SG-1
Molecular genetics of multiple system atrophy: results from the Japan Multiple System Atrophy Research Consortium

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Objective: To elucidate the natural history and the molecular mechanisms of multiple system atrophy (MSA).

Background: The Japan Multiple System Atrophy Research Consortium (JAMSAC) was established in 2005 to elucidate the natural history and the molecular mechanisms of MSA. Although MSA has widely been considered as a nongenetic disorder, identification of multiplex MSA families suggests involvement of genetic components.

Methods: MSA patients fulfilling the criteria of Gilman were enrolled in the study. Additional criteria based on MRI findings are adjunctively employed. We employed UMSARS, parts of ICARS, parts of UPDRS and Barthel index for evaluation of clinical features and the severity of MSA. For molecular genetic studies, two approaches were employed: 1. Enrollment of six multiples MSA families for linkage analysis and whole-genome sequencing to identify causative genes, and 2. Exome sequencing and subsequent association studies in 437 MSA cases and 342 control subjects to investigate the association of rare coding variants with MSA.

Results: We evaluated the rating scales from 171 patients (93 men, and 78 women) whose mean age at onset was 58.5 years (range 40-79). About 70% of MSA patients were MSA-C in the Japanese population, whereas MSA-P shares only 30% of the patients. There is a significant correlation between the duration from onset and variable rating scales (P<0.0001). Parametric linkage analysis revealed that there was no single locus showing linkage compatible with autosomal recessive inheritance, indicating genetic heterogeneities in multiplex MSA families. Whole-genome sequencing of the proband in one of the multiplex families generated 187.5 Gb of short reads and 3,492,429 variants. In the exome-association studies, we identified 139,224 functional SNVs (nonsense, missense, or splice-site variants) with allele frequencies less than 5% in the controls. These variants are used for genome-wide association studies to identify disease-relevant functional SNVs.

Conclusions: MSA-C is more frequent in the Japanese population compared with those in European of North American populations. Identifications of causative genes involved in multiplex families and of susceptibility genes based on exome-association studies are expected to provide new insights.
into the molecular basis of MSA. To boost genetic research in MSA, further global collaborations with other MSA study groups are needed.

SG-2
The Movement Disorder Society Study Group on Multiple System Atrophy: Mission and goals

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Objective: The overall aim of the Movement Disorder Society (MDS) Study Group on Multiple System Atrophy (MoDiMSA-SG) is to provide a framework for global collaborative research on multiple system atrophy (MSA).

Background: In the last decades, clinical and preclinical MSA research has frequently been limited to single sites reflecting a lack of collaboration at an international level.

Methods: We will provide an administrative framework for global collaborative MSA research assigning short-term goals to focused working groups. The coordination of the study group will involve regular telephone conferences as well as study group meetings during the annual MDS congress. In addition, we will actively recruit leading academic centres into the network.

Results: We plan to develop a minimal data set, including disease-specific validated rating scales for harmonized data acquisition. Second, we intend to launch a global MSA patient registry. Third, we will provide standard operating procedures for the storage of biomaterial enabling us to subsequently launch studies with a focus on the discovery of diagnostic and surrogate (bio)markers, as well as determination of environmental and genetic underpinnings. Finally, we will develop consensus (best-practice) guidelines for diagnosis and management in MSA (based on the principles of evidence-based medicine). To this end, working groups have been initiated.

Conclusions: MoDiMSA-SG brings the leading MSA research centres together and, for the first time, provides a global platform for collaborative MSA research.

SG-3
Dynamics of red flags in multiple system atrophy: An analysis of the EMSA-SG natural history study cohort

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**Objective:** To prospectively study the presence and dynamics of clinical red flags in patients with MSA.

**Background:** MSA is an adult-onset atypical parkinsonian disorder characterized by early autonomic failure associated with either levodopa-refractory parkinsonism (MSA-P) or cerebellar ataxia (MSA-C). Certain clinical features such as early instability, rapid progression, Pisa syndrome, disproportionate antecollis, contractures of hands or feet, diurnal or nocturnal inspiratory stridor, inspiratory sighs, severe dysphonia or dysarthria, severe dysphagia, and emotional incontinence have been proposed as clinical pointers or red flags suggesting a diagnosis of MSA in subjects with parkinsonism. Finally, MSA red flags may be assigned to six categories (early instability, rapid progression, abnormal postures, bulbar dysfunction, respiratory dysfunction, emotional incontinence).

**Methods:** 141 patients with a clinical diagnosis of MSA were recruited in a natural history study conducted by EMSA-SG. Patients were followed up for two years with a complete neurological examination every six months. During follow-up, an extensive MSA red flags checklist was completed by the treating investigator.

**Results:** At baseline, all patients had bulbar symptoms. Early instability was present in 70.2%, a rapid progression was observed in 60.7%, abnormal postures occurred in 42.4%, respiratory dysfunction was noted in 45.0% and 26.9% experienced emotional incontinence. All of these red flags categories became more common during follow-up. The presence of abnormal postures (including the Pisa syndrome, disproportionate antecollis and contractures of hand or feet) separated MSA-P from MSA-C patients with a positive predictive value of 81.1%. Conversely, severe dysarthria was more common in MSA-C (p = 0.006). Out of 14 patients who converted from possible to probable MSA during follow-up, 71.4% could have been diagnosed at baseline already utilizing possible Gilman criteria plus the presence of at least two categories of red flags.

**Conclusions:** MSA red flags were frequently present at baseline visit and steadily increased during follow-up. The utilization of MSA red flags may be useful to support an early diagnosis of probable MSA.

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**SG-4**

**Progression of autonomic failure in multiple system atrophy: An analysis of the EMSA-SG Natural history study cohort**

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**Objective:** To prospectively study the progression of autonomic failure in patients with multiple system atrophy (MSA).
**Background:** MSA is a fatal neurodegenerative disorder that is characterised clinically by marked autonomic failure, parkinsonism and cerebellar ataxia in various combinations. Previous studies indicated rapid progressive autonomic failure affecting primarily orthostatic and urogenital domains.

**Methods:** 141 consecutive patients with a clinical diagnosis of MSA were recruited in a natural history study conducted by the European MSA study group (EMSA-SG). The consensus diagnostic criteria were applied retrospectively. The follow-up period was two years with a comprehensive neurological examination every six months. Autonomic failure was assessed by the Composite Autonomic Symptom Scale (COMPASS), the COMPASS Change Scale (COMPASS-CSS) and the autonomic subscore of the Unified MSA Rating Scale (UMSARS).

**Results:** At baseline - on average 5.5 years after symptom-onset – measurement of self-perceived impairment using COMPASS indicated the presence of severe autonomic failure. During follow-up autonomic failure steadily progressed, particularly in the urogenital domain as reflected by increasing COMPASS-CSS and UMSARS autonomic subscores. In addition, COMPASS-CSS OH subscore indicated that MSA patients also perceived a deterioration of OH symptoms during their disease course.

**Conclusions:** Severe autonomic failure was evident at baseline already and steadily worsened during follow-up, particularly in OH and urogenital domains. These observations are in line with previous studies showing a marked autonomic involvement in MSA patients. Rigorous symptomatic treatment of autonomic symptoms is required to alleviate MSA-associated disease burden.

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**SG-5**

**Randomized treatment trial of Rifampicin in MSA patients**

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**Objective:** To determine the efficacy of Rifampicin on multiple system atrophy (MSA) in a Phase III study.

**Background:** MSA is a rapidly progressive disorder characterized by autonomic failure with parkinsonism and/or cerebellar ataxia. Its hallmark is glial cytoplasmic inclusions consisting of aggregated α-synuclein. In a transgenic mouse model of MSA, Rifampicin inhibits formation and disaggregates α-synuclein fibrils and improves both behavioral and neuropathological changes.
Methods: We undertook a randomized, double-blind, placebo-controlled 12-month clinical safety/efficacy study of 100 patients with possible or probable MSA, 50% consigned to active drug (Rifampicin 300 mg BID), 50% to placebo (Riboflavin capsules BID). Subjects recruited from 10 US sites. Inclusion criteria include subjects of either gender; ages 30 to 80 years; <4 years from diagnosis; expected survival ≥3 years; MMSE >24. Primary outcome measure was rate of change from baseline to 12 months in total UMSARS I score (minus Q11). Interim analysis was planned after 30 subjects had completed 12 months of study.

Results: 100 subjects were randomized: 43% women and 57% men, mean age 61.7±9.2 (mean±std dev), age range 41.7 to 79.9 years, 48% possible MSA, 52% probable MSA. There were 3 serious adverse events, 2 on placebo and one on Rifampicin, none considered likely due to treatment. 9 subjects withdrew from study. Interim analysis of primary endpoint, the rate of change (slope) of UMSARS I, was 0.47±0.48 in placebo (N=15) and 0.62±0.85 in Rifampicin (N=15), P=0.76. This analysis was performed in all patients who had completed the protocol. The analysis of all evaluable subjects found a slope of 0.54±0.59 in placebo (N=50) vs. 0.53±0.72 (N=48) in Rifampicin, P=0.69. The DSMB recommended the study stop as futility criteria were met.

Conclusions: Rifampicin was well-tolerated. The study fulfilled statistical criteria for futility and is undergoing closure.

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SG-6
Multiple system atrophy: Prognostic indicators of survival

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Objective: To determine the early clinical features that predict survival in multiple system atrophy (MSA) based on autopsy cases.

Background: Although autonomic failure is a frequent early clinical feature of MSA its prognostic role is not fully established.

Methods: Retrospective survival analysis in 49 MSA cases (median age at onset, 56.1 years; 16 women) confirmed by autopsy at Mayo Clinic. Clinical records were reviewed for age at onset, sex, clinical phenotype, and early development of motor disability, autonomic symptoms and severe dysautonomia. When available, the 10-point composite autonomic severity score (CASS) derived from the autonomic reflex screen provided laboratory quantification of generalized autonomic failure and the thermoregulatory sweat test (TST) quantitated body surface anhidrosis.

Results: Phenotype was MSA-P in 65% and MSA-C in 35%. Onset was autonomic in 50%, parkinsonian in 30% and cerebellar in 20% with a median survival time of 8.6 (95% CI, 6.7-
10.2) years. On Kaplan-Meier analysis, survival time was shorter in patients with early laboratory evidence of generalized (CASS≥6) autonomic failure (7.0 [95% CI, 3.9-9.8] vs. 9.8 [95% CI, 4.6-13.8] years; P=0.036) and early requirement of bladder catheterization (7.3 [95% CI, 3.1-10.2] vs. 13.7 [95% CI, 8.5-14.9] years; P=0.003) compared to those without these clinical features. On Cox proportional analysis, prognostic indicators of shorter survival were older age at onset (HR, 1.04, 95% CI, 1.01-1.08; P=0.03), age-adjusted early requirement of bladder catheterization (HR, 7.9; 95% CI, 1.88-38.63, P=0.004) and age-adjusted early generalized (CASS≥6) autonomic failure (HR, 2.8; 95% CI, 1.01-9.26; P =0.047). Gender, phenotype, and early development of gait instability, aid-requiring ambulation, orthostatism, neurogenic bladder or significant anhidrosis (TST≥40%) were not indicators of shorter survival.

Conclusions: Our data suggests that early development of severe autonomic failure more than triples the risk of shorter survival in patients with MSA after adjusting for age.


SG-7
The setting up of a multi-specialty international Parkinson’s Non-Motor Research Group: The MDS Non Motor Study Group

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2. Research Unit and CIBERNED, Alzheimer Center Reina Sofia Foundation, ISCIII, Madrid, Spain

Background: Till 2004 there were:
1. no specific validated instruments either self- or health care professionals (HCP) completed for Parkinson’s disease (PD)
2. no validated global measure for non motor symptoms (NMS) burden in clinical trials. These issues have become increasingly relevant because it is now established that:
   a. PD is as much a non motor disorder as a motor disorder
   b. Non-dopaminergic systems are involved probably before motor symptoms emerge
   c. NMS are the key determinant of quality of life¹

Objectives: The PDNMG was formed from a multi-speciality group of international experts:
1. To develop and validate specific comprehensive (not piecemeal) tools for non motor assessment in clinic/ clinical trials
2. To use these instruments and address impact on quality of life in PD
3. Setting up and performing clinical studies of characterization of non motor endophenotypes
4. Develop research towards animal models of NMS of Parkinson’s
Methods: PDNMG was set up by KRC in 2004 with an international multispecialty group led by KRC and Pablo Martinez-Martin, supported and endorsed by Parkinson’s UK and adopted by MDS as a formal study group in 2013.

Results: Publication of NMSQuestionnaire (NMSQuest, 2006) and NMS scale (NMSS, 2007), the first validated tools for NMS self declaration and HCP completed tool. Now in worldwide use and recommended via MDS, NINDS, Parkinson’s UK.
1. Use of NMSS in international clinical trials as non motor outcomes (e.g. RECOVER, CONFIDENT, PANDA)
2. Global validation of NMSS (Europe, USA, Asia, South Africa, Japan)
3. Key NMS prevalence studies (Martinez-Martin et al, 2007)
4. Recent publication of NMSB staging addressing endophenotypes
5. Over 20 peer reviewed publications to date

Conclusion: The PDNMG has been highly successful in signposting the importance of NMS in PD at a time where focus was entirely on motor symptoms and NMS only existed in isolated symptoms category such as cognitive problems and depression. The adoption of PDNMG by MDS will lead to formalization of the role of PDNMG and cutting edge clinically relevant, real life research in the area of NMS of Parkinson’s.


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SG-8
A prospective observational study of dopamine agonist withdrawal syndrome in Parkinson's clinic: The EuroDaws study

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Objective: We have started a European multicentre prospective study (EuroDaws) addressing frequency of Dopamine Agonist Withdrawal Syndrome (DAWS) in people with Parkinson's disease (PwP) as retrospective case note surveys indicate a high prevalence of 14-18%.

Background: Recently, DAWS has been reported (symptoms similar to addictive drug
withdrawal) in PwP who decrease or stop their dopamine agonist (DA) treatment.

**Methods:** In the preliminary phase of this study, 16 patients (12 m/4 f, mean age 71.2 ± 10.8 yrs; PD duration 11.0 ± 5.3 yrs) were noted to have decreased/ stopped their dopamine agonists and the Non Motor Symptoms Questionnaire (which addresses core features of DAWS) was administered at clinical follow up at 1 month.

**Results:** Five out of 16 patients (31%) reported DAWS with symptoms of anxiety, sweating and depression after the withdrawal of Ropinirole, Pramipexole, and Cabergoline which were stopped owing to impulse control disorders or hallucinations.

**Conclusions:** In this first prospective evaluation of DAWS in the clinic, preliminary data indicates a high rate after discontinuation of a range of DAs. Continuation of EuroDaws would hopefully address the issue in a larger cohort of PwP across Europe.

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**SG-9**

**The EuroInf Study: A multi-centre European comparative study of apomorphine versus intrajejunal levodopa infusion in a real life cohort of Parkinson's patients**

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**Objective:** Intrajejunal levodopa infusion (IJL) and sub-cutaneous apomorphine infusion (Apo) are established treatments for advanced Parkinson's disease (PD).

**Background:** We initiated a novel case control study to compare motor and non motor effects of these therapies (EuroInf study) and to report multi-centre European data from a real life setting of intrajejunal levodopa (44 patients) and apomorphine infusion (43 patients) in matched cases with advanced PD

**Methods:** IJL: 44 advanced PD cases,( age: 62.66±9.09 yrs, mean duration of disease: 16.06±6.7yrs, median Hoehn &Yahr (H&Y) stage: 3), Apo: 43 cases,( age 62.25±10.60 yrs, disease duration 14.04±4.4 yrs, median HY: 3), were assessed with Unified PD Rating Scale (UPDRS) III and IV, Non Motor Symptoms Scale (NMSS) and Parkinson's disease questionnaire (PDQ-8) scores before initiation of therapy and after 6 months of therapy.

**Results:** Both groups were matched in terms of age, duration of PD, median HY stage, levodopa equivalence dose. Effect size of both interventions on UPDRS III&IV, and PDQ-8 scores were big (>0.8). Concerning the NMSS, differential effects were observed with sleep/fatigue and
gastroenterological/urinary symptoms showing greater response to IJLI, while mood was better improved with apomorphine with no worsening of hallucinations.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Change Baseline-Follow up</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Difference in Score</td>
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<tr>
<td></td>
<td>Duodopa</td>
</tr>
<tr>
<td>UPDRS- Part 3</td>
<td>-12.23±11.45</td>
</tr>
<tr>
<td>UPDRS- Part 4</td>
<td>-5.57±3.53</td>
</tr>
<tr>
<td>NMSS</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>-1.5±3.14</td>
</tr>
<tr>
<td>Sleep/Fatigue</td>
<td>-8.05±10.87</td>
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<tr>
<td>Mood/Apathy</td>
<td>-3.91±12.10</td>
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<tr>
<td>Perceptual/Hallucinations</td>
<td>-1.59±4.27</td>
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<tr>
<td>Attention/Memory</td>
<td>-2.61±6.86</td>
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<tr>
<td>Gastrointestinal</td>
<td>-5.23±6.02</td>
</tr>
<tr>
<td>Urinary</td>
<td>-6.02±8.98</td>
</tr>
<tr>
<td>Sexual functioning</td>
<td>-3.41±7.59</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>-4.98±8.66</td>
</tr>
<tr>
<td>Total score</td>
<td>-37.30±36.13</td>
</tr>
<tr>
<td>PDQ-8 Summary index</td>
<td>-16.62±20.29</td>
</tr>
</tbody>
</table>

**Conclusions:** To our knowledge this is the first case control comparative multicentre study comparing IJLI and Apo in advanced PD. We report a robust improvement in motor and quality of life scores with a large effect size with both therapies while a differential effect on NMSS is noted. Specifically of note is that apomorphine infusion improved mood dysfunction and did not worsen hallucinations.

**Previously Presented:** This is a follow up dataset analysis to the first EuroInf data presented at the MDS congress in Dublin, 2012. The NMSS analysis is novel.
Objective: A multicentre real observational study of tolerability (at least 6 months use) and impulse control disorders (ICD) if dopamine agonists (DA) with a focus on extended release formulations: rotigotine skin patch (RTG), ropinirole (ROP IR/XL) and pramipexole (PPX IR/PR) across several European centres.

Background: Tolerability/retention rate and occurrence of impulse control disorder on prolonged release DA therapy are unknown in real life clinical populations of people with Parkinson's (PwP).

Methods: Prospective case note/interview based survey of patients across all stages and age groups initiated on above DA.

Results: 425 cases were included for analysis (median age 69 yrs, range: 37-90; median duration of disease 6 yrs, range: 0-37), 31.5% of which were ≥75 yrs (old PD).

1. Tolerability rates were high with no significant differences between the groups in young or old PD.

<table>
<thead>
<tr>
<th>Tolerability rates for extended release DA's</th>
<th>PPX PR</th>
<th>ROP XL</th>
<th>RTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>% on DA</td>
<td>17.9</td>
<td>39.1</td>
<td>8.4</td>
</tr>
<tr>
<td>Mean dose (mg)</td>
<td>2.8</td>
<td>12.4</td>
<td>8.4</td>
</tr>
<tr>
<td>Tolerability (&lt;75 yrs)</td>
<td>93.5%</td>
<td>93.1%</td>
<td>86.8%</td>
</tr>
<tr>
<td>Tolerability (≥75 yrs)</td>
<td>95.2%</td>
<td>90.7%</td>
<td>79.2%</td>
</tr>
</tbody>
</table>

2. ICD rates were judged by questionnaires and interviews. Rate of ICD with RTG was significantly lower than with any other extended or immediate release DA except for PPX PR. Rate of ICD for PPX PR was significantly lower than for PPX IR.
59.6% of the reported ICD cases have been exposed to shorter acting agonists previously and discontinuation rates with ICD were low.

Conclusions: Tolerability rate of all prolonged release DAs are high including older (≥75yrs) PwP who are often excluded from DA use. For the first time a relatively low rate of ICD with use of prolonged release DA is reported, especially for RTG.


SG-11
Criteria for mild cognitive impairment in Parkinson's disease: Applicability and validity

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Objective: on behalf of the MDS Study group “Validation of Mild Cognitive Impairment in Parkinson Disease”.

Background: Dementia in Parkinson's disease (PD) is a serious health issue and a major concern for many patients. Mild cognitive impairment (MCI) is considered a transitional stage between normal cognitive functioning and dementia. In 2012 diagnostic criteria for MCI in PD (PD-MCI) were proposed by the Movement Disorder Society (MDS). The next step is to validate these criteria and to investigate whether they can be applied to obtain a uniform and valid definition of PD-MCI. The definition of this clinical entity is important both for the early identification and management of those at risk for the development of dementia and for future research on etiology, disease course, and disease modifying or causative treatment.
**Methods:** The MDS Study group “Validation of Mild Cognitive Impairment in Parkinson Disease” is an international consortium that will pool existing cross-sectional and longitudinal data of more than 3000 PD patients and more than 1000 controls. These data will be analyzed to determine the applicability of the PD-MCI criteria.

**Results:** Therefore, the presence of PD-MCI will be scored using the levels I and II of the MDS PD-MCI criteria. For validity we will determine whether PD-MCI predicts further cognitive decline as well. Moreover, since currently there is no consensus on the details (e.g. precise tests and cut off scores) that would determine PD-MCI, we will study which method (e.g. cut off scores, cognitive profile) best predicts conversion to dementia.

**Conclusions:** The criteria will be discussed and preliminary results of the study concerning the applicability and validity will be presented.

**Previously Presented:** Presented at 9th international congress on mental dysfunction and other non-motor features in Parkinson's disease and related disorders, Seoul, April 18-21 2013.

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**SG-12**

**The Movement Disorders Society-Endorsed PSP Study Group**

**Authors:** Günter U. Höglinger*, Kailash Bhatia, Adam L. Boxer, Dennis Dickson, Lawrence Golbe, Keith A. Josephs, Irene Litvan, Brit Mollenhauer, Huw R. Morris, Ulrich Müller, Wolfgang Oertel, Maria Stamelou, Gerard Schellenberg, John C van Swieten, Jennifer Whitwell, David Williams, for the MDS PSP Study Group

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**Objectives:**

1st To provide an evidence-based revision of the diagnostic criteria for PSP.

2nd To promote cooperative clinical research into PSP.

3rd To promote clinical trials aiming to cure PSP.

**Background:** PSP is an adult-onset neurodegenerative disorder with cerebral tau pathology leading to an akinetic-rigid syndrome with oculomotor dysfunction, postural instability, frontal lobe and bulbar dysfunction. The diagnostic gold standard is pathological diagnosis (Hauw et al., Neurology. 1994;44:2015-9). The clinical diagnosis remains a challenge. The National Institute of Neurological Disorders and Stroke and the Society for PSP (NINDS-SPSP) criteria have been proposed for the clinical diagnosis (Litvan et al., Neurology 1996; 46:922-930). Validation of these criteria in independent sets of patients demonstrated a high positive predictive value, albeit low sensitivity particularly during the early course of the disease (Osaki et al., Mov Disord. 2004;19:181–189; Respondek et al., Mov Disord. 2013 doi: 10.1002/mds.25327). Particularly, the NINDS-SPSP criteria do not allow the recognition of the recently described variable phenotypic PSP presentations.
No curative treatment options are available at present. Clinical research into this rare disorder is limited in power due to its fragmentation.

**Aims:** We aim to improve the diagnostic criteria for PSP, to create clinical research networks, and to initiate measures facilitating therapeutic clinical trials in PSP.

**Methods:** We initiated the establishment of international S3-guidelines for the clinical diagnosis of PSP based on published evidence. Secondly, we aim to characterize the earliest clinical signs and symptoms occurring over the disease course of pathologically confirmed PSP. Thirdly, we are undertaking studies to facilitate clinical trials in PSP, including an improvement of early diagnosis for early recruitment and protocol development and refinement for clinical trials.

**Results:** Working groups have been created for ‘clinical course’, ‘neuropsychology’, ‘oculomotor dysfunction’, ‘MR imaging’, ‘nuclear medicine’, ‘genetics’, ‘biomarker’. Key questions and search terms have been defined for a systematic literature research. A retrospective analysis of original clinico-pathological datasets has been initiated. Clinical research networks have been initiated in the US, UK and Germany.

**Conclusions:** The MDS PSP Study Group has set up studies to improve early diagnosis and treatment of PSP.

**Deep brain stimulation of the pedunculopontine area in Parkinson’s disease and progressive supranuclear palsy (PPN DBS Working Group)**

Elena Moro\(^1,2\), Joachim Krauss\(^3\), Michael S. Okun\(^4\), Tipu Aziz\(^5\), Andres M Lozano\(^6\), Bastiaan R. Bloem\(^7\), Bettina Debû\(^2\), on behalf of the MDS PPN DBS Working Group

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\(^4\) Division of Neurology, Gainesville, Fl, USA
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**Background:** Postural instability and gait difficulties (PIGD) are severely debilitating symptoms that inevitably affect almost all patients with advanced Parkinson’s disease (PD). These symptoms emerge much earlier in the disease for progressive supranuclear palsy (PSP). These PIGD symptoms generally respond suboptimally to medical treatment and can be alleviated temporarily prior to axial disease progression by subthalamic nucleus and globus pallidus internus deep brain stimulation (DBS). Pedunculopontine nucleus area (PPNa) DBS has recently been tested as an alternative DBS target site, however the initial results were mixed. These results have raised a number of issues regarding patient selection, target localization, optimal parameter settings and outcome measures.
**Objective:** It will be important to clarify the benefits and limitations using the current literature and also the worldwide experience implanting PPNa DBS.

**Methods:** The MDS PPNa DBS working group consists of neurologists, neurosurgeons, neurophysiologists, gait specialists, bioengineers, and neuropsychologists with experience in PPN DBS. The main objective is to develop an instrument (core assessment protocol, CAP) that will provide movement disorder centers implanting DBS devices with a common set of pre- and post selection criteria and outcome measurements for both PD and PSP patients selected for PPNa DBS. Additionally, the group aims to provide recommendations for intra-operative targeting and post-operative management.

**Results and Conclusions:** Following a systematic and thorough review of available evidence-based studies, conclusions will be drawn and recommendations made for patient selection (inclusion/exclusion criteria), management and evaluation (short and long term), as well recommendations for surgery procedures and targeting (intra-operative recording and stimulation, appropriate imaging, adequate surgical hardware).