Clinical and physiological parameters were obtained at the baseline, after the fifth rTMS session, and one and 3 weeks later. Statistical analysis was performed using the Wilcoxon non parametric test.

**Results:** Clinical scales significantly improved by 25-30% after the fifth session of rTMS (p<0.05, compared to baseline). This beneficial effect persisted at +1 week (p<0.02) and +3 weeks (p<0.05) after the end of the stimulation series. Tremor amplitude, obtained from Fast Fourier Transform power analysis of the Acc and extensor carpi radialis EMG signals, also decreased significantly (p<0.01 and 0.05, respectively), and lastingly after the 5 rTMS sessions (p<0.05 at +1 and +3 weeks, for Acc and EMG). Mean tremor frequency (6.0 ± 0.8 Hz) was not modified by rTMS. No adverse effects of rTMS were observed.

**Conclusion:** This pilot study further supports that cerebellar dysfunction may be involved in the pathogenesis of ET and modulation of the cerebellar output is a promising therapeutic target in this setting. In a unique previous study (Gironell et al, 2002), a short lasting (<1h) beneficial effect of a single session of 1Hz cerebellar stimulation was shown. Here we demonstrate for the first time, enduring (>20 days) therapeutics effect on ET by repeating rTMS sessions over a week. Further investigations, including placebo controlled designs with chronic stimulation are needed.

### Tango and Parkinson's disease: limitations in the evaluation of efficacy and new prospectives in the rehabilitative approach

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Since some years ago, it was not completely certain the utility of rehabilitation for Parkinson's disease (PD) patients, so that in a review of all rehabilitative approaches in PD (Rubinstein TC, 2002), it appeared that goals of treatments were not always successful.

The point is that, as documented by anatomopathological studies (Braak H, 2010), PD is, at the beginning and probably intrinsically, a not motor disease, but, probably much more, is a cognitive-emotional disease, in consideration of the high incidence of depression (Fang F, 2010) and mild cognitive impairment (Sollinger AB, 2010), since the early stages.

By starting "era" studies of external cues (McIntosh GC, 1997), it changes the wind, beginning a view of approach involving the whole body, so that working on associative cortical areas, it is possible to influence the quality of gait.

Our group found in Argentine Tango a potential rehabilitative tool for Parkinson's disease patients. This music, so full of imagination, would facilitate the planning of movement, because, in few seconds, the dancer needs to think about and soon apply a dancing image. Much more, tango might help to ameliorate the social life and the self-esteem. Finally, this dance contains itself same motor schemes lost in course of disease so that replying them, it may help for motor recovery.

On this line, by a collaboration with teachers of tango, patients, bioengineers, physiotherapist, psychologists, and we neurologist, it has been created a DVD version manual ([www.tangonauti.it](http://www.tangonauti.it)), which includes a number of selected dancing movements believed useful for PD patients.

For 5 weeks, each patient and his partner (10/10) followed 1 hour per day for 5 days per week home-protocol included in DVD and 2 hours per week of session all together with 2 teachers of Tango.

The UPDRS motor score pre/post 5 weeks was ameliorate in speech, posture, and gait items in all patients. Concerning the quantitative data, we found not homogenous findings: kinematic analysis shows an amelioration of flexed posture of the hip and cadence of gait, while any change was found, evaluating the single and choice reaction of time immediately after the class of tango.

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[www.tangonauti.it](http://www.tangonauti.it)

### Analysis of FDG and FP-CIT PET measures for 32 MSA patients: In vivo evidence for trans-synaptic degeneration

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**Background:** We compared the severity of regional pathology in living patients with early MSA, using [18F]FDG and [18F]FP-CIT PET.

**Methods:** [18F]FDG PET and [18F]FP-CIT PET were performed in 32 patients with early stage of MSA (age=58.1 ±8.17 years, disease duration =3.2 ±1.74y; 19 probable, 13 possible). Subjects were divided into three groups (13 with cerebellar ataxia only; "pure" MSA-c, 5 with parkinsonism only; "pure" MSA-p, and 14 with both symptoms; MSA-m). Regional FDG uptake was obtained as a ratio of the global cortical uptake of FDG. Striatal FP-CIT binding was expressed as a ratio of the occipital binding. Each PET measure was compared between MSA subgroups and age-matched normal subjects.

**Results:** FP-CIT binding ratio in the putamen was significantly lower in the pure MSA-p (3.20 ±0.72, p<0.0001 for vs pure MSA-c, vs normal), MSA-m (2.68 ±0.98, p<0.0001 for vs pure MSA-c, vs normal), and pure MSA-c (6.81 ±0.97, p=0.0016 vs normal) than the normal (8.44 ±1.87). FDG binding ratio in the putamen was significantly subnormal in the pure MSA-p (0.99 ±0.08, p=0.002 vs normal), MSA-m (1.08 ±0.10, p<0.001), but not in pure MSA-c (1.21 ±0.92 vs 1.29 ±0.24 for normal); FDG binding ratio in the cerebellum was significantly subnormal in all MSA subgroups: pure MSA-c (0.62 ±0.05, p<0.001 vs normal) < MSA-m (0.66 ±0.07, p<0.001) < pure MSA-p (0.77 ±0.08, p=0.045; vs normal 0.97 ±0.26). FP-CIT binding ratios in the putamen correlated positively with FDG uptake ratios in the putamen (r=0.602, p=0.0003), but not with FDG uptake ratios in the cerebellum.

**Conclusion:** We showed that: (1) FP-CIT binding in the putamen was subnormal even in "pure" MSA-c patients with cerebellar ataxia only; (2) conversely, FDG uptake in the cerebellum was subnormal in "pure" MSA-p with parkinsonism only. These findings suggest that MSA-c and MSA-p are in a spectrum of the same disorder. Furthermore, significant positive correlation between FP-CIT and FDG PET measures in the putamen supports the notion of "linked degeneration" of presynaptic nigrostriatal and postsynaptic striatal projection neurons in MSA.

### Analysis of Asp331Tyr variant of PLA2G6 in Taiwanese Parkinson's disease

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**Introduction:** Mutations of PLA2G6 have been recently documented in association with dystonia-parkinsonism but absent iron deposit in the basal ganglia on brain imaging. In our previous investigation on Asp331Tyr variant in a group of early onset Parkinsonism (EOPD), we found 1 case with homozygous variant from a consanguineous marriage and 4 cases of heterozygous variant. Now we extend to screen this variant in a large scale of sporadic PD for the possible genetic susceptibility.

**Subjects and methods:** An informed consent was obtained in each participant. Of 956 sporadic patients (woman/man= 387/569) with

Parkinson's disease (PD) were included in this extension study. PD patient was included based on the UK Brain Bank criteria. Of 802 healthy controls (woman/man =483/319) were also screened and most of them was the spouse of PD patient. The PLA2G6 c.G991T variant in exon 7 was screened by a TaqMan allelic discrimination method and Assays-by-Design on Applied Biosystems 7300 Real Time PCR System.

**Results:** We have identified 8 heterozygous Asp331Tyr variant; 4 (0.4%, 4 men) in the patient group and 4 (0.5%, 3 men and 1 woman) in the control group. There was no difference of frequency of this mutation between PD and control groups (P value =0.535, odd ratio=0.835, 95% CI: 0.210-3.33). Those 4 patients with heterozygous variant manifested with typical Parkinson's disease and responded effectively to levodopa therapy. The onset of symptoms of 2 patients was before 50.

**Conclusion:** In the present extended study in a large scale of PD population, the frequency of Asp331Tyr variant was not higher in the sporadic PD than in the control.

## LB-23

### The French national experience for Wilson's disease: Epidemiological study of a cohort of 330 patients

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**Background:** Wilson's disease (WD) is a rare inherited disease with an efficient treatment if it is early conducted. Improving the knowledge of this disease is a priority of the French national reference centre for a better access to diagnosis and treatment.

**Objective:** Improve the knowledge of WD by an epidemiological study on the French cohort.

**Methods:** We registered all patients followed by all the French centers working with the national reference centre.

**Results:** 330 patients (1-77 years old) have been listed by the French national reference center for Wilson's disease (sex ratio: 1). Mean age at diagnosis was 19 years. First symptoms were neurological for 38.5% of the patients, hepatic for 43.9% and renal, psychiatric or haematologic for 7%. Seventeen percent were diagnosed after familial screening. At time of diagnosis, Kayser-Fleischer ring was observed in 95% of patients with neurological symptoms, in 55% of hepatic presentation and in 26% of the presymptomatic form. Mean coeruloplasminemia was low (0.08 g/L) but 5% of patients had normal values (>0.2 g/L). Urinary excretion of copper was increased in 96% of the patients (>40 µg/24h). Genetic investigation was not conclusive in 13.1% of the families (only one or no mutation founded). First treatment was D-Penicillamine in 85% of the cases. After a mean follow up of 15 years the treatment was D-Penicillamine for 44.4% of the patients, Trientine for 14.4%, Zinc for 26.7% and association of chelator and zinc for 8.9%. Liver transplantation has been realized for 5.6% of the patients. The major cause of death was infectious complications for 50% of the cases followed by hepatic decompensation (25%) and liver carcinoma (16.6%).

**Conclusion:** This cohort included about 1/3 of the WD patients in France. In order to ameliorate the recruitment of Wilson's disease patients, coordination of all health professionals with a multidisciplinary approach needs to be improved.

## LB-24

### Postmortem brain urate levels are reduced in Parkinson's disease

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**Introduction:** Increasing laboratory, clinical and epidemiological evidence suggest that urate may play an important role in neurodegenerative disease. In Parkinson disease (PD) higher levels (but still within normal range) of blood and CSF urate have been associated with a slower rate of disease progression. Elevated urate may also be linked to reduced progression of cognitive decline and risk of dementia, including Alzheimer's disease (AD). Urate is a natural antioxidant found abundantly in blood and human brain tissue and likely crucial to limiting oxidative damage. As oxidative stress is thought to contribute to loss of nigrostriatal dopamine neurons in PD and the pathophysiology of other neurodegenerative disorders, brain and blood urate levels may be important in determining disease susceptibility and progression. In this study we explore the hypothesis that low brain urate levels may be associated with PD and related neurodegenerative disorders, including AD and dementia with Lewy bodies (DLB).

**Methods:** We analyzed human post-mortem brain tissue obtained from the ADRC/Harvard NeuroDiscovery Center neuropathology core from PD, AD, and DLB patients and age-matched non-neurodegenerative disease controls (n=73). Urate pathway analytes were measured in multiple brain regions, including frontal and temporal cortex, striatum, cerebellum, and white matter, using HPLC with electrochemical and UV detection. Mean levels were compared across groups using one-way ANOVA by ranks.

**Results:** Age was well-matched among groups (mean 80.5±9.7 yrs). Mean postmortem interval (PMI) for samples was 16.3 hrs (range 2.0-65) and different only for AD (10.7±5.2 hrs). Our preliminary findings show significant differences in brain urate levels among controls, PD, and DLB cases (p<0.05). Consistent with levels in serum, brain urate in control tissue is higher in males than in females. Among males urate is significantly lower in PD tissue compared to control (p<0.05), whereas in females urate levels are unchanged. Measurement of urate precursors, inosine, hypoxanthine, and xanthine, showed no differences among groups. Differences could not be explained by PMI or age.

**Conclusion:** Although preliminary and inconclusive with respect to disease associations, these findings demonstrate ability to detect and measure urate and multiple precursors in postmortem brain. Analysis of more samples and additional urate analytes (adenosine and allantoin) will be needed to verify and expand upon these findings.

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## LB-25

### Phenotype of the e1F4G1 mutation in familial Parkinson's disease

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**Objective:** To characterise the phenotype of an Irish patient with a novel genetic mutation causing familial Parkinson's disease (PD).

**Background:** Genome-wide analysis of a multi-incident Northern French family with autosomal dominant parkinsonism has implicated a novel locus on chromosome 3q26-27. Linkage and disease susceptibility is caused by amino acid substitution (p.R1205H) in eukaryotic translation initiation factor 4-gamma protein (eIF4G1). Translation initiation protein is impaired due to a mutation in exon 24 of the gene. eIF4G1 has been identified as an important regulatory factor in cell size and cycle progression, its absence in vitro studies results in autophagy. It is postulated that eIF4G1 mutations impair the ability of dopaminergic neurons to respond to stress through changes in translation of existing mRNAs that are essential for cell survival. The phenotype of this novel mutation has not yet been described.

**Design/Methods:** A 61 year old Irish man, with onset of symptoms age 34 and no family history of PD was evaluated following identification of this novel genetic mutation. He meets the UK Brain Bank criteria for a diagnosis of PD.

**Results:** eIF4G1 is a new genetic mutation discovered in PD. The phenotype of this mutation in an Irish patient consists of; onset with dystonia (age 34), levodopa responsiveness, marked dyskinesias, responsiveness to deep brain stimulation and no cognitive impairment.

**Conclusion/Relevance:** There is increasing evidence for a genetic basis for PD with up to seven genetic mutations being reported in the last decade. eIF4G1 is a novel genetic mutation whose phenotype has not yet been described; this is the first description of a patient with eIF4G1 mutation.

## LB-26

### Group patient visits for Parkinson's disease: a randomized comparative effectiveness trial

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**Objective:** To establish the feasibility and evaluate the benefits of using group patient visits for individuals with Parkinson's disease

**Background:** Group visits are shared medical appointments among individuals with a common, usually chronic, medical condition. Previous trials of group visits in other conditions have demonstrated greater patient and provider satisfaction, improvements in quality of life, and decreased health care utilization. This novel method of care delivery has yet to be evaluated in Parkinson's disease.

**Methods:** We conducted a 12-month, randomized controlled trial of group patient visits versus usual (one-on-one) visits for patients with Parkinson disease. Group visits lasted approximately ninety minutes, which included five minutes of introductions, a 45 minute educational session, and a ten minute break. The remaining time was spent addressing patient concerns, discussing research opportunities, and planning subsequent group sessions. Patients randomized to group visits met individually with the study physician

for brief ten minute visits prior to or after the group session. Those receiving group visits attended four sessions with their current physicians over twelve months; the usual care group continued to see their same physician as needed.

The primary outcome measure was feasibility as measured by the ability to recruit participants for the study and by the proportion of participants who completed the study. Secondary outcome measures included quality of life, patient satisfaction, depression, and caregiver burden.

**Results:** The three study physicians enrolled thirty patients and 27 caregivers into the study. Participants randomized to group visits and usual care had similar baseline characteristics. Thirteen of the 15 patients randomized to group visits and 14 of the 15 randomized to usual care completed the 12-month study.

Change in quality of life, patient satisfaction, depression, and caregiver burden did not differ significantly between both groups. At the study's conclusion, 13 individuals expressed preference for group visits, 10 for usual visits, and four were undecided.

**Conclusion:** Group patient visits are a feasible means of providing care to individuals with Parkinson disease and may offer an alternative for some patients and physicians.

## LB-27

### European-HD burden study (EURO HDB) – Preliminary results for Italy and France

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**Objective:** To evaluate patient health status, patient and caregiver quality of life (QoL), cost of illness, and drivers of costs and QoL in Huntington's disease (HD). To our knowledge, this is the first comprehensive, European observational study (Euro-HDB) to establish these burdens.

**Methods:** Euro-HDB is being conducted in eight European countries, including France and Italy. We developed and validated two self-reported questionnaires for the study: one for patients and one for their caregiver. The patient questionnaire includes the Huntington Self-Assessment Instrument (HSAI), a comprehensive specific tool that assesses clinical characteristics, QoL and healthcare resource utilization. Two generic QoL instruments (5-dimension EuroQol questionnaire and 36-item Short Form Health Survey) are also included to allow comparisons between HD and other disorders.

**Results:** The study is ongoing. To date, 201 patients and their caregivers have been enrolled in France and 124 in Italy. About half of patients are male (51% and 47%); average age is 54 and 56 years. Over half of patients have no occupational activity (57% and 80%). All levels of disease severity are represented. The main drivers of costs are loss of productivity and patient absence from work, which represent over half of total costs. In France, hospitalization and nursing home costs are the primary sources of medical costs, followed by practitioner visits and services. For severe patients, medical resource utilization diminishes while caregiver involvement increases significantly. This shift is greater in Italy than in France. In both countries, patient and caregiver QoL are affected greatly and to the same extent regardless of the instrument used. For patients, physical, mental and social QoL domains are all seriously affected; QoL scores were worse in Italy than France. Full details will be presented.

**Conclusion:** Euro-HDB is the first study to comprehensively assess the cost of illness of HD and shows that it is associated with significant costs.

## LB-28

### **A randomized, placebo-controlled clinical trial to assess the effects of rasagiline in patients with multiple system atrophy of the Parkinsonian subtype (MSA-P): Baseline characteristics and enrollment status**

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**Objective:** To report enrollment data on a protocol to assess the efficacy of rasagiline on symptom progression in multiple system atrophy of the parkinsonian subtype (MSA-P).

**Background:** MSA is a neurodegenerative disorder characterized by a combination of Parkinsonian, autonomic and cerebellar symptoms. Currently, treatment of MSA-P is limited to partially effective symptomatic therapies. Rasagiline is a MAO-B inhibitor indicated for the treatment of Parkinson's disease (PD). Preclinical studies have demonstrated neuroprotective properties of rasagiline, including attenuation of nigral, striatal and cerebellar Purkinje cell loss in a transgenic mouse MSA model. The ADAGIO delayed-start study showed that early treatment with rasagiline 1mg/d slowed the clinical progression of PD.

**Methods:** This is a 48 weeks, phase IIb, multi-centered (39 sites, 12 countries), randomized, double-blind study comparing 1mg of rasagiline to placebo (1:1) in 140 subjects with possible or probable MSA-P based on Gilman Consensus Criteria. The primary endpoint is change from baseline to study end in the Unified Multiple System Atrophy Rating Scale. Secondary assessments include: Clinical Global Impression of Improvement, Composite Autonomic Symptom Scale-Select, Beck Depression Inventory, MSA Quality of Life scale, Montreal Cognitive Assessment Scale, orthostatic vitals and a weekly falls diary. Safety and tolerability will be assessed through AEs, ECG, labs, and percent of subjects who discontinue.

An imaging sub study will use MRI-based indices of disease progression, including changes in putamenal diffusivity on serial DWI.

**Results:** As of end of April 2010, 80 patients have been screened, of which 63 were enrolled. One patient had an early termination. Current randomized population at baseline (mean±SD): age 64.7±8.2 years; total UMSARS Score (Parts I+2) 37.0±9.2 points; time from MSA diagnosis 0.8±0.8 years; time from first symptom of 3.6±2.4 years. Overall, 47% fulfill Consensus Criteria for possible MSA-P and 53% for probable MSA-P.

**Conclusion:** This will be one of the largest placebo-controlled trials conducted in MSA-P and the first to use both clinical and imaging outcomes to assess the efficacy and impact of rasagiline on disease progression in this understudied condition.

sustained vowel and monologue were obtained from digital hand-held sound level meter (Radio Shack, model 33-2055) placed 30 cm from the patient's mouths.

**Results:** All patients improved considerably in vocal sound pressure level during sustained vowel and monologue and there was no significant statistical difference between both groups. GI = Vowel sustained: pre: 70.2 db SPL and post: 84.3 db SPL – Monologue: pre: 65.4 dB SPL and post: 74.1 dB SPL. GII= Vowel sustained: pre: 69.1 dB SPL and post: 83.8 dB SPL – Monologue: pre: 65.6 dB SPL and post: 73.8 dB SPL.

**Conclusion:** This preliminary study suggests that LSVT LOUD can be applied in an adapted modality with no decrease of its therapeutic efficacy. According to the concept of the existence of a relationship of non-declarative memory and motor learning, vocal training distributed throughout a long period of time may be more effective in promoting learning of the ability to produce stronger vocal loudness and thus achieve more adequate vocal performance. These results indicate the persistence of the ability to acquire and retain motor learning in PD and support the notion that a distributed practice may reinforce the results of the treatment due to an increase in the time of exposure for the process of memory consolidation. Another important aspect favoring the distributed modality is a better adherence to treatment since a critical component to the traditional LSVT LOUD is the daily attendance to a rehabilitation center. This regimen may be troublesome for many patients especially those with difficulties with transportation and may lead to treatment interruption. Emphasis should be stressed on some conditions for the success of the method, mainly high motivation, preserved cognitive status and willing to maintain home training.

## LB-29

### **The Lee Silverman voice treatment method in the rehabilitation of hypophonia in Parkinson's disease: new perspective**

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*Hypophonia is a common symptom in Parkinson's disease (PD) and may sometimes impair verbal communication.*

**Objective:** to investigate the efficacy of an adapted version of Lee Silverman Voice Treatment (LSVT LOUD) for the treatment of hypophonia.

**Method:** Forty male patients aged 54 to 72 were randomly distributed in two groups with 20 patients each. All patients were in stages 2 or 3 (Hoehn & Yahr). Group I were treated with the traditional LSVT LOUD of massive practice (four sessions per week during four weeks); and group II were treated with an adapted LSVT LOUD of distributed practice (one session per week for 16 weeks). Pre and post measures of vocal intensity (SPL) of a