How to test ocular movements in PSP

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Bedside Screening: PSP

• initially slowing of vertical saccades
• slowing of downward saccades is considered the hallmark of PSP and is included in the diagnostic criteria
• PSP patients’ eyes might tonically drift in response to the visual cue in the direction of the slow phase of the nystagmus (loss of reflexive saccades)
• advanced disease: possibly complete ophthalmoplegia
• markedly hypometric vertical and horizontal saccades
• smooth pursuit at least moderately impaired
• prominent fixation instability with small-amplitude horizontal square wave jerks
• markedly diminished blink rate
• eye-opening and eye-closing apraxia
• ‘lazy lid phenomenon’ (S. Lorenzl)

Anderson & McAskill, Nat Rev Neurol 2013
non-invasive: Video-Oculography

EyeLink® I

EyeSeeCam®

Oculomotor Lab in Ulm

stimulus presentation
Reactive (vertical) saccades

Pathologically reduced peak eye velocity (<200°/s)

Patellar saccades

PSP patient

Peak eye velocity (>400°/s)

Healthy control

Gorges et al., J Ophthalmol 2014
PSP: subtypes RS und PSP-P

Fig. 1 Plot of factors for components 1 and 2 derived from factor analysis. ASYM = asymmetric onset; TREM = tremor; L-DOPA = response to levodopa; BRADYK = bradykinesia; DYST = extrapyramidal symptom; DYSK = dyskinesia; VISUAL = non-specific visual symptoms; PI = postural instability; SNGP = supranuclear gaze palsy; S/P = abnormal saccadic or pursuit movements; SPEECH = speech disturbance.

Williams et al., Brain 2005
Saccadic Eye Movements

- Functional networks: saccades
- Selection of saccades based on Hikosaka & Wurtz 1983

Diagram showing brain structures involved in saccadic eye movements, including:
- Parietal cortex
- Frontal cortex
- Basal ganglia
- Superior colliculus
- Brainstem
- Ocular muscles
Pathophysicsiology of vertical gaze palsy in PSP

lesions of burst neurons in riMLF (rostral interstitial nucleus of the medial longitudinal fascicle) for vertical saccades

- decreased firing rate
- decreased saccade velocity.
VOG: velocities of reactive saccades in PSP

PD and controls did not differ

PSP-P and RS significantly slower than PD and controls

PSP-P and RS with no significant differences

individual level: in 10 out of 12 RS and 4 out of 5 PSP-P patients peak velocity below 5%-Percentile of the controls

Pinkhardt et al., J Neurol (2008)
Individual variability of SNGP in PSP
NB:
Slow vertical saccades not in all PSP patients
Executive control: anti-saccade

Eye Position /° –20 0 20

Time / s 0.02 0.2 0.4 0.6 0.8 1.0

stimulus

Executive control: anti-saccade

Eye Position /° –20 0 20

Erro...
VOG helps to differentiate PD and PSP-P already in early stages and clinically similar presentation (saccade velocity).

Williams et al. described SNGP in PSP-P (if any) to occur late in the disease course – based upon clinical examination.

PSP-P and RS could not be differentiated by VOG in this retrospective study.
Oculomotor functions in Parkinsonian syndromes

Literature

In `atypical` Parkinsonism, oculomotor pathology occurs with large overlap.

PD patients also show pathological pursuit and pathological reactive saccades.
VOG: SPEM in MSA

MSA vs. PD vs. CTL
SPEM horizontal: significant difference between MSA, PD and CTL
[0.375 Hz > 0.125 Hz]

MSA-C vs. MSA-P
No significant difference for Gain and Phase angle between MSA-C and MSA-P
(49% of MSA with OPCD and SND (Ozawa et al., Brain 2004)

Comparison of smooth pursuit eye movement deficits in multiple system atrophy and Parkinson’s disease

Elmar H. Pinkhardt · Jan Kassubek · Sigurd Süssmuth · Albert C. Ludolph · Wolfgang Becker · Reinhart Jürgens
Parkinsonism and oculomotor deficits: differential diagnostics

Pinkhardt & Kassubek, Parkinsonism Rel Disord (2011)
Utility of eye movement recordings in PSP

Anderson & McAskill, Nat Rev Neurol (2013)
Conclusion I: Present knowledge

- With respect to the subdivision of the clinical PSP syndrome to RS and PSP-P, a clinically assessable vertical gaze palsy is not described as a leading symptom in early PSP-P.

- By hands of VOG, nearly similar oculomotor deficits have been shown in both RS and PSP-P with a prominent decreased saccadic velocity (vertical > horizontal), decreased gain of saccades, and smooth pursuit eye movements even in the early course of the disease when motor symptoms of PSP-P are very similar to PD.

- VOG is useful in clinical diagnostics, also with respect to other entities, although overlapping findings exist.

Anderson & McAskill, Nat Rev Neurol (2013)
Conclusion II: Present knowledge deficits

• Prospective longitudinal data in early stages of PSP-P and RS are lacking and should be acquired in order to assess the biomarker potential of oculomotor alterations in PSP and other Parkinsonian syndromes.

→ correlation to other technical parameters (e.g. MRI)

• For that purpose, more experience in multi-center data acquisition and postprocessing needs to be gained

→ first studies exist (AL-108 PSP Study, Allon Therapeutics)