Transcranial sonography in movement disorders

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TCS of brain parenchyma

Method

- High-end ultrasound system
- 2.5-MHz phased-array transducer
- Image resolution axial: 0.7 (0.3) mm - lateral: 3 (1) mm

Walter et al. Neuroimage 2008
TCS of brain parenchyma
Parameter settings

- Penetration depth 14 – 16 cm
- Focus position 7 – 8 cm
  axial resolution 0.3 - 0.7 mm
  lateral resolution 1 – 3 mm
- Dynamic range 45–50 dB
- Post-processing: moderate
  suppression of low echo signals
- Time gain compensation:
TCS of brain parenchyma
Intracranial bleeding

Computed tomography

TCS

8.2 x 3.0 cm
7.9 x 2.9 cm
TCS of brain parenchyma
Malignant brain tumors
Detektion abh. von Lage und Knochenfenster sowie Echogenität
Nekrose, solide Anteile und perifok. Ödem haben untersch. Echogenität
Klinikum, 14/10/2004
1. Method of TCS in movement disorders
Neurodegenerative diseases
Course of investigation

- 3) Cella-media level:
  - Lateral ventricle (Cella media)
- 2) Thalamus level:
  - Thalamus
  - Lenticular nucleus
  - Caudate nucleus
  - 3rd ventricle
  - Frontal horn of lateral ventricle
- 1) Midbrain level
  - Substantia nigra
  - Red nucleus
  - Brainstem raphe

Walter et al. Ultrasound in Medicine & Biology 2007;33:15-25
Evaluation of midbrain structures

- Substantia nigra
- Red nucleus
- Brainstem raphe
Evaluation of midbrain structures
Substantia nigra (SN)

Grading by size of SN echogenic area

SN echogenic size measurements ipsilateral to insonation

Normal SN echogenicity
SN hyperechogenicity

SN hyperechogenicity is characteristic for PD (> 90%)

Evaluation of midbrain structures
Substantia nigra (SN)

Ultrasound systems Siemens Sonoline Elegra and Acuson Antares

• Normal SN echogenicity: A ≤ 0.19 cm² A ≤ 0.23 cm²
  (upper standard deviation in normal population)
• Moderate SN hyperechogenicity: A = 0.20 - 0.24 cm² A = 0.24 - 0.29 cm²
• Marked SN hyperechogenicity: A ≥ 0.25 cm² A ≥ 0.30 cm²
  (above 10% percentile in normal population)


Normal range of SN echogenic area needs to be estimated separately for each ultrasound system!
2. Clinical relevance of substantia nigra echogenicity
Substantia nigra hyperechogenicity in Parkinson’s disease: specificity

Key motor symptoms:
- Rigidity
- Tremor
- Bradykinesia
- Postural instability

James Parkinson 1817

70% of SN neurons are degenerated when PD is clinically diagnosed.

Can SN hyperechogenicity on TCS be used for preclinical diagnosis of PD?
Substantia nigra hyperechogenicity in Parkinson’s disease: specificity

is characteristic for PD as compared to:

- age-matched healthy subjects
  Berg et al. 2001
- non-degenerative brain diseases
  Walter et al. 2002
- essential tremor
  Stockner et al. 2007
Substantia nigra hyperechogenicity in Parkinson’s disease: specificity

- Berg 1999 (n=301)
- Walter 2006 (n=55)
- Berg 2001 (n=79)
- Berg 2001 (n=103)
- Walter 2006 (n=97)

Bar chart showing the percentage of subjects with substantia nigra hyperechogenicity in normal subjects and PD patients.
Substantia nigra hyperechogenicity in Parkinson’s disease: clinical correlates

• Larger SN echogenic size correlates with
  – increased iron content in the SN
  – earlier PD onset
  – slower PD progression

• SN echogenic size does not correlate with
  – PD duration
  – PD severity and complications
  – FP-CIT SPECT in PD patients

=> SN hyperechogenicity is not a result from cell degeneration
Substantia nigra hyperechogenicity in Parkinson’s disease: clinical correlates

Larger SN hyperechogenicity correlates with
- earlier PD onset
- hereditary parkinsonism
- slower PD progression
- genetic determination?

Mov Disord 2004;19:1445-1449

Mov Disord 2006;21:94-98
Substantia nigra hyperechogenicity in Parkinson’s disease: supports differential diagnosis

- SN hyperechogenicity discriminates PD from
  - Multiple-system atrophy and progressive supranuclear palsy
  - Posttraumatic parkinsonism
    Kivi et al. *Mov Disord* 2005
  - Essential tremor
  - Dopa-responsive dystonia
    Hagenah et al. *Neurology* 2006
  - Welding-related parkinsonism
    Walter et al. *Mov Disord* 2008
  - Vascular parkinsonism
    Walter et al. (unpublished)

- SN hyperechogenicity does **not** discriminate PD from
  - Corticobasal degeneration
    Walter et al. *Neurology* 2004
  - Dementia with Lewy bodies
    Walter et al. *J Neurol* 2006
Substantia nigra hyperechogenicity in healthy adults: indicates impaired dopaminergic function

- Preclinical correlates
  - 10% of (young) healthy adults, reduced $^{18}$F-dopa uptake on PET
  - parkinsonism induced by neuroleptics
    Berg et al. *Biol Psychiatry* 2001
  - motor retardation in elderly subjects
    Berg et al. *Neurology* 2001
  - abnormal FP-CIT-SPECT in hyposmic subjects
    Sommer et al. *Mov Disord* 2004
  - motor asymmetry in depressed non-parkinsonian subjects
    Walter et al. *Brain* 2007

$\Rightarrow$ Preclinical risk marker for PD
Substantia nigra hyperechogenicity and depression: Increased risk of later developing PD?

Non-Parkinsonian patients with depression: increased frequency of marked SN hyperechogenicity.

PD patients with history of depression prior to PD onset: clearest correlation of larger SN echogenicity with earlier PD onset ($r = -0.6$, $p < 0.05$).

Walter et al. *Brain* 2007
Substantia nigra hyperechogenicity and depression: Increased risk of later developing PD?

Larger SN hyperechogenicity in depression correlates with higher degree of motor abnormalities characteristic for early PD.


- Tapping asymmetry
- Reduced word fluency
Evaluation of midbrain structures
Brainstem raphe

• Normal (B): highly echogenic, continuous line
• Hypoechogenic (A): interrupted or invisible from both sides

• Depressive disorders (SSRI responders), depression in PD

• Urinary incontinence in PD
3. Clinical relevance of midbrain raphe echogenicity
Midbrain raphe reduced echogenicity in Parkinson’s disease: clinical correlates

- Normal (fig. B): highly echogenic, continuous line
- Hypoechogenic (fig. A): interrupted or invisible from both sides (6-8% of normal population)

- Characteristic for major depression, and for depression in PD
Midbrain raphe reduced echogenicity in depressive disorders: clinical correlates

- No relationship to diagnostic category
- Clear relationship to better SSRI response

Thalamus level
Ventricle widths

Normal values
• 3rd ventricle:
  < 7 mm  (< 60 years)
  < 10 mm  (> 60 years)
• Frontal horn of lateral ventricle:
  < 17 mm  (< 60 years)
  < 20 mm  (> 60 years)

Dilatation
• Brain atrophy
• Hydrocephalus
• 3rd ventricle dilatation typical for progressive supranuclear palsy

Thalamus level
Evaluation of basal ganglia

Ventricle widths

3rd ventricle
Frontal horn

Basal ganglia
Thalamus
Lenticular nucleus
Caudate nucleus

normal: isoechogenic to adjacent brain parenchyma
abnormal: increased echogenicity (hyperechogenicity)
Thalamus level
Lenticular nucleus hyperechogenicity

... can be diffuse or dot-like
4. Clinical relevance of lenticular nucleus echogenicity
Lenticular nucleus hyperechogenicity
Clinical relevance

• In dystonia:
  – discriminates idiopathic from kinesiogenic and psychogenic dystonia
    Naumann et al. *Neurology* 1996

• In parkinsonism:
  – supports discrimination of atypical parkinsonian syndromes (MSA, PSP) and of welding-related parkinsonism from idiopathic PD

• In Wilson’s disease:
  – present already in asymptomatic stages
  – correlates with severity of neurological symptoms
    Walter et al. *Neurology* 2005
Lenticular nucleus hyperechogenicity discriminates atypical parkinsonism from PD

Combination of hyperechogenic LN and normal echogenic SN

Combination of 3rd ventricle dilatation >10 mm and hyperechogenic LN

PD (n=138), probable MSA-P (n=21), probable PSP (n=22)

Wilson's disease

- Asymptomatic

- Moderate disease

- Severe disease

Walter et al. *Neurology* 2005, 64:1726-1732
Thalamus level
Caudate nucleus hyperechogenicity

• frequent in:
  – Huntington's disease (10-20%)
  – Late PD (60%): levodopa-induced psychosis
  – DLB (90%)
  – PSP (80%)
  – CBD (100%)

Postert et al. JNNP 1998
Walter et al. Neurology 2003, 2004,
Mov Disord 2007
5. Clinical relevance of caudate nucleus echogenicity
Caudate nucleus hyperechogenicity
Clinical relevance

• In Parkinson’s disease:
  – correlates with occurrence of levodopa-induced psychosis
    Walter et al. Mov Disord 2007

• In Huntington’s disease:
  – discriminates HD from secondary forms of Chorea
    Postert et al. JNPP 1998
    Walter et al. (unpublished)
6. Clinical relevance of **DBS electrode** localization
TCS in deep brain stimulation (DBS)

Perioperative monitoring of DBS electrode implantation

Microelectrode

Macroelectrode

Microelectrode 2

Microelectrode 3

Macroelectrode
TCS in deep brain stimulation (DBS)
Electrode [Ø 0.8 mm] artifacts in axial section

- Artifact in axial direction 2.0-2.5 mm
- Artifact in lateral direction 4-5 mm
- Repetition artifact
TCS in deep brain stimulation (DBS)
Postoperative measures
Summary

- **Substantia nigra hyperechogenicity** correlates:
  - in healthy adults with subclinical nigrostriatal dopaminergic deficit
  - in PD patients with earlier onset and slower progression of disease

- **Midbrain raphe reduced echogenicity** correlates:
  - in depressive disorders with better SSRI response
  - in PD patients with increased risk of depression and of urge incontinence

- **Lenticular nucleus hyperechogenicity** correlates:
  - in dystonia and Wilson’s disease with severity of motor symptoms
  - in Parkinsonian disorders with postsynaptic rather than presynaptic etiology

- **Caudate nucleus hyperechogenicity** correlates:
  - in Chorea with primary rather than secondary forms
  - in PD patients with increased risk of levodopa-induced psychosis

- **DBS electrode localisation** allows:
  - Intraoperative prevention of vessel damage/bleeding
  - Postoperative detection of dislocation