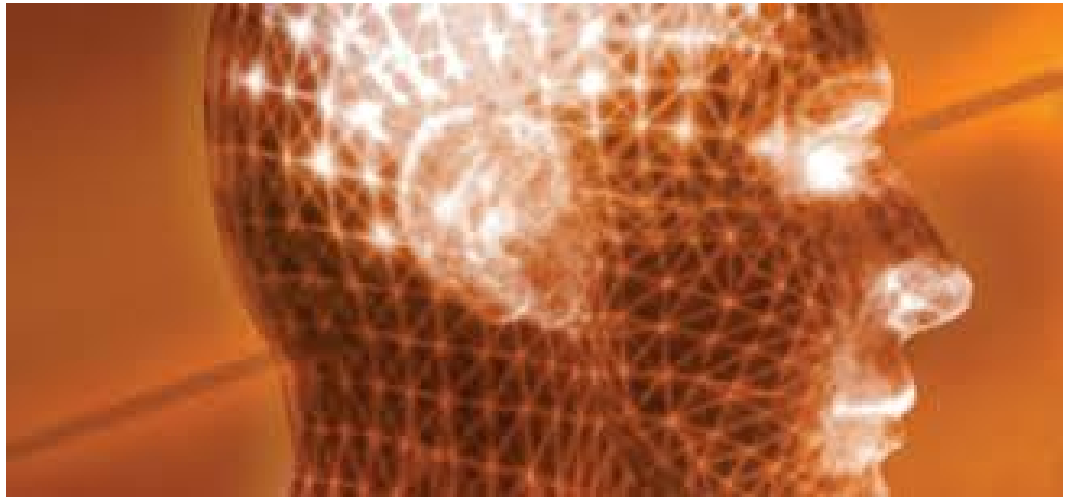
Day 2

Plenary:
Non motor manifestations of Parkinson‘s disease



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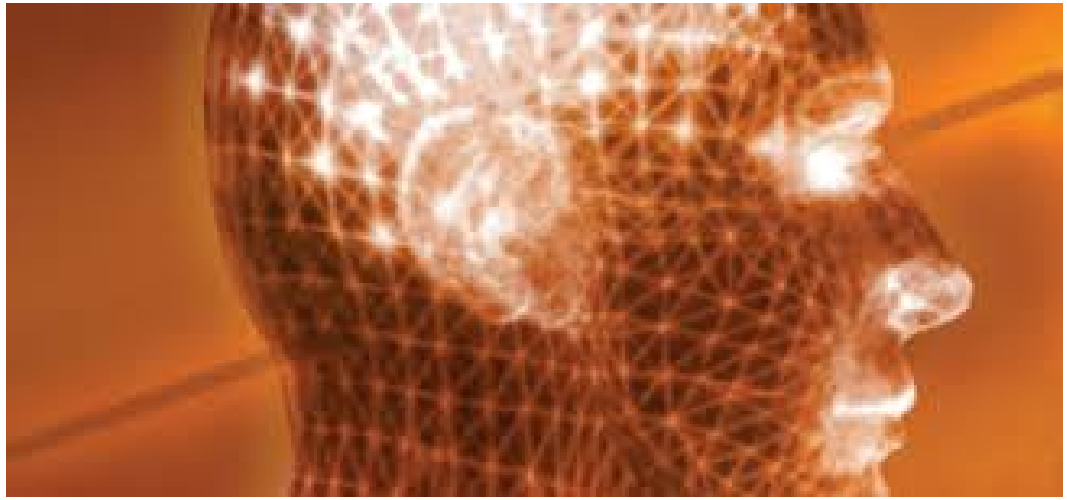
Plenary Day 2 – Non-motor manifestations of PD

Lecture 3

Antonio Strafella (Canada)



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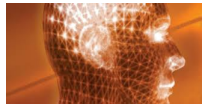
Contribution of functional imaging to the understanding of non-motor manifestations of PD

Many similarities to the lecture within Science and advocacy of Day 0*



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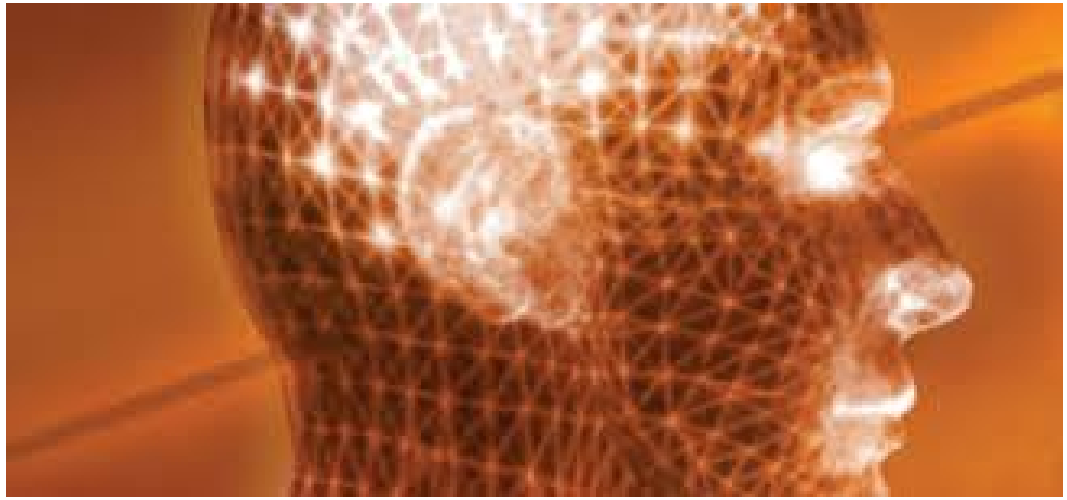
Contribution of Functional Neuro Imaging in Non Motor Manifestations

- Increase reporting of cognitive dysfunction and impulse control disorders
- Cause significant distress for patient and family
- To date mechanisms causing abnormal behaviour is poorly understood

Non-motor manifestations of PD

Ray Chaudhuri

Plenary Session



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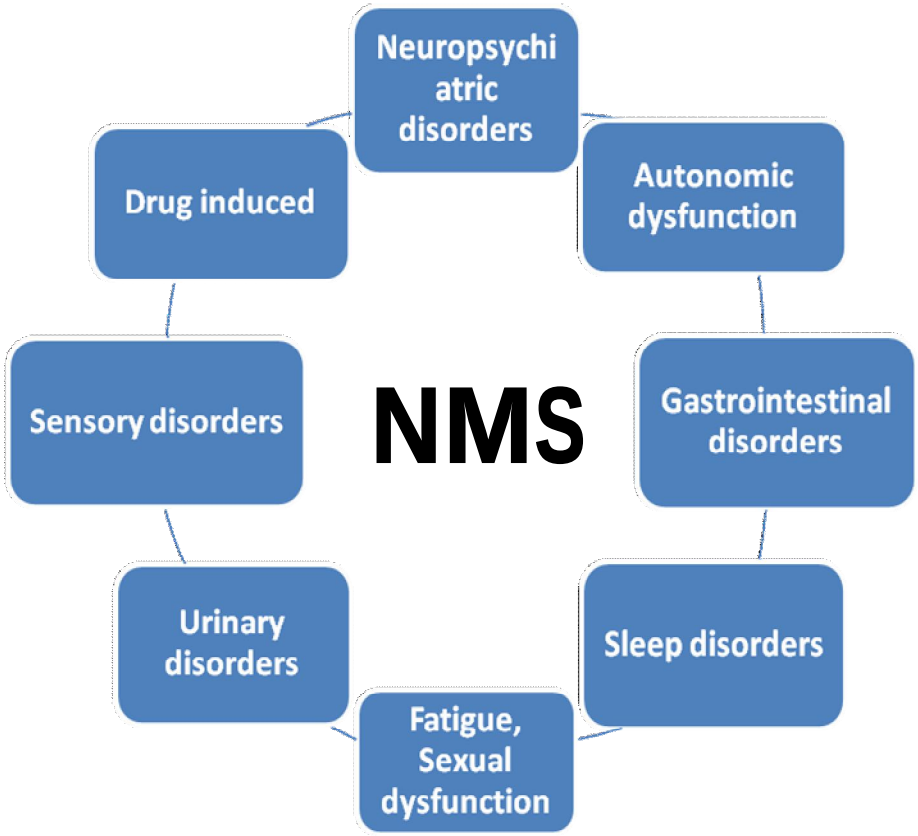
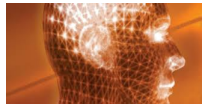
Non-motor symptons in Parkinson‘s



Report on 3rd World Parkinson Congress by Mo Morgan, Simon Wilkinson, Werner Remmele



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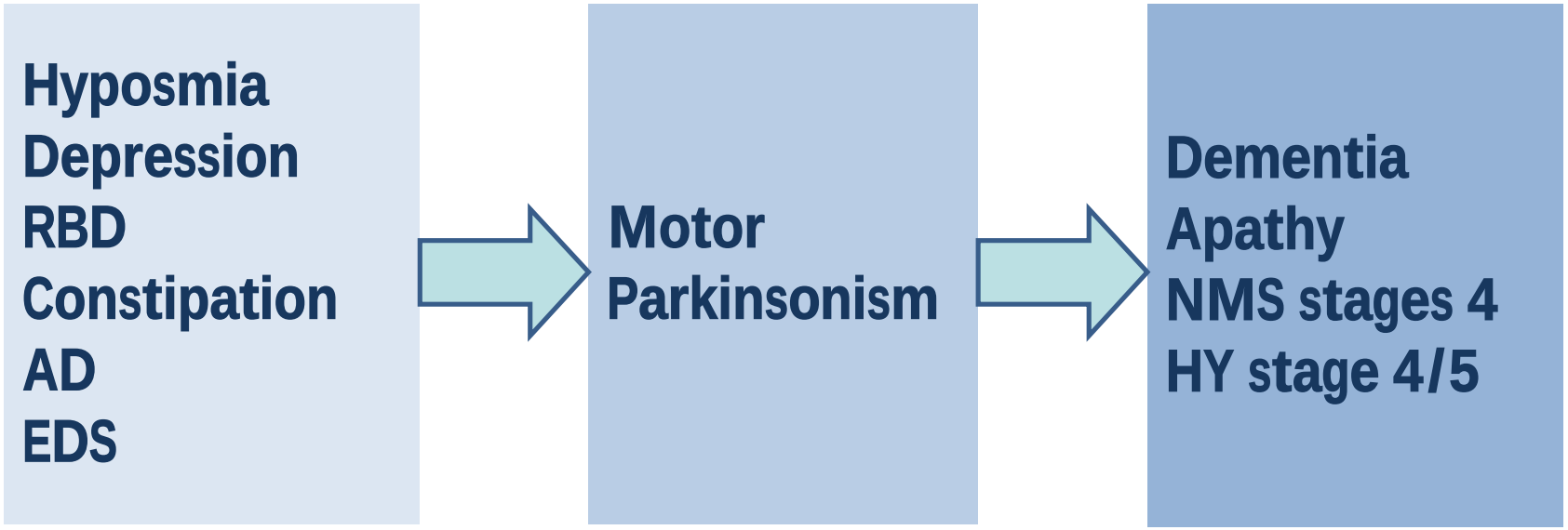
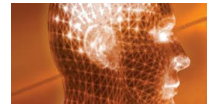
Non-motor symptons in Parkinson‘s





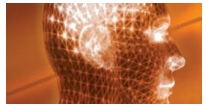
Non-motor symptoms - tools

The first validated NMS questionnaire:

NMSQuest
Empowering patients across the world to declare NMS to HCP
Worldwide use
Chaudhuri et al 2006
http://www.parkinsons.org.uk/content/non-motor-symptoms-questionnaire

The first validated NMS scale (NMSS)

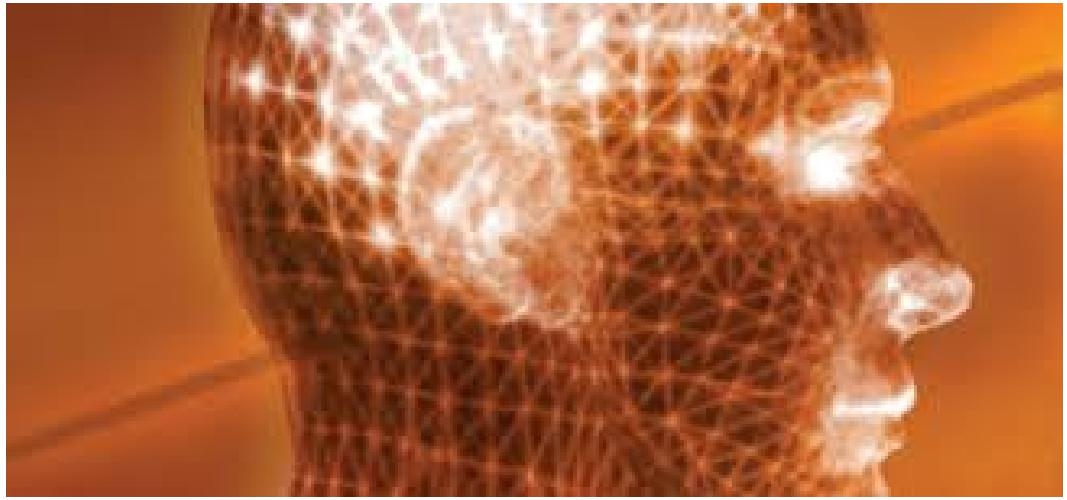
Worldwide use for clinical trials and epidemiology
Chaudhuri et al 2007/2009



Dementia and psychiatric manifestations in PD

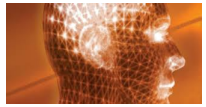
David Burn

Plenary Session



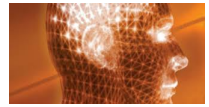
Non Motor Symptoms

	Patients
Depression	35%
Anxiety	40%
Apathy	35%
Psychosis (Hallucinations)	Up to 60%
Psychosis (Delutions)	5 – 10%
Delirium	
Dementia	
Mild cognitive impairment	40%



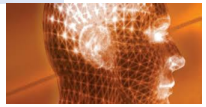
Depression

- Often co-exists with anxiety
- May predate onset of motor symptoms
- Heterogeneous
- May associate with motor phenotype
- Aetiology
- Psychosocial
- Neurobiological
- Anatomical
- neurochemical



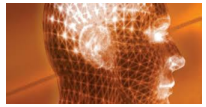
Psychosis - Treatment

- Stopping drugs is often the first step
- Review current medication
  - E.g. stop anticholinergics, selegiline, amantadine (gradual)
- Treatment not always required
- Non-pharmacological
  - Environmental considerations
- Pharmacological
  - Avoid ‚typical' neuroleptics
  - Cholinesterase inhibitor
  - ...



PDD Profile

- Executive dysfunction and ‚bradyphrenia' often dominant
  - Lack of mental flexibility, inability to multitask, complete simple tasks, mental slowness
- Memory and visuospatial deficits
- Fluctuating attention
  - Variability in performance
- High neuropsychiatric burden
  - Depression, apathy, visual hallucination, sleep-wake disorders
- Postural instability and falls



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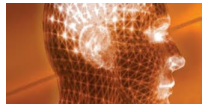
What do PD nurse specialists spend their time on?

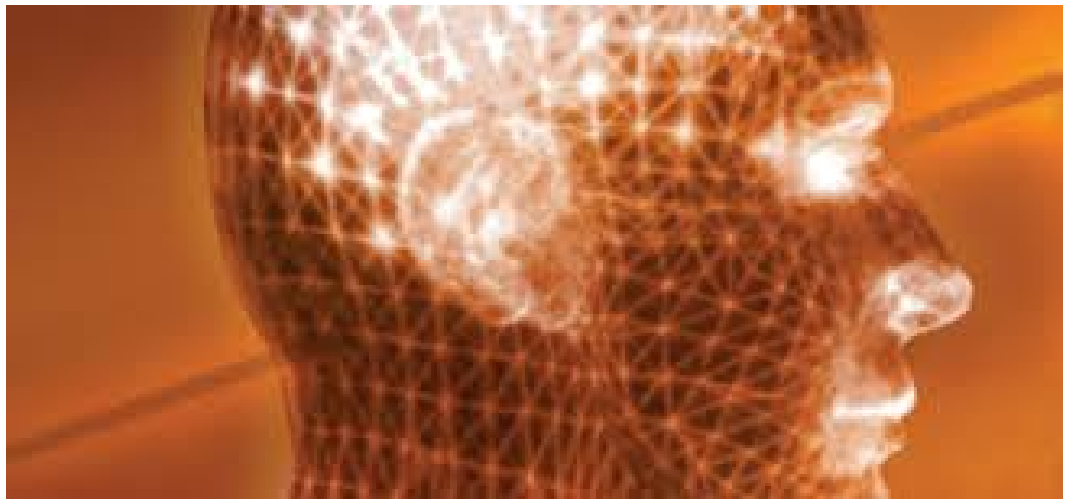
- Neuropsychiatric symptoms
  - May predate motor features
  - Increase as cognitive decline progresses
  - Are often underdiagnosed
- Cognitive impairment
  - May affect 35 – 40% people at time of diagnosis
  - Full blown dementia in up to 80% (!)
  - Largest area of unmet therapeutic need in PD



Non Motor Symptoms & PD

Meet the experts
Round Table

Host: Ronald Pfeiffer



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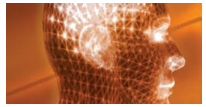
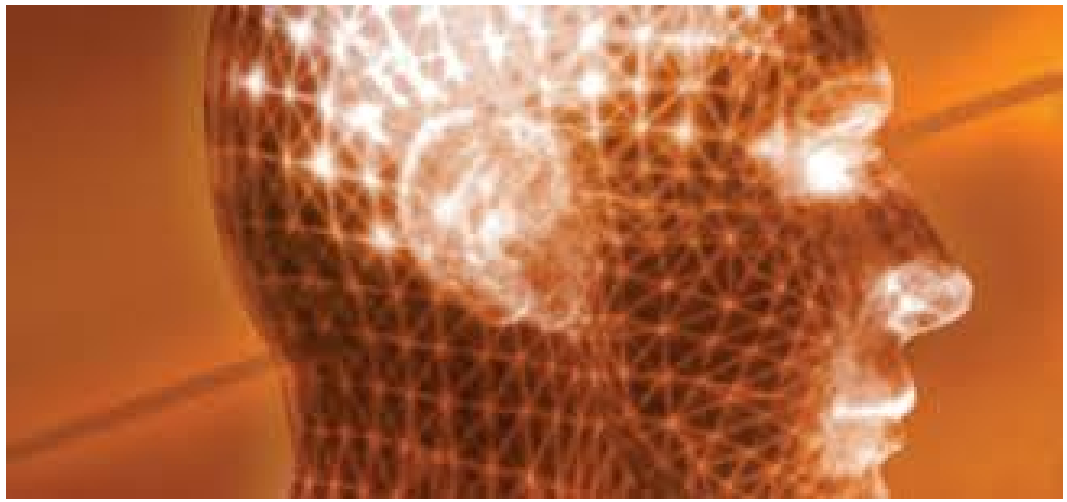
Round Table Discussion on NMS

- Vision and double vision
- Difficulties to focus or bring eyes in
- Impaired contrast
- Extreme crying
- Saliva problems
- Bladder problems
- Running eyes and running nose
- Peristalsis problems
- ‚Phone' feeling



Poster

CAN DANCE FOR PARKINSON'S IMPROVE COGNITIVE FUNCTIONING IN PWP?



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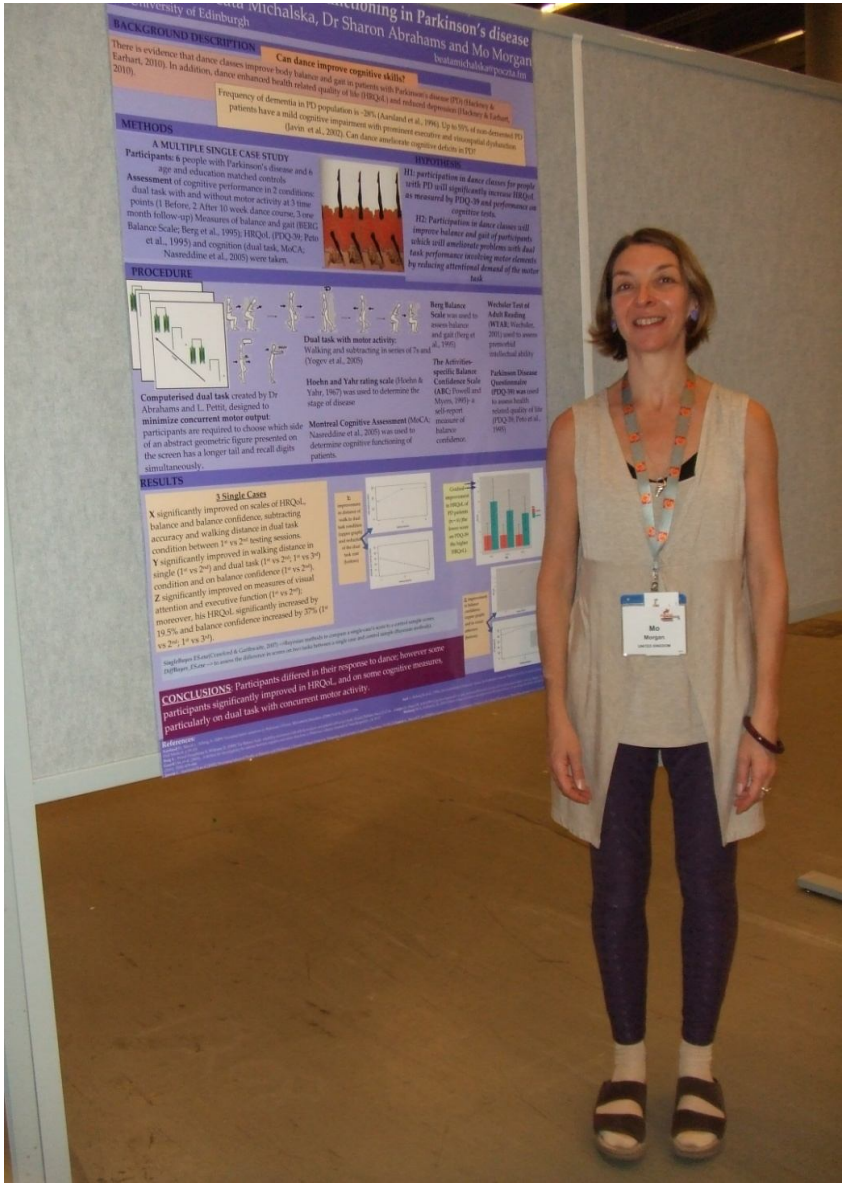

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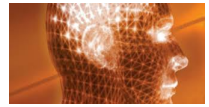
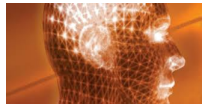


Parkinson‘s Disease Clinical Trials

- No drug has yet been established to have a neuroprotective effect in PD
- Some clinical trials have shown positive results from neuroprotective agents
- Results could not be determined whether benefit was due to Pharmacologic or regulatory effects of the study agent



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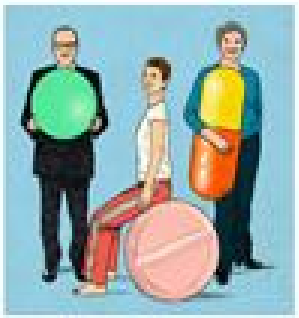
Parkinson‘s Disease Clinical Trials

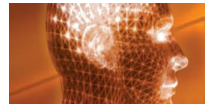


Results are an average for a diverse group.

Clinical Trials results are the strongest Anchor to the TRUTH – is there or is there NOT an effect of the intervention we are dealing with?

A responder in a trial is an abstraction.

To translate the abstraction to a real patient is the challenge of Personalized Medicine.



What do we measure in PD Clinical trials and how do we try to translate it back to the patient?

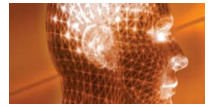
- Objective measures
- Rating Scales

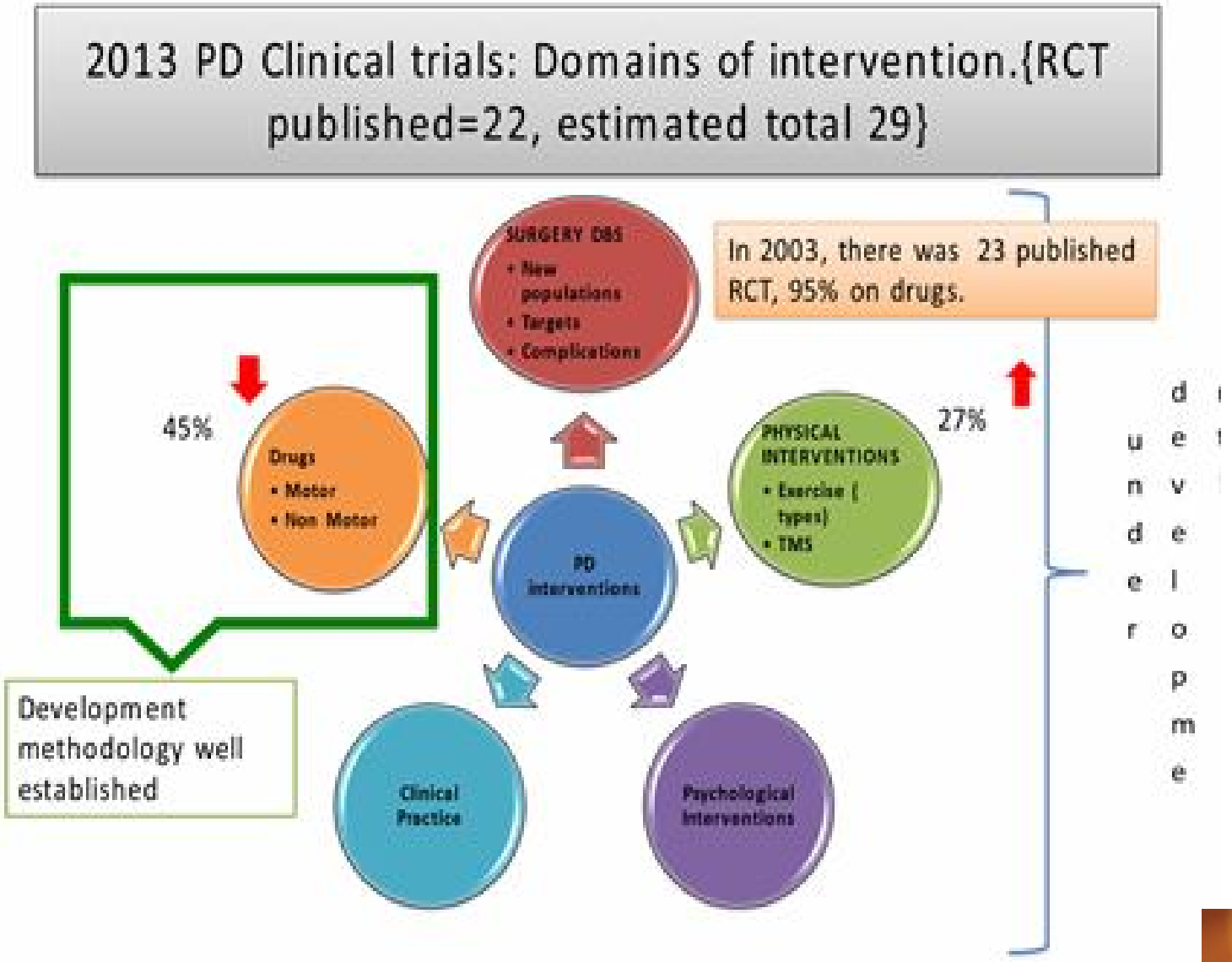
- Time diff: speed
- Movement: quantity

- Scores
- Subscores

Points

1. Face and construct validity of measurement tools
2. Clinical relevance of Effect sizes estimated in Clinical trials




2013 PD Clinical trials: Domains of intervention.{RCT published=22, estimated total 29}
SURGERY DBS
• New populations
• Targets
• Complications
In 2003, there was 23 published RCT, 95% on drugs.
45%
Drugs
• Motor
• Non Motor
27%
PHYSICAL INTERVENTIONS
• Exercise (types)
• TMS
PD interventions
Clinical Practice
Psychological Interventions
Development methodology well established
under development

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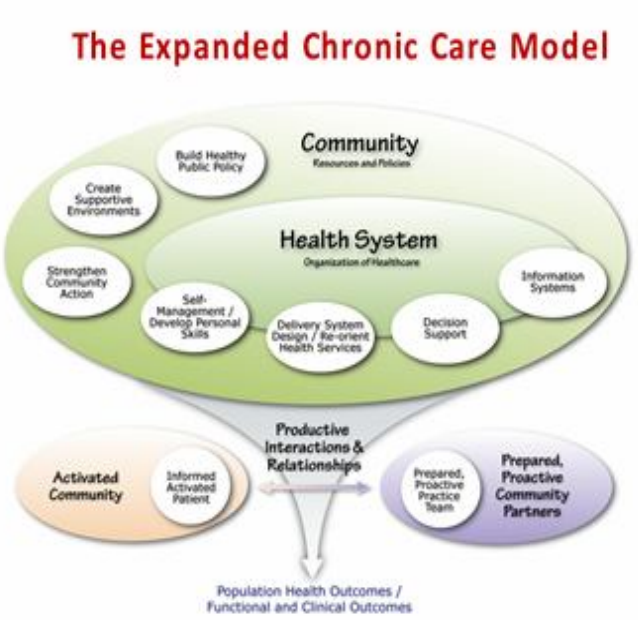
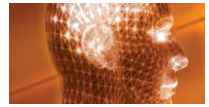
Ways for people with PD to become empowered

- Self Efficacy-AGAIN!
- Confidence to deal with medical management
- Health care provider to increase patient skill and confidence in managing their health





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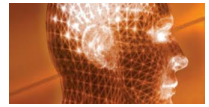
Self Efficacy – AGAIN!

"One's belief that one can perform a specific behaviour or task in the future"

Dr Albert Bandura



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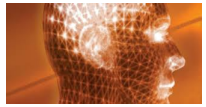
Meta-analysis of the Stanford CDSMP conducted by US Centers of Disease Control

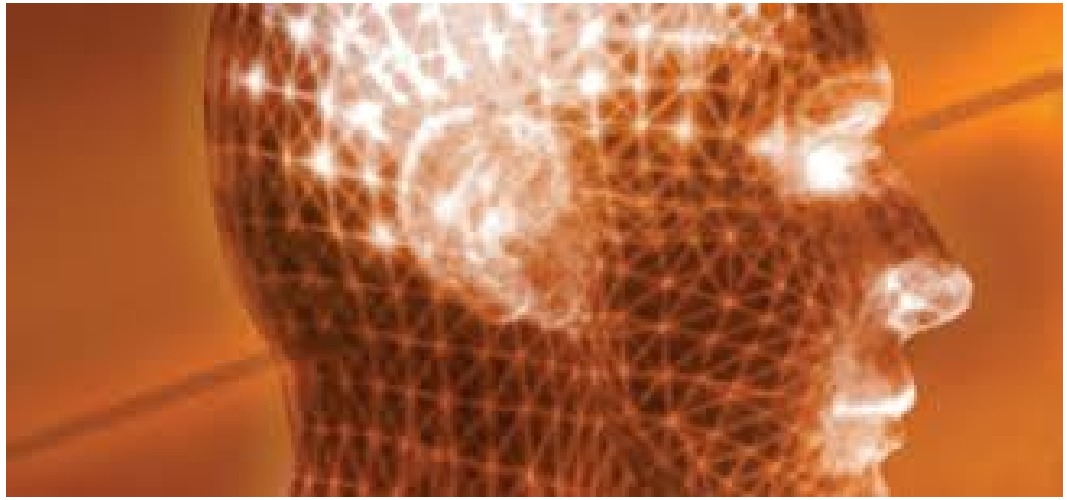
- Chronic Disease Self-Management Program
- 23 studies
- Between 1999 and 2009
- 5 countries
- 3000 subjects in RCT's
- 5,688 subjects in longitudinal studies
- Studied impacts at 6 and 12 months



Benefits and Risks of Genetic Testing

Workshop

Presenter:
Oksana Suchowersky



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Workshop: Benefits and risks of genetic testing

Clinical vs Research genetic testing

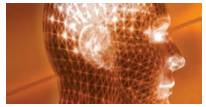
Decision factors:

- Patient
- Family and partner
- Outside, e.g. insurance

Conflicts

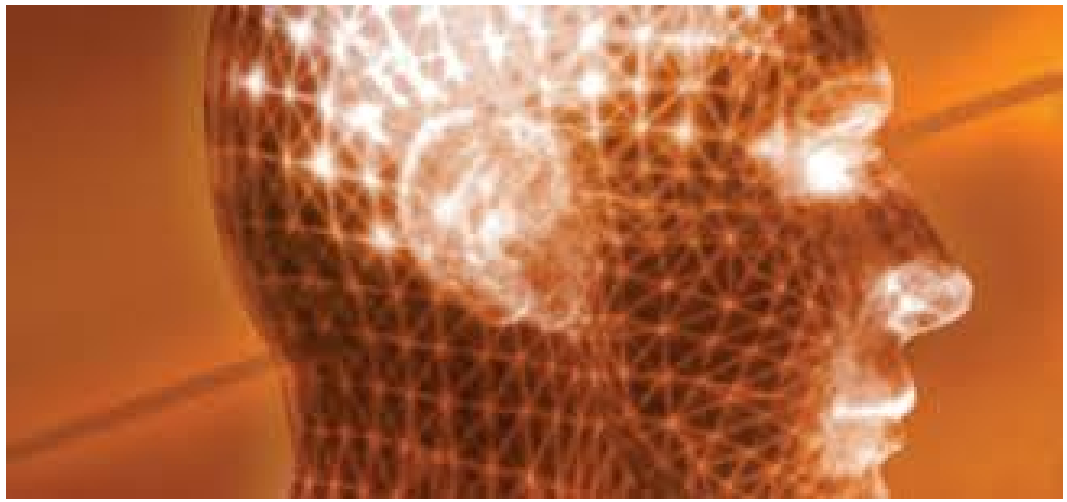
- Unexpected results

Need for counseling



Workshop
Dance for Parkinson‘s: Why and How?

Gammon Earhart,
David Leventhal,
Maura Fisher,
Diane Cote,
Joanabbey Sack

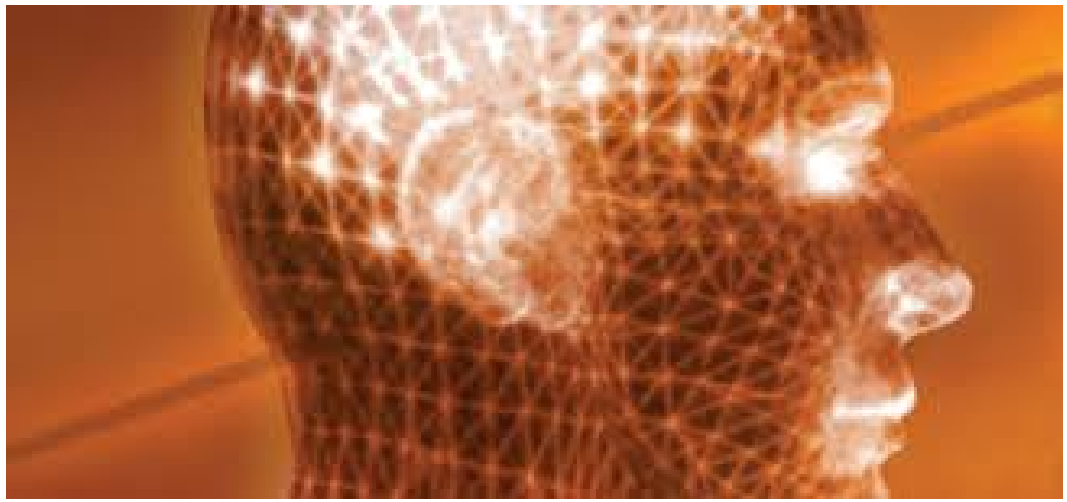


Dance for Parkinson‘s©

David Leventhal (DL) of the Mark Morris **Dance** Group (MMDG)

Accompanied live by **William Wade,** musical director at MMDG

Also featuring **Claudine Naganuma** (Dance for Parkinson‘s, California) and **Mo Morgan** (me! Dance for People with Parkinson‘s, Edinburgh)*



Acknowledgements - David Leventhal, Olie Westheimer, Maria Portland Kelly, and every person who dances with Parkinson‘s anywhere in the world

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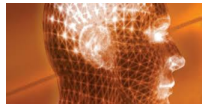
What is **Dance for Parkinson‘s©**?

- **Dance** for Parkinson‘s©, is a dance/movement class devised specifically for people with Parkinson‘s led by professionally trained dancers that partners, spouses, care-givers and friends can participate in too

- the original monthly class started 12 years ago by DL and John Heginbotham (JH) of the MMDG* in conjunction with Olie Westheimer , Executive Director of the Brooklyn Parkinson‘s Group (BPG)



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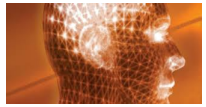
WPC 2010 to WPC 2013

- WPC Glasgow 2010, Olie presented a session which included a video of the Edinburgh Dance for Parkinson's group performing at Dancebase during Fringe Festival 2010 .
- 5 UK practitioners led 2 sessions of Dance for Parkinson's with 30 people in the small Renewal Room
- UK Network was born.
- over 100 communities now throughout the world - USA, Australia, Canada, Germany, Italy, India, Israel and UK, practicing Dance for Parkinson's*
- numerous training days as a network*a led to inaugural UK introductory weekend *b at Roehampton College, London University, June 2013*c
- over 40 participants attended from UK, Europe and American guests*d
- now over 30 practitioners throughout the UK and growing*e ....

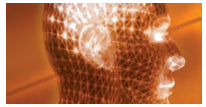


Montreal 2013

- the overwhelming response from participants in Glasgow resulted in a vastly bigger room being devoted to movement/creative activities in Montreal accommodating lots more people

- Renewal Room activities ranged from yoga, tai chi, clay therapy, Pam Quinn‘s Movement Lab‘, laughter workshops to singing, voice therapy and everything in between!

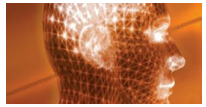
- ... well over 60 people danced and moved together in the Dance for Parkinson‘s session....*



here we are at the end of class…..

Outcome + evidence?!

- Many people were dancing in this way for the first time, others in the session had particpated in the very first class in Brooklyn and are still dancing – more of that later.....
- Everyone had an absolute ball enjoying what they could do – all classes focus on this enjoyment of being in the now and enjoying what **can** be done*a
- Having managed to persuade a YP UK volunteer to come to the Dance for Parkinson's class*b. She expressed how she felt she wouldn't be ´good enough' and almost didn't come... She is now set to join up with a current practitioner to co-teach with her!
- She was so inspired and is so inspiring*c .....



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Caught in the act! ....the joy of dance!

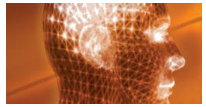
PARKINSON'S UK CHANGE ATTITUDES. FIND A CURE. JOIN US.

Acknowledgements – in no particular order...

Only to say an enormous thank you to the branch for having the courage to back our class. We are the fifth longest running class originating here in the UK and still the only one in Scotland – hopefully this will change within the coming years....

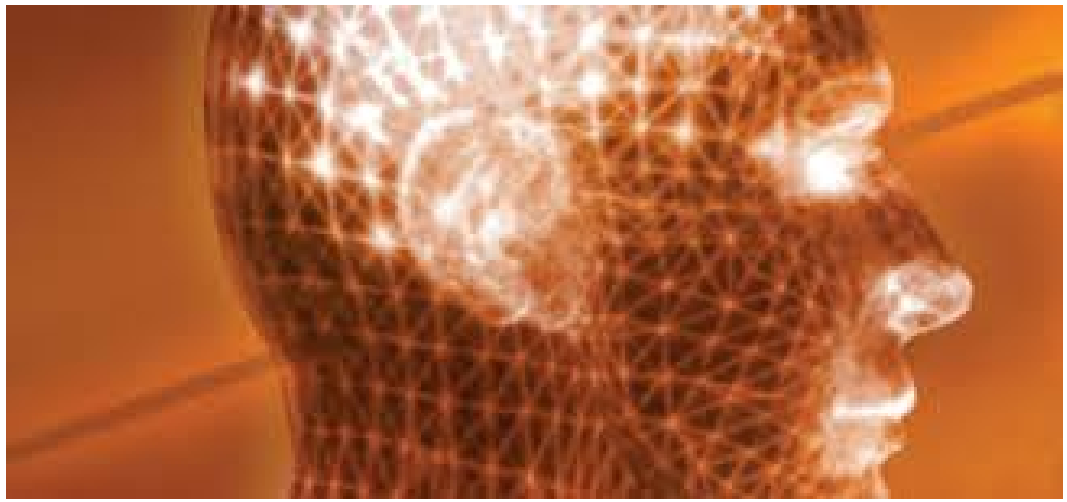
To thank DL for dragging me in to the centre of a very large circle of people at the beginning of the session (to represent the UK) and ´lead‘ along with Claudia from California and himself.

Olie and Maria and all at Brooklyn Parkinson‘s Group, Pam Quinn and all other Dance for Parkinson‘s practitioners and participants at WPC who welcomed me so warmly



Other!

More socialising....*



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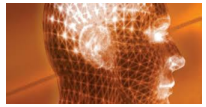
The Westin Hotel

Meeting other practitioners!

Independent practitioners in Toronto*

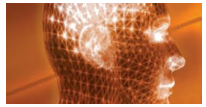
Research project*

National Ballet School of Canada, Toronto*



Poster Tour

- Several hundred posters on exhibition
- Covered scientific, health, quality of life, education, care delivery, dance (Mo)
- Several stood out, especially educating first line responders
- Startling demonstration given by exhibitor of DB Stimulation on/off effects



Training Police About Parkinson's

Stop and Assist

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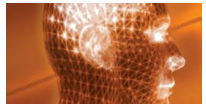
Stop and Assist is a program for police which increases their understanding of Parkinson's disease. To the untrained, people with Parkinson's can appear threatening, require forceful intervention or be in need of emergency medical services; however, this is seldom the case. Through this presentation, the police become aware of how the disease develops and how to assist.

Objectives for People with Parkinson's

To ensure people living with Parkinson's receive proper treatment by police.
To encourage people to participate in public with self esteem and confidence.
To maintain physical and social access into the everyday world.

Objectives for Police Personnel

To recognize people with Parkinson s disease.
To interpret behaviours correctly and respond appropriately.
To ensure the safety of all people.



PARKINSON'S UK CHANGE ATTITUDES. FIND A CURE. JOIN US.

Safety and Efficacy Study of ADS-5102 in Levodopa-Induced Dyskinesia (EASED Study)

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Background

- ADS-5102 is a proprietary long-acting capsule formulation of amantadine HCl in development for the treatment of levodopa-induced dyskinesia (LID).
- Administered once-nightly at bedtime, ADS-5102 provides a slow initial increase in amantadine plasma concentration, resulting in high concentration during daytime hours when LID can be troublesome and low concentration overnight.
- The present study was designed to evaluate the safety and efficacy of three dose levels of ADS-5102 oral capsules dosed once-nightly for the treatment of LID in Parkinson's disease (PD) patients.

Objectives

- Investigate the safety and efficacy of 3 dose levels of once-nightly administration of amantadine HCl extended release (ADS-5102) for the treatment of LID in PD.

Methods

- Randomized, double-blind, placebo-controlled, parallel-group study conducted at 31 U.S. clinical trial sites (NCT 01397422).
- PD patients with troublesome LID were randomized to placebo or one of three dose levels of ADS-5102 (260 mg, 340 mg, 420 mg), dosed once-nightly for 8 weeks.
- The primary outcome measure was the change from baseline to Week 8 in the Unified Dyskinesia Rating Scale (UDysRS) total score.
- Secondary outcome measures included the change from baseline in 24-hour PD patient diaries and the MDS-Unified Parkinson's Disease Rating Scale (MDS-UPDRS).
- An ANCOVA model was used to assess the statistical significance of the changes in the outcome measures.

Key Inclusion criteria

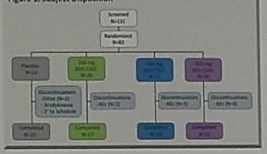
- 30–85 years old with PD
- Score of at least 2 on part IV, item 4.2 (functional impact of dyskinesia) of the MDS-UPDRS at screening and Day 1
- At least two 30 minute intervals of ON Time with troublesome dyskinesia between the hours of 9 am–4 pm, documented on a 24-hour PD diary
- Current PD medications, including levodopa preparations, were to be unchanged for 30 days prior to screening, and during the study

Key Exclusion criteria

- History of deep brain stimulation
- History of exclusively diphasic, off state, myoclonic, dystonic or akathetic dyskinesia without peak dose dyskinesia
- Presence of cognitive impairment, as evidenced by a MMSE of less than 24
- Estimated GFR <50 mL/min/1.73 m^2 (measure of renal function)
- Current treatment with apomorphine or dopamine receptor antagonists
- Use of amantadine within 30 days prior to screening, or documented inability to tolerate amantadine

Results

Figure 1. Subject Disposition



- 83 subjects were randomized in the study. The efficacy analysis population included 80 subjects; one subject was excluded from each of the active treatment groups according to pre-defined criteria
- The demographics and baseline characteristics appeared to be balanced across treatment groups

Table 1. Demographics and Baseline Characteristics

		Placebo (N=22)	260 mg ADS-5102 (N=20)	340 mg ADS-5102 (N=21)	420 mg ADS-5102 (N=20)
Age (yrs), Mean (SD)		65.5 (10.2)	67.5 (8.6)	64.7 (10.0)	66.4 (9.4)
Sex n (%)	Male	14 (63.6)	8 (40.0)	13 (61.9)	10 (50.0)
Ethnicity n (%)	Hispanic	1 (4.5)	2 (10.0)	0	2 (10.0)
	Not Hispanic	21 (95.5)	18 (90.0)	21 (100)	18 (90.0)
Race n (%)	White	20 (90.9)	18 (90.0)	20 (95.2)	17 (85.0)
Time since PD Diagnosis (yrs), Mean (SD)		10.7 (7.1)	8.9 (3.4)	9.3 (4.9)	9.0 (3.5)
Duration of Levodopa Treatment (yrs), Mean (SD)		9.0 (7.0)	6.9 (3.7)	8.2 (5.3)	8.3 (3.2)
Duration of LID (yrs), Mean (SD)		4.1 (4.1)	3.3 (2.6)	4.4 (3.4)	3.6 (2.0)
FSS, Mean (SD)		4.9 (1.2)	4.4 (1.5)	4.8 (1.4)	4.8 (1.1)
MMSE, Mean (SD)		28.6 (1.8)	28.6 (2.0)	28.8 (1.5)	28.2 (2.0)
Hoehn and Yahr, Mean (SD)		2.5 (0.74)	2.5 (0.89)	2.5 (0.60)	2.4 (0.75)
UDysRS, Total, Mean (SD)		39.2 (17.8)	39.8 (13.5)	43.8 (12.1)	41.9 (12.0)

Analysis of primary outcome measure

- The study met its primary endpoint; both the 340 mg and 420 mg dose levels significantly reduced LID as measured by change in the UDysRS total score over 8 weeks vs placebo (p=0.005 and p=0.013, respectively) as shown in Figure 2.

Figure 2. UDysRS Total Score Change from Baseline to Week 8

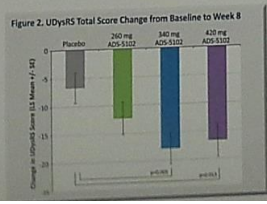
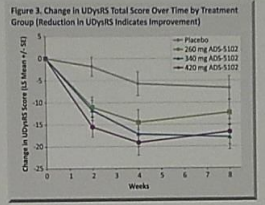


Figure 3. Change in UDysRS Total Score Over Time by Treatment Group (Reduction in UDysRS Indicates Improvement)

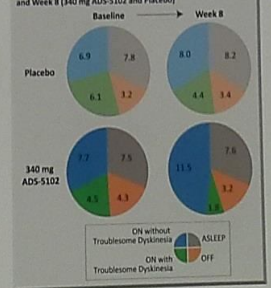


- A statistically significant reduction in LID was seen as early as two weeks following the first dose of ADS-5102 as shown in Figure 3.

Analysis of patient diary data

- At week 8, the ON time without troublesome dyskinesia, as measured by diaries, was 11.0 hours, 11.5 hours, and 12.1 hours for the 260 mg, 340 mg, and 420 mg dose levels, respectively, compared to 8.0 hours for placebo. This represents an increase of about 3 hours over placebo compared to baseline values. These changes were statistically significant and are shown below in Figure 4.

Figure 4. 24-Hour PD Diary Parameters (Mean Hours) at Baseline and Week 8 (340 mg ADS-5102 and Placebo)



Additional Efficacy Analyses

- A dose response was confirmed for the treatment groups in mean change from baseline to Week 8 in total UDysRS total score at Week 8 (p<0.01).
- ADS-5102 significantly reduced the UDysRS total objective score (parts III, IV) as compared to placebo at both the 340 mg and 420 mg dose levels (p=0.004 and p=0.0004, respectively).
- Using MDS-UPDRS (part IV, item 4.1 and 4.2), ADS-5102 reduced the time spent with dyskinesia (not significant) and resulted in a statistically significant improvement in the functional impact of dyskinesia in all treatment groups.

- There was no statistically significant change in MDS-UPDRS Combined Score (Part I, II, III) suggesting there was no worsening of PD.
- Clinician's Global Impression of Change showed significant improvement at the 340 mg dose level (p=0.004).
- No significant treatment group differences were noted in the FSS or the PDQ-39.

Safety Results

- The safety population included all 83 randomized and treated subjects. The most common AEs were constipation, dizziness, hallucinations, and dry mouth. There was no difference from placebo in the incidence of sleep-related adverse events.

Table 2. Most Common Adverse Events

Preferred Term, n (%)	Placebo (N=22)	260 mg ADS-5102 (N=20)	340 mg ADS-5102 (N=21)	420 mg ADS-5102 (N=20)
Constipation	2 (9.1)	7 (35.0)	5 (23.8)	3 (15.0)
Dizziness	1 (4.5)	3 (15.0)	6 (28.6)	3 (15.0)
Hallucination	0	4 (20.0)	5 (23.8)	4 (20.0)
Dry mouth	0	3 (15.0)	4 (19.0)	2 (10.0)
Fall	3 (13.6)	1 (5.0)	3 (14.3)	3 (15.0)
Confusion	1 (4.5)	1 (5.0)	3 (14.3)	2 (10.0)
Headache	1 (4.5)	1 (5.0)	3 (14.3)	1 (5.0)
Nausea	1 (4.5)	1 (5.0)	3 (14.3)	1 (5.0)
Asthenia	1 (4.5)	0	3 (14.3)	1 (5.0)

Conclusions

- The study met its primary endpoint. Both the 340 mg and 420 mg ADS-5102 dose levels significantly reduced LID, as early as week 2, as measured by the change in UDysRS total score over 8 weeks versus placebo (p=0.005 and p=0.013, respectively)
- ADS-5102 significantly increased ON Time without Troublesome Dyskinesia at the 260 mg, 340 mg and 420 mg dose levels as measured by patient diaries (p=0.004, p<0.008 and p=0.018, respectively), consistent with the changes observed in the UDysRS
- Both the 340 mg and the 420 mg ADS-5102 dose levels significantly reduced the UDysRS Total Objective Score (III, IV) (p=0.004 and p=0.0004, respectively)
- ADS-5102 resulted in statistically significant improvements in the functional impact of dyskinesia at the 260 mg, 340 mg, and 420 mg dose levels by MDS-UPDRS (part IV, item 4.2) (p<0.014, p=0.002, p<0.001, respectively).
- Treatment with ADS-5102 did not result in clinical worsening of PD as measured by the MDS-UPDRS combined score (parts I, II, and III).
- ADS-5102 was generally well tolerated and reported adverse event terms were consistent with PD and the known amantadine safety profile.

Acknowledgements and Disclosures

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