September 20 – 23
2016

- Plenary Session: An update of brain circuits in Parkinson’s and **Deep Brain Stimulation**

Deep Brain Stimulation
Andres M Lozano, University of Toronto

- Deep brain stimulation is the delivery of an electrical current to an area of the brain - in PD bilateral to the subthalamic nucleus (STN)
- 150,000 PD patients have received it worldwide and currently 10,000 patients per year

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- 150,000 PD patients have received it worldwide and currently 10,000 patients per year
- Best Outcome – Better quality of life with reduced motor fluctuations, tremor, rigidity, akinesia, gait and postural problems. **Non-motor symptoms are resistant to surgery (Sleep problems, depression etc)**

Deep Brain Stimulation
Andres M Lozano, University of Toronto

- **MRI guided Focused Ultrasound** (trans-skull penetration – i.e. **no surgery**) showed promising results in for essential tremor (n=40) (NEJM, 375,8 2016).

MRI guided Focused Ultrasound

Pretreatment

Post treatment

- Parallel Session: Disease modification - an update on clinical trials

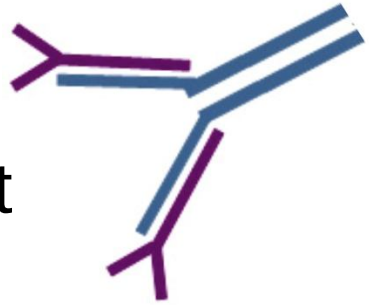
aSyn vaccines, passive immunization and novel small molecules (Eliezer Masliah)

aSyn vaccine - active immunization

- **PD01A AFFITOPE** (small aSyn peptide) – (Mandler, 2014)
  - tested in mouse models (Thy1.2-haSyn and pdgf-haSyn)
  - reduce cerebral aSyn
  - ameliorate neurodegeneration and dopaminergic loss in striatum
  - promote aSyn clearance by microglia
- Phase I trial in 12 PD patients showed vaccine to be safe
- 50% of patients developed aSyn antiboides in blood and CSF
- Phase IIA in PD and new trial in multiple system atrophy (MSA) patients.

aSyn vaccine - passive immunization

Prothena/Roche

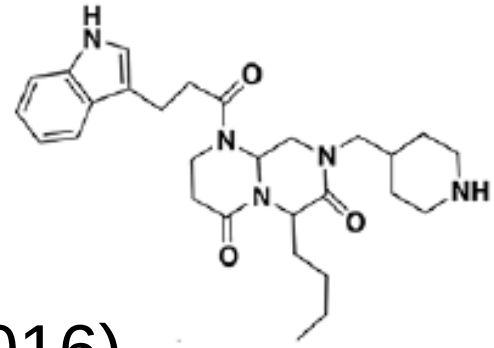


- **PRX002 vaccine** - humanized 9E4 antibody that recognises aSyn 118-126
- Phase 1A = 30 patients; Safe and well tolerated
- Reduced aSyn levels in plasma after 1 administration
- Phase 1B ongoing - ascending dose in PD patients.

- Many reports from other groups on anti-aSyn antibodies protecting against dopamineric neurons loss

Small molecules against aSyn

Neuropore/UCB



- **NPT200-11 drug** – similar to NPT100-18A
- NPT100-18A experiments (Price et al, Brain, 2016)
  - reduce aSyn oligomer formation
  - reduce reduced aSyn toxicity,
  - ameliorate behaviour (mThy1-haSyn mouse model)
- Phase I complete = 8 patients; Safe and well tolerated
- Phase II in planning stages

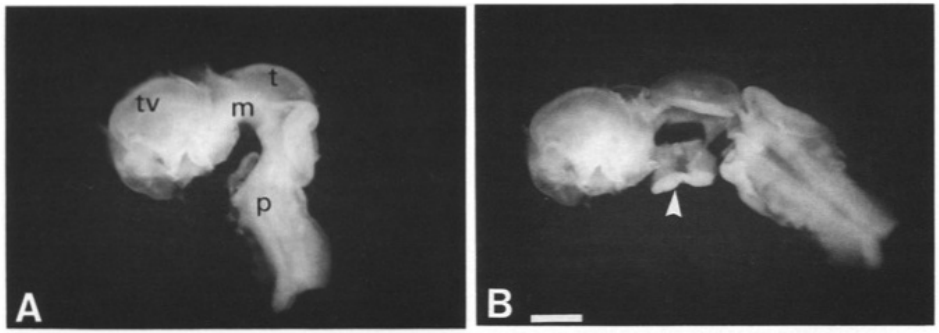
Clinical Trials with therapeutics against aSyn

Company	Drug	Preclinical efficacy	Preclinical PK/PD/ADME	Phase I	Phase II
Prothena/Roche	PRX002 passive a-syn immunization				
AFFiRiS/MJFox	PD-01A Active a-syn vaccine				
Neuropore/UCB	NPT200-11 a-syn stabilizer				
Neurophage/ MJFx/others	Npt-088 Phage anti-fibrilation			?	
Neuroimmune /Biogen	passive a-syn immunization			?	

- Plenary Session Day 3 – Stem cells and iPS cells: where are we?

Cell Based therapies for Parkinson's Disease: Past present and future (Roger Barker)

- Cell replacement of lost DA neurons in PD
- PAST - Fetal transplants in PD patients – variable results:
  - different doses of cells
  - different delivery method
  - different immunosupression
  - different primary end points



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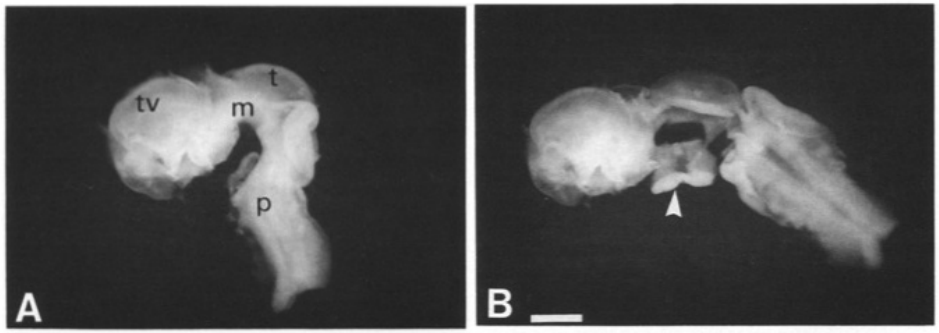
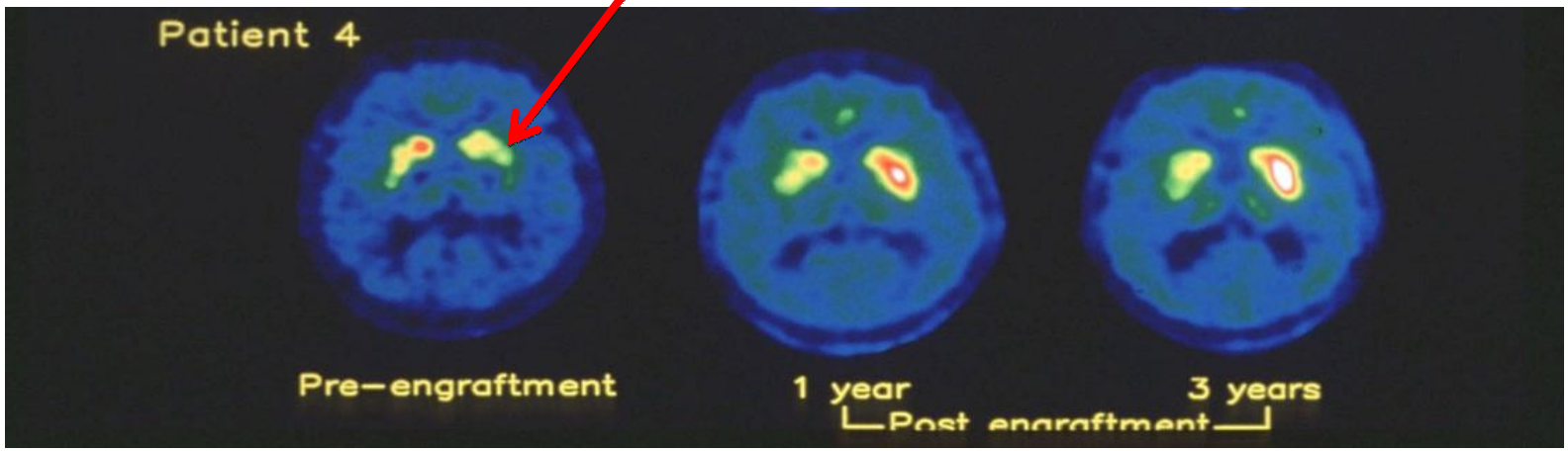


unilateral graft here



(^{18}F-DOPA PET)

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  - different immunosupression
  - different primary end points
- PRESENT - TRANSEURO using fetal grafts
  - better selection of patients (<65, <10 years duration, minimal LIDs)
  - same dose of cells, same delivery method,
  - same immunosupression, same 3 year end point (2020)

Cell Based therapies for Parkinson's Disease: Past present and future (Roger Barker)

- About 16 transplants between May 2015 – September 2016
- At least *15 cancellations due to insufficient tissue*

Cell Based therapies for Parkinson's Disease: Past present and future (Roger Barker)

- **FUTURE – Stem cells (hESCs or iPSCs)**
- avoid ethical and logistical issues
- controlled differentiation into a defined cell product
- dopaminergic neurons from hESCs have similar efficacy to fetal ventral midbrain transplants

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- **GForce-PD** = global initiative in coordinating stem cell-based treatments for PD.
- - CiRA - iPSC in PD trial in 2017 (**Japan**)
- - NYSTEM trial hESC in PD in 2018 (**USA**)
- - NeuroStemCellRepair hESC in PD in 2018/2019 (**UK/Sweden**)

June 2019