Transcranial sonography in movement disorders

Uwe Walter

1st Residential Training of the
European Society of Neurosonology and Cerebral Hemodynamics
September 7-12, 2008
Bertinoro, Italy

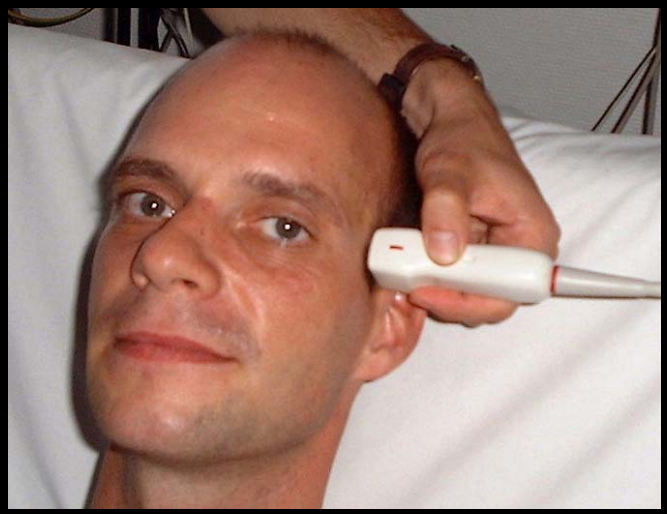
Department of Neurology

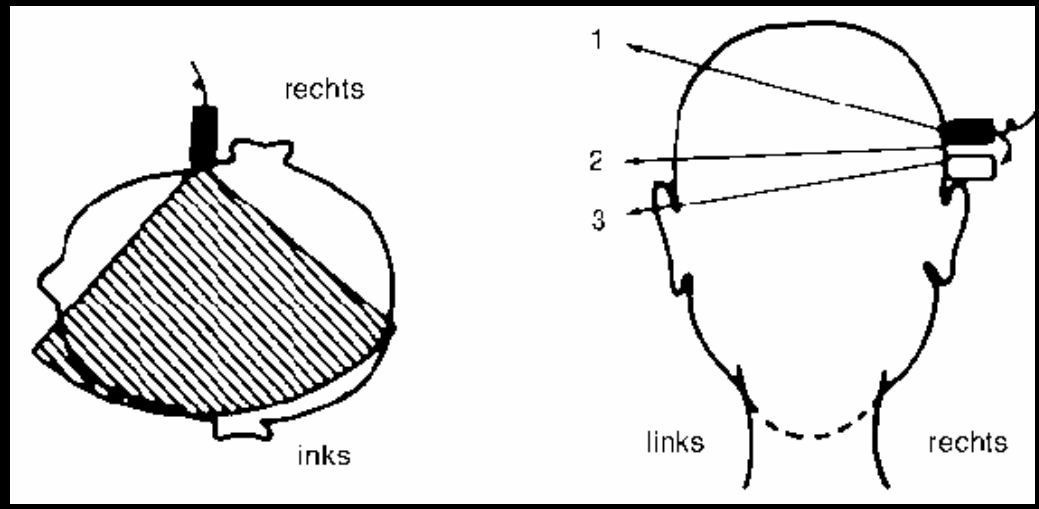
University of Rostock, Germany

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





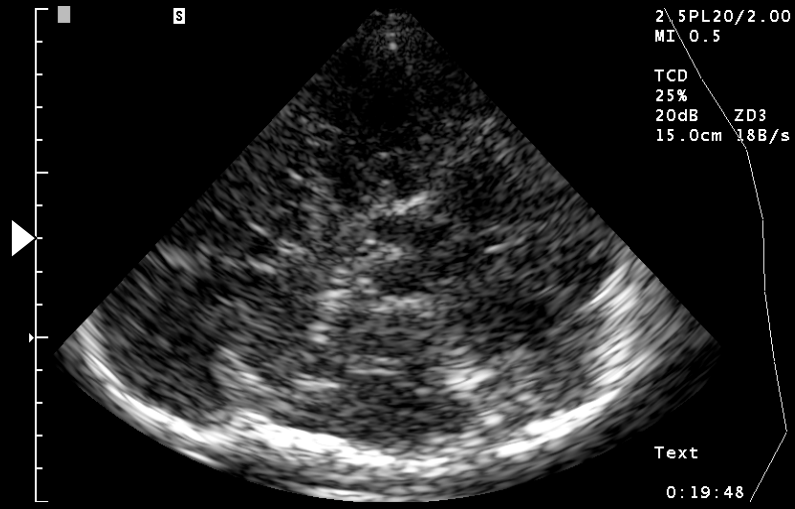
TCS of brain parenchyma

Parameter settings

- Penetration depth 14 – 16 cm
- Focus position 7 – 8 cm

  axial resolution 0.3 - 0.7 mm

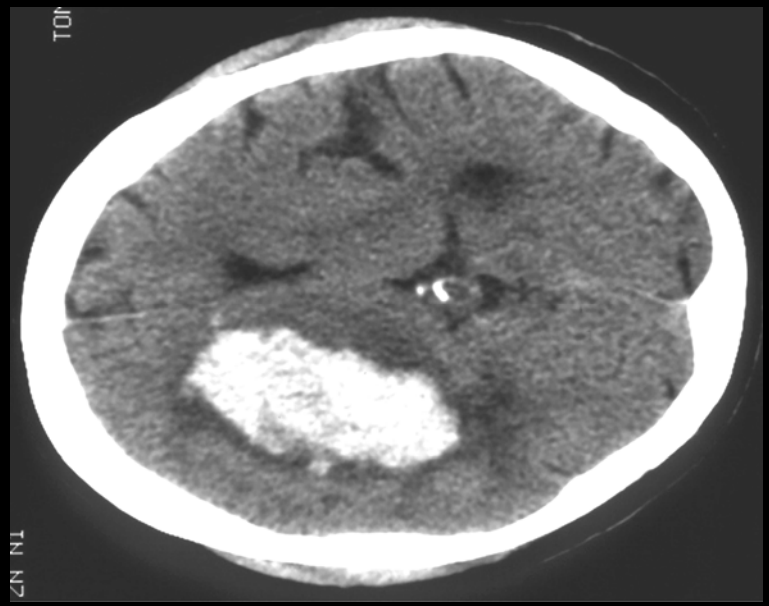
  lateral resolution 1 – 3 mm
- Dynamic range 45–50 dB
- Post-processing: moderate suppression of low echo signals
- Time gain compensation:



TCS of brain parenchyma

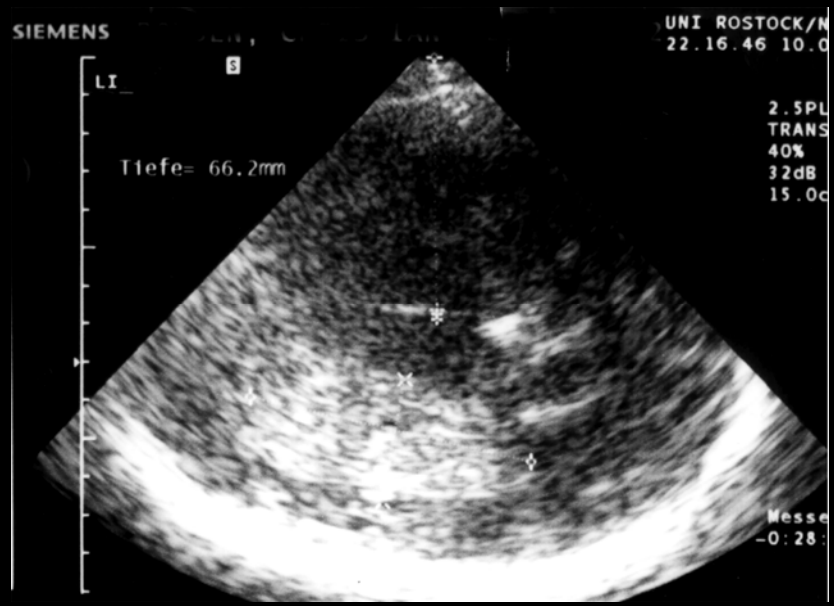
Intracranial bleeding

Computed tomography



8.2 x 3.0 cm

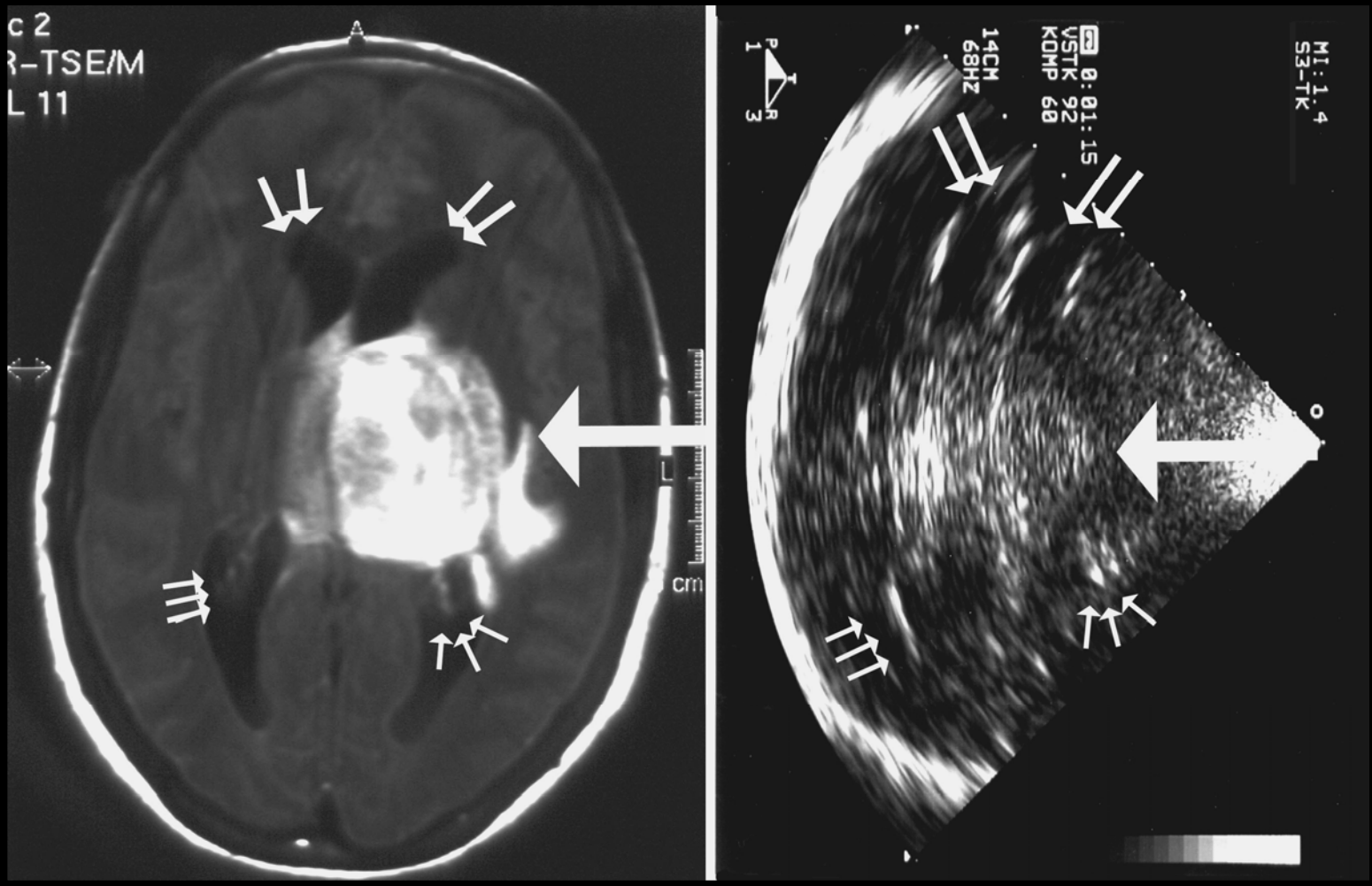
TCS



7.9 x 2.9 cm

TCS of brain parenchyma

Malignant brain tumors



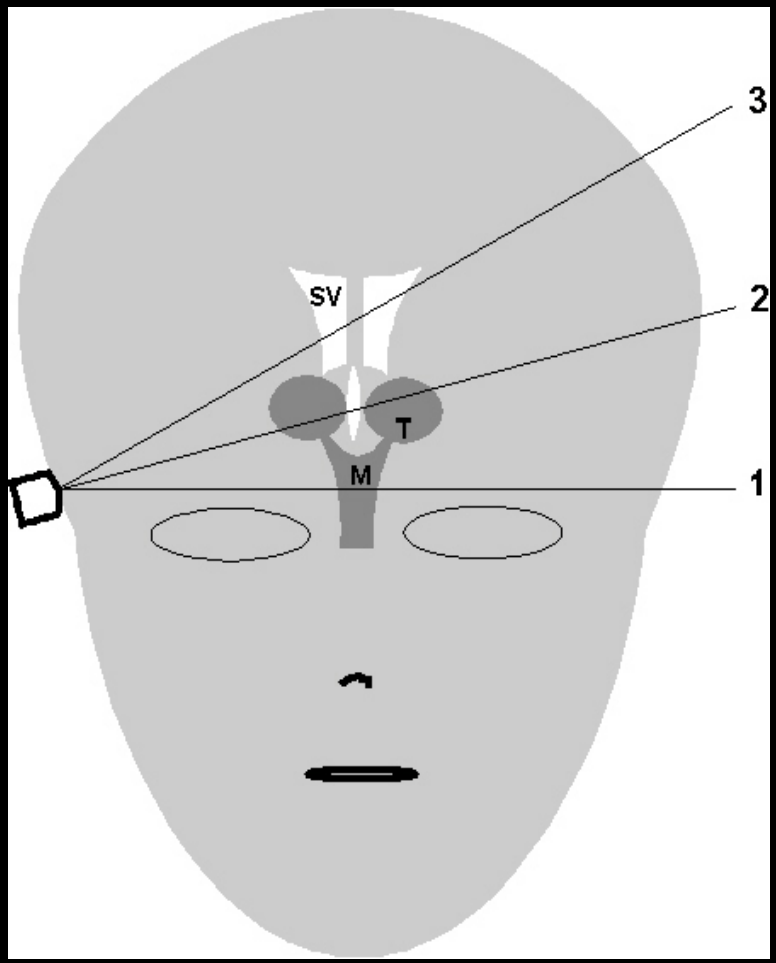
K1

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

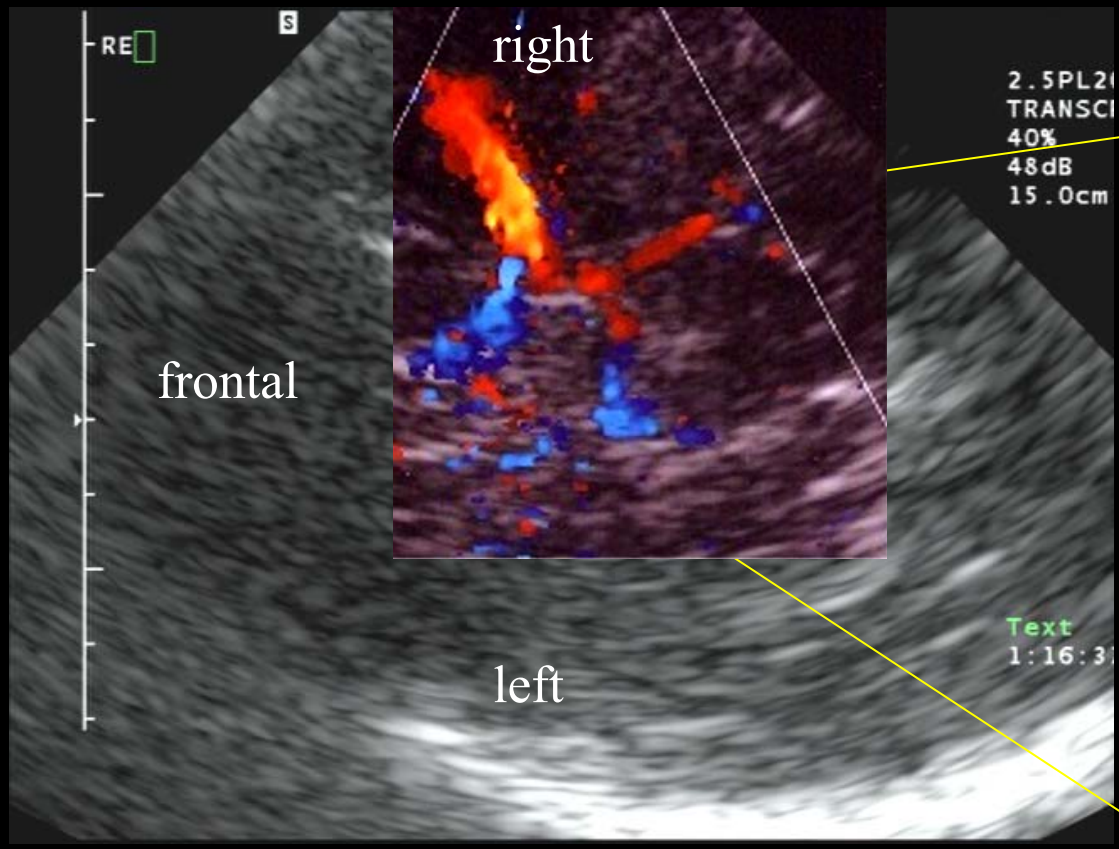
Course of investigation



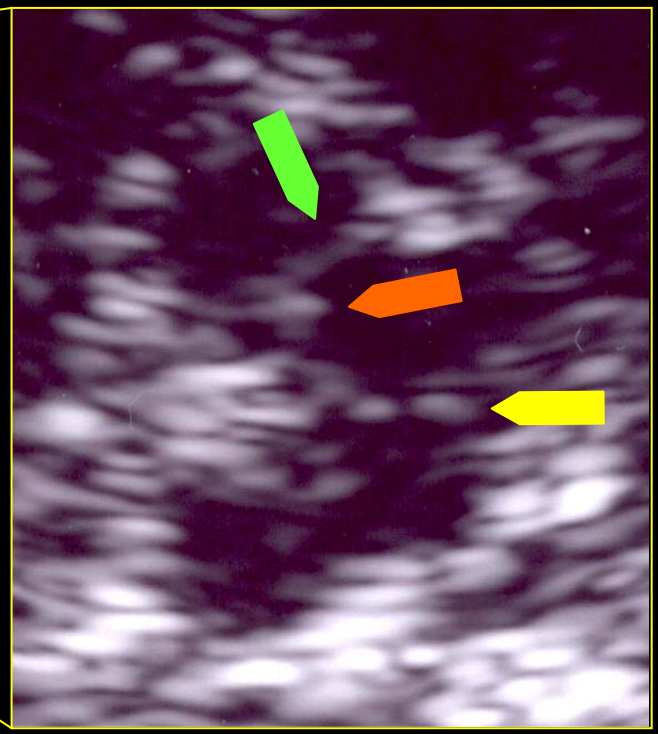
- 3) Cella-media level:
  - Lateral ventricle (Cella media)
- 2) Thalamus level:
  - Thalamus
  - Lenticular nucleus
  - Caudate nucleus
  - 3rd ventricle
  - Frontal horn of lateral ventricle
- 1) Midbrain level
  - Substantia nigra
  - Red nucleus
  - Brainstem raphe

Walter et al. *Ultrasound in Medicine & Biology* 2007;33:15-25

Evaluation of midbrain structures



- **Substantia nigra**
- **Red nucleus**
- **Brainstem raphe**

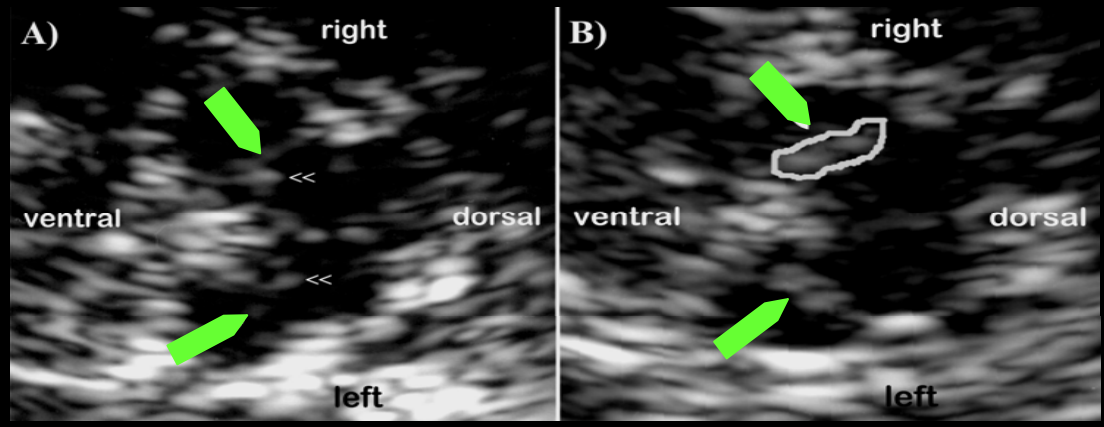


Evaluation of midbrain structures

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%)

Becker et al. 1995; Berg et al. 2001; Walter et al. 2002, 2003

Evaluation of midbrain structures
Substantia nigra (SN)

Ultrasound systems Siemens Sonoline Elegra and Acuson Antares

- Normal SN echogenicity: $A \leq 0.19$ cm² $A \leq 0.23$ 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: $A \geq 0.25$ cm² $A \geq 0.30$ cm²

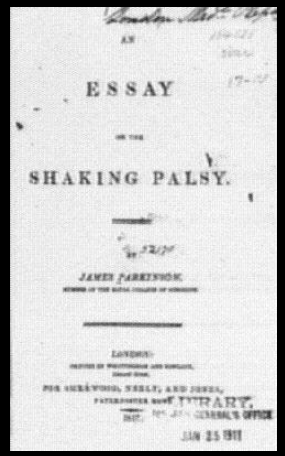
  (above 10% percentile in normal population)

Berg et al. 1999; 2001; Walter et al. 2002, Niehaus et al. 2006

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

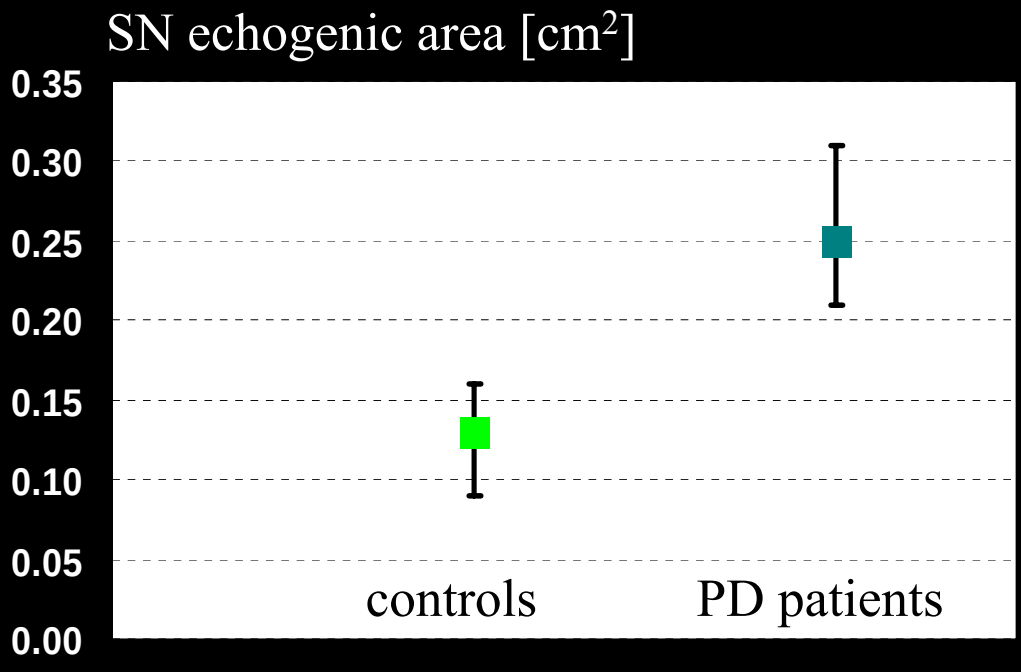
  Berg et al. 2001

- non-degenerative brain diseases

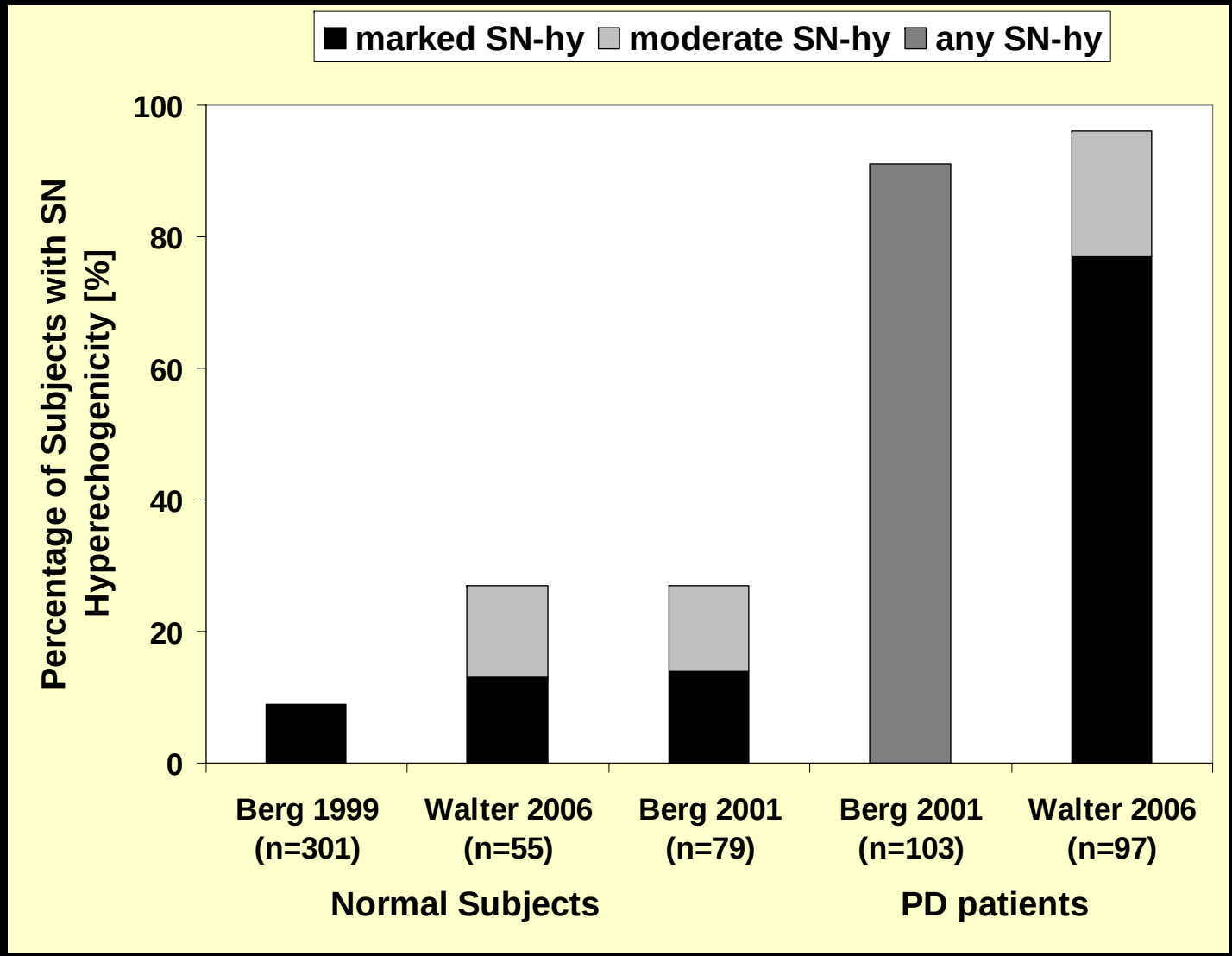
  Walter et al. 2002

- essential tremor

  Stockner et al. 2007



Substantia nigra hyperechogenicity
in Parkinson‘s disease: specificity



Substantia nigra hyperechogenicity
in Parkinson‘s disease: clinical correlates

- Larger SN echogenic size correlates with
  - increased iron content in the SN — Berg et al. *Arch Neurol* 2002
  - earlier PD onset — Berg et al. *J Neurol* 2001; Walter et al. *Mov Disord* 2004, 2007
  - slower PD progression — Schweitzer et al. *Mov Disord* 2005

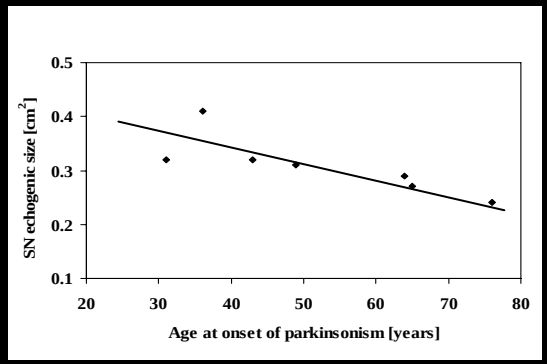
- SN echogenic size does not correlate with
  - PD duration — Berg et al. *Mov Disord* 2004
  - PD severity and complications — Walter et al. *Mov Disord* 2007
  - FP-CIT SPECT in PD patients — Spiegel et al. *Brain* 2006

=> SN hyperechogenicity is not a result from cell degeneration

Substantia nigra hyperechogenicity
in Parkinson‘s disease: clinical correlates

Larger SN hyperechogenicity correlates with

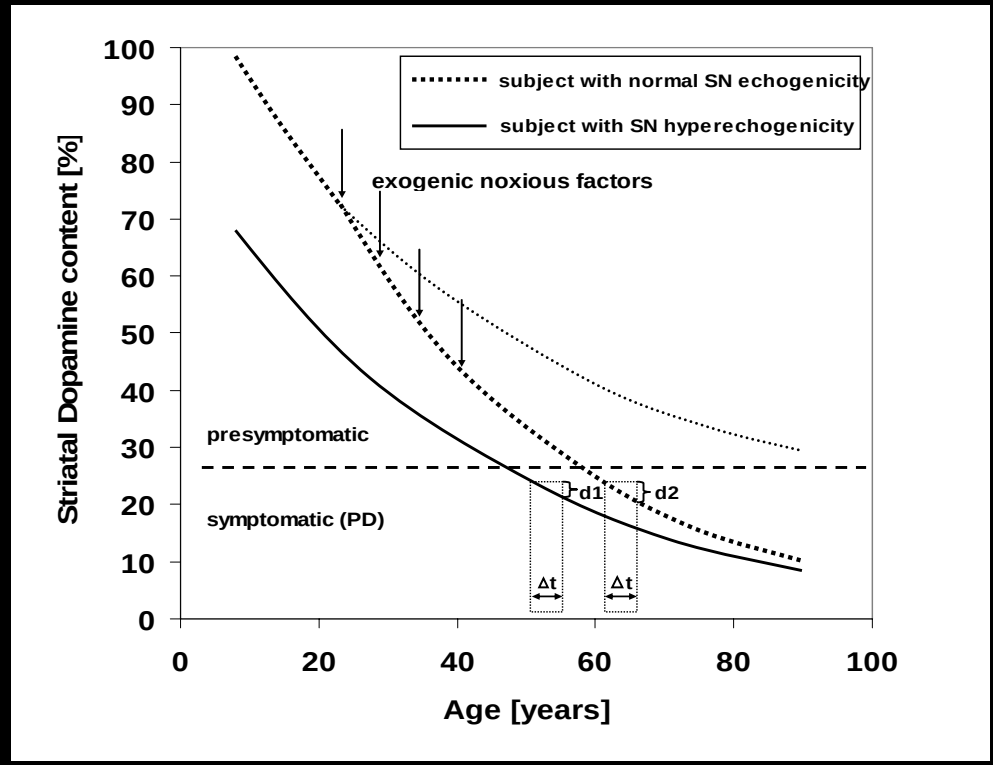
- earlier PD onset
  hereditary parkinsonism



Mov Disord 2004;19:1445-1449

- slower PD progression

- genetic determination?



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 — Walter et al. *Neurology* 2003, 2004; *Arch Neurol* 2007; Behnke et al. *JNNP* 2005; Okawa et al. *Arch Int Medicine* 2007; Gaenslen et al. *Lancet Neurol* 2008
  - Posttraumatic parkinsonism — Kivi et al. *Mov Disord* 2005
  - Essential tremor — Stockner et al. *Mov Disord* 2007; Doepp et al. *Mov Disord* 2007
  - 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

    Berg et al. *Neurology* 1999 ; Walter et al. *Mov Disord* 2004
  - 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

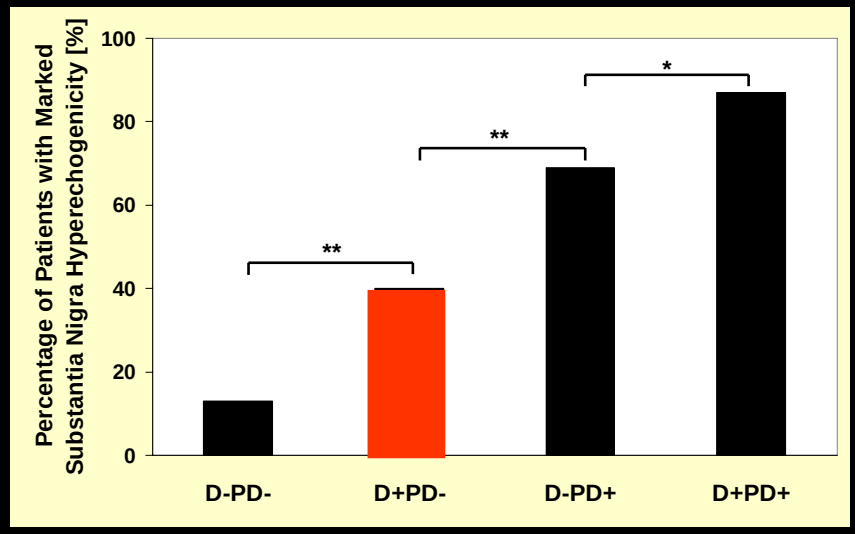
    Sommer et al. *Mov Disord* 2004
  - motor asymmetry in depressed non-parkinsonian subjects

    Walter et al. *Brain* 2007

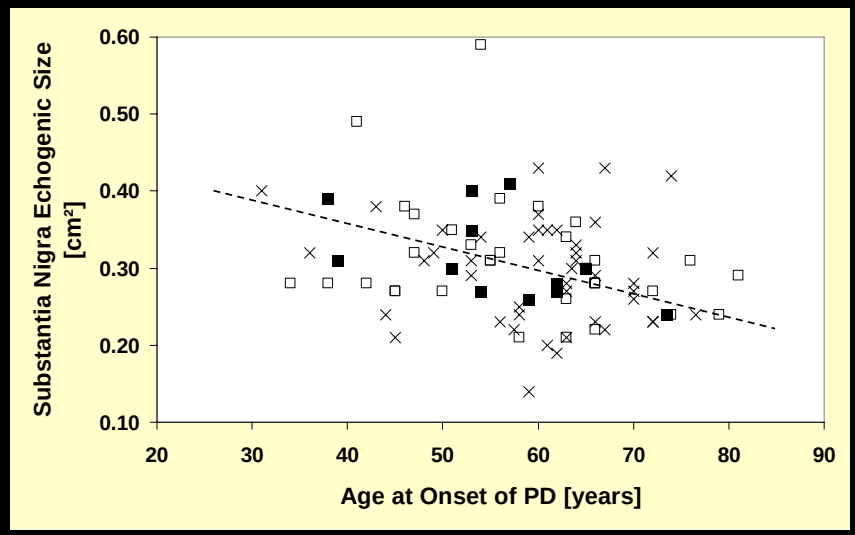
=> Preclinical risk marker for PD

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 ($r = -0.6$, $p < 0.05$).

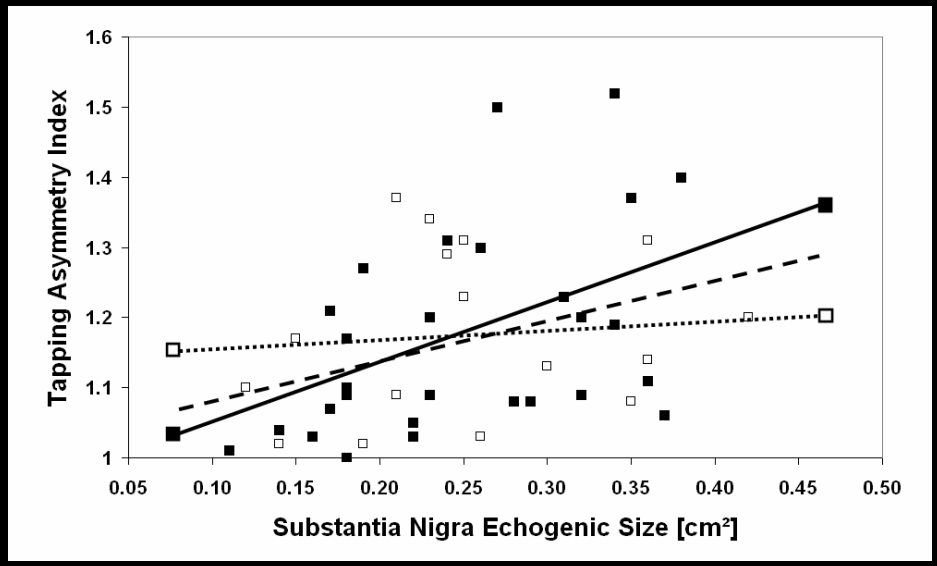


Walter et al. *Brain* 2007

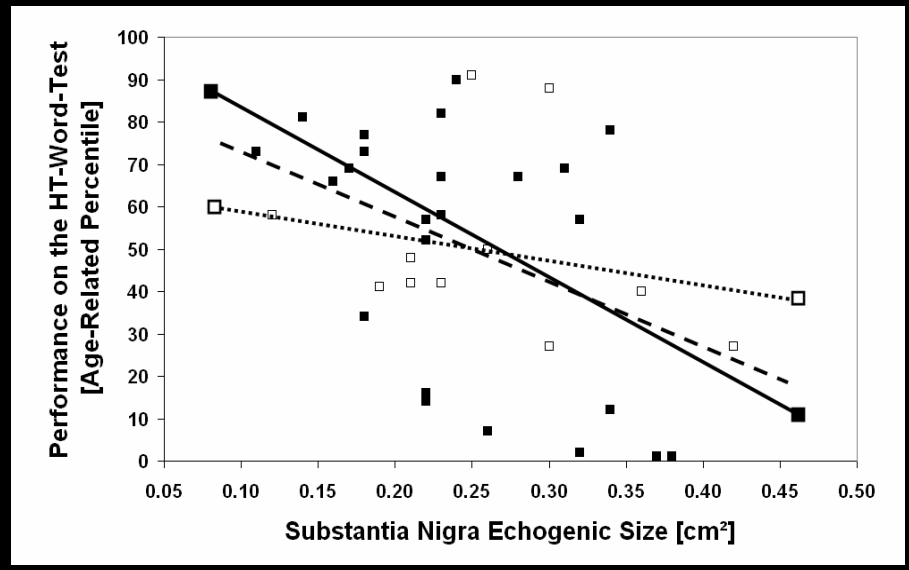
Substantia nigra hyperechogenicity

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



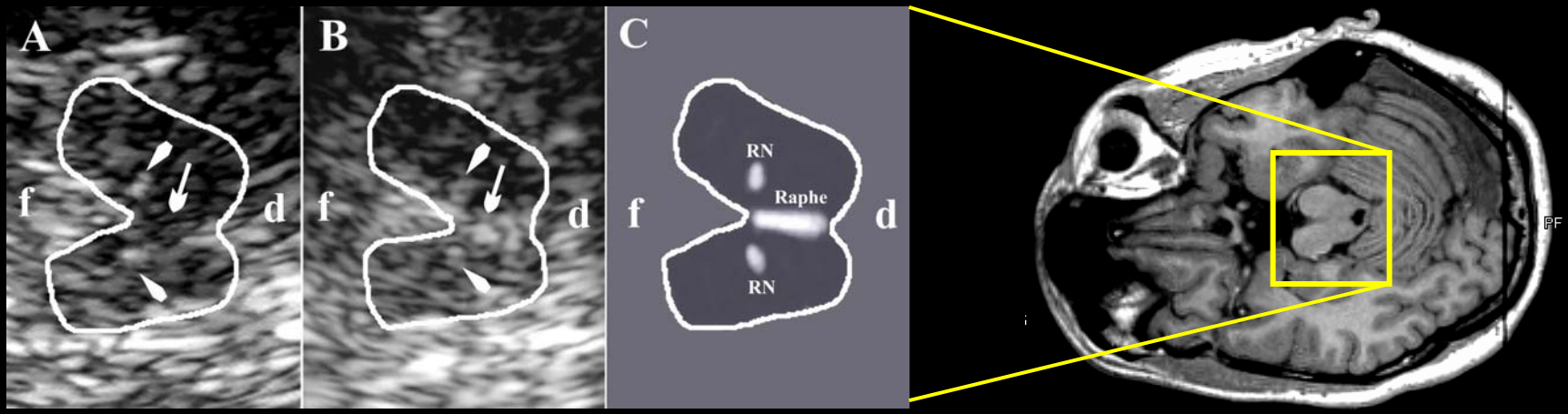
Reduced word fluency

Walter et al. *Eur Arch Psychiatry Clin Neurosci* 2008

Evaluation of midbrain structures

Brainstem raphe

- Normal (B): highly echogenic, continuous line
- Hypoechogenic (A): interrupted or invisible <u>from both sides</u>



- Depressive disorders (SSRI responders), depression in PD

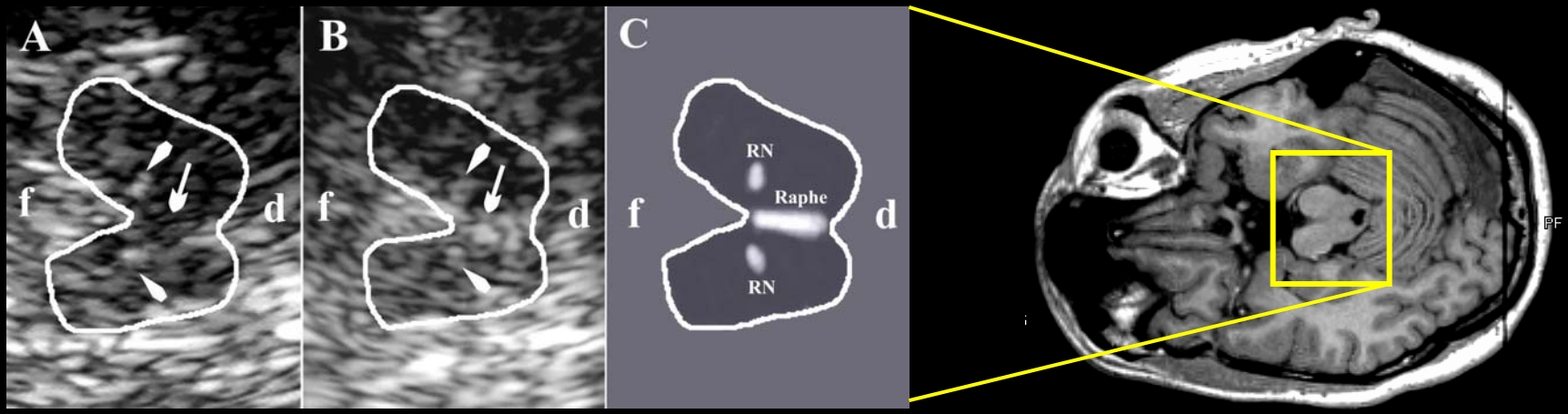
  Becker et al. *Biol Psychiatry* 1995, Walter et al. *Psychiatry Res* 2007, *Brain* 2007

- Urinary incontinence in PD Walter et al. *Eur J Neurol* 2006

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 <u>from both sides</u> (6 -8% of normal population)

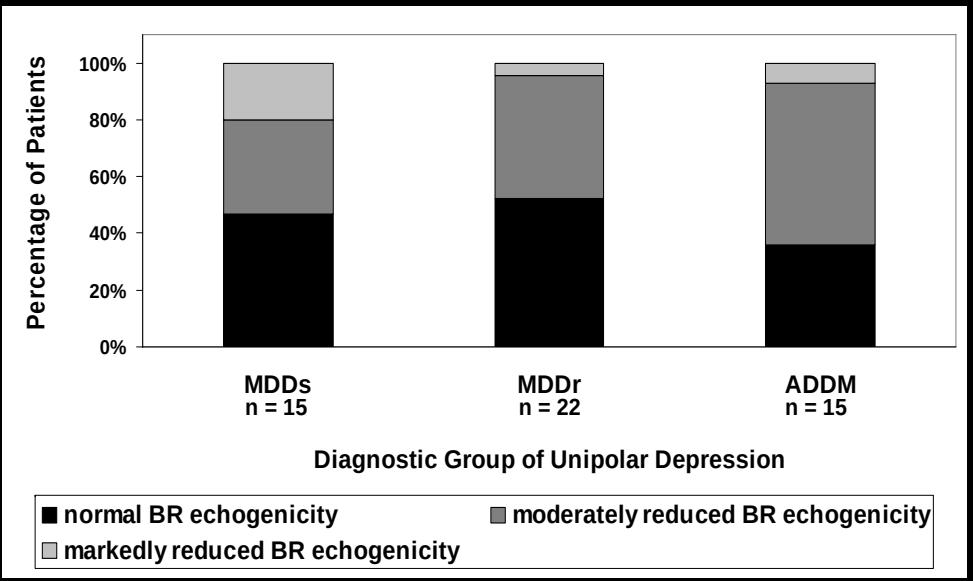


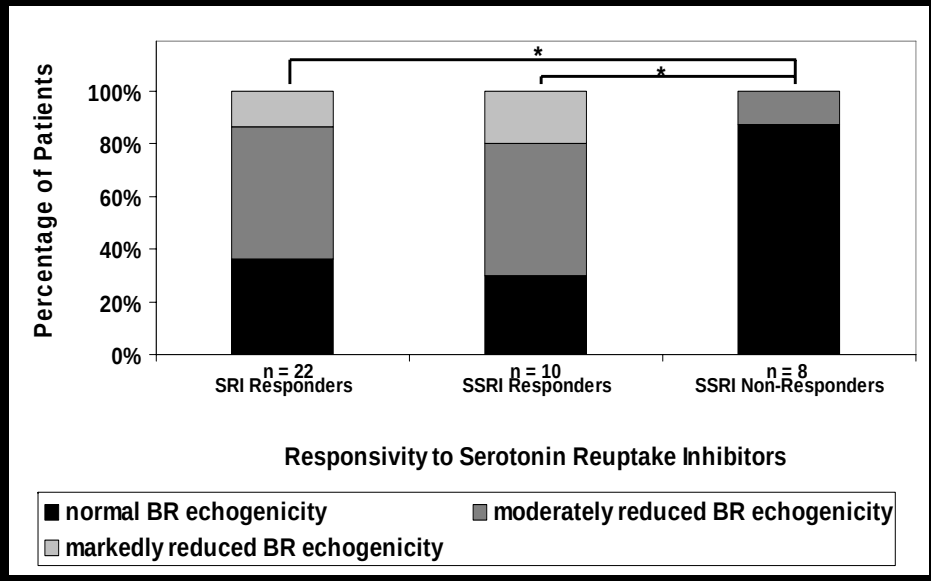
- Characteristic for major depression, and for depression in PD

  Becker et al. *Biol Psychiatry* 1995; Berg et al. *J Neurol* 1999; Walter et al. *Mov Disord* 2007, *Brain* 2007
- Urge incontinence in PD Walter et al. *Eur J Neurol* 2006

Midbrain raphe reduced echogenicity
in depressive disorders: clinical correlates

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





Walter et al. *Psychiatry Res Neuroimaging* 2007

Thalamus level
Ventricle widths

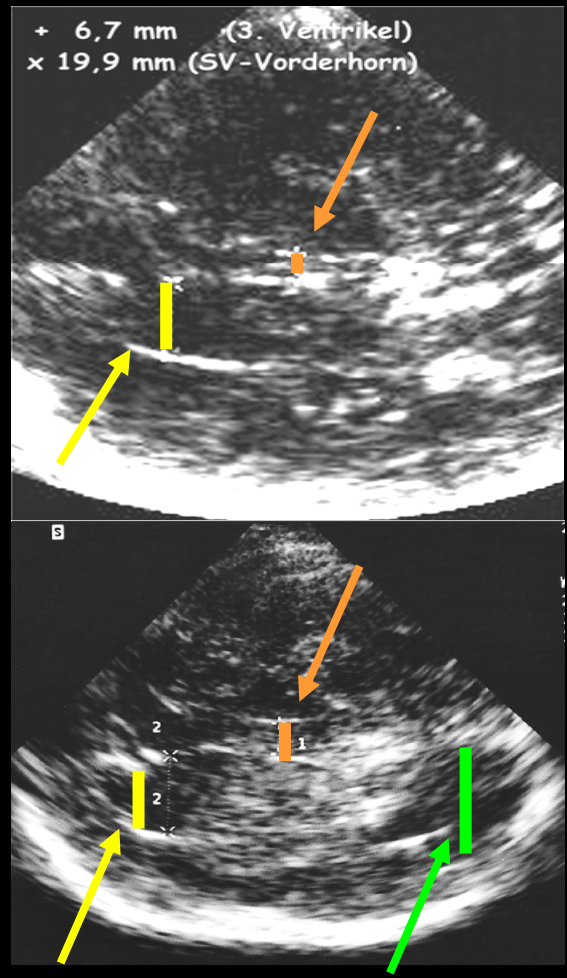
Normal values

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

Seidel et al. *J Neuroimaging* 1995

Dilatation

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



Thalamus level

Evaluation of basal ganglia

Ventricle widths

3rd ventricle

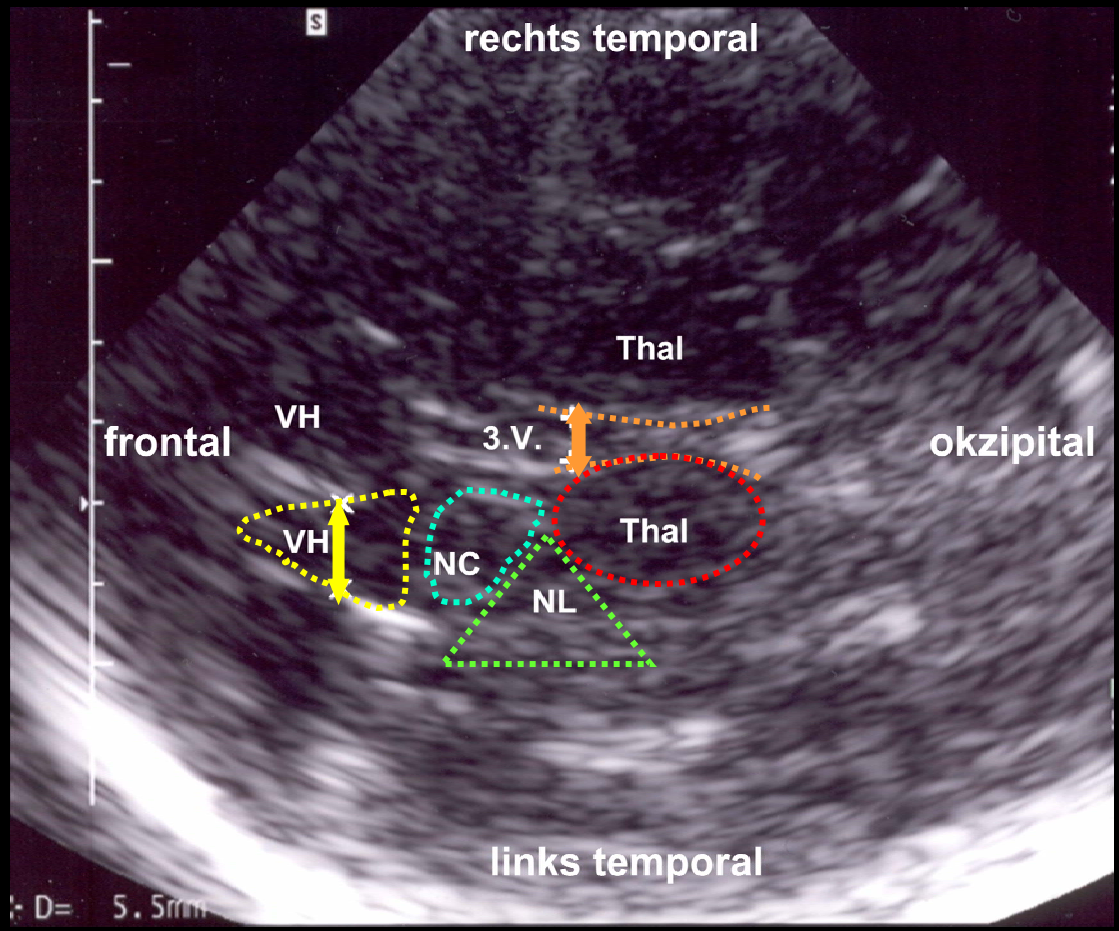
Frontal horn

Basal ganglia

Thalamus

Lenticular nucleus

Caudate nucleus

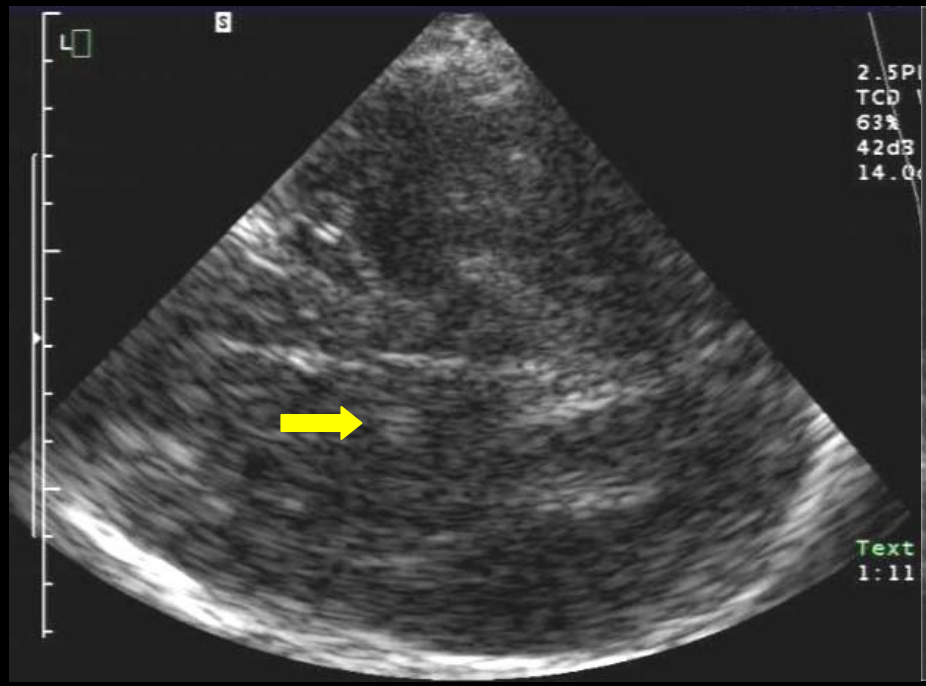


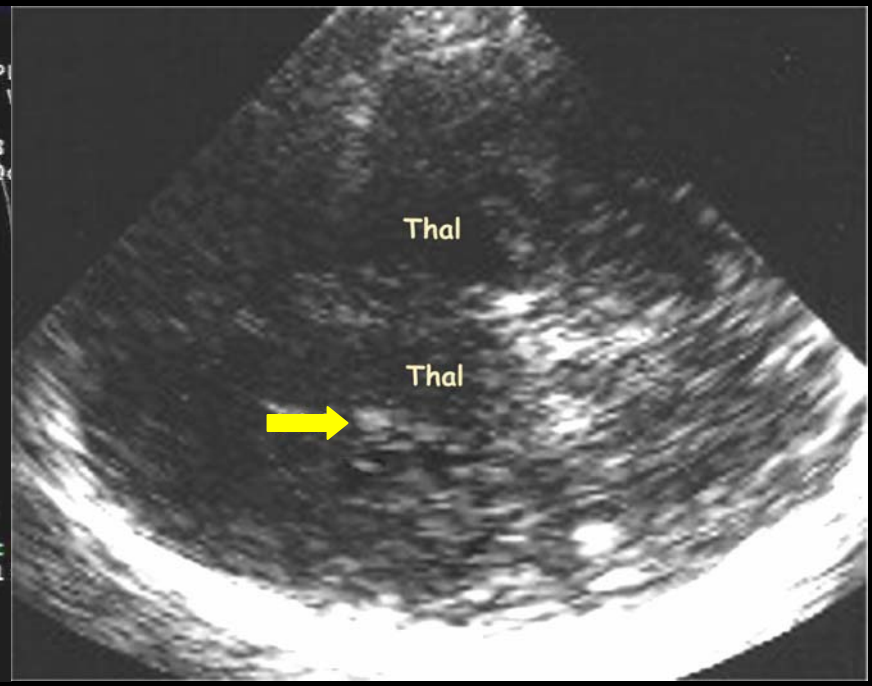
normal: isoechogenic to adjacent brain parenchyma

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

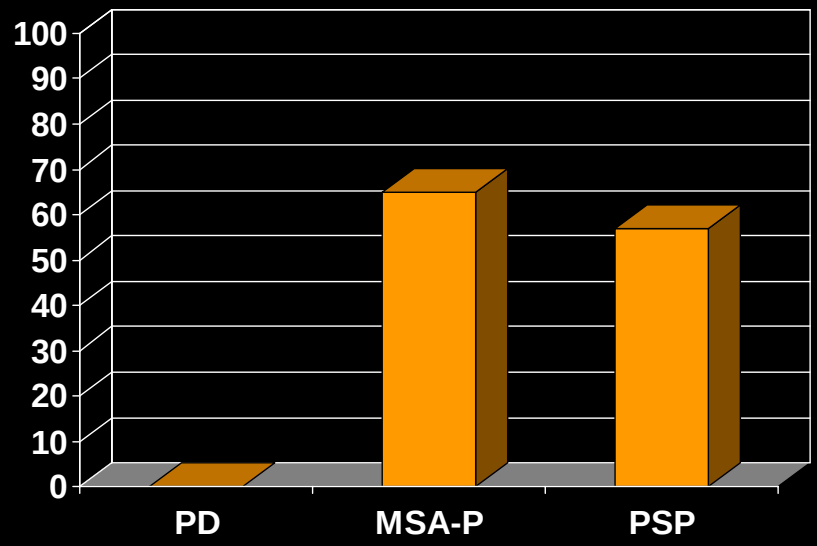
- In parkinsonism:
  - supports discrimination of atypical parkinsonian syndromes (MSA, PSP) and of welding-related parkinsonism from idiopathic PD Walter et al. *Arch Neurol* 2007, *Mov Disord* 2008

- In Wilson‘s disease:
  - present already in asymptomatic stages
  - correlates with severity of neurological symptoms

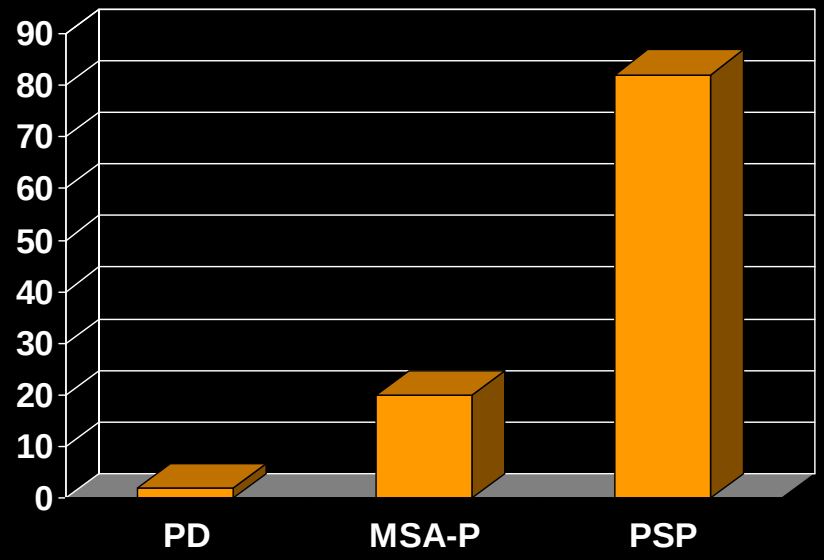
Walter et al. *Neurology* 2005

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

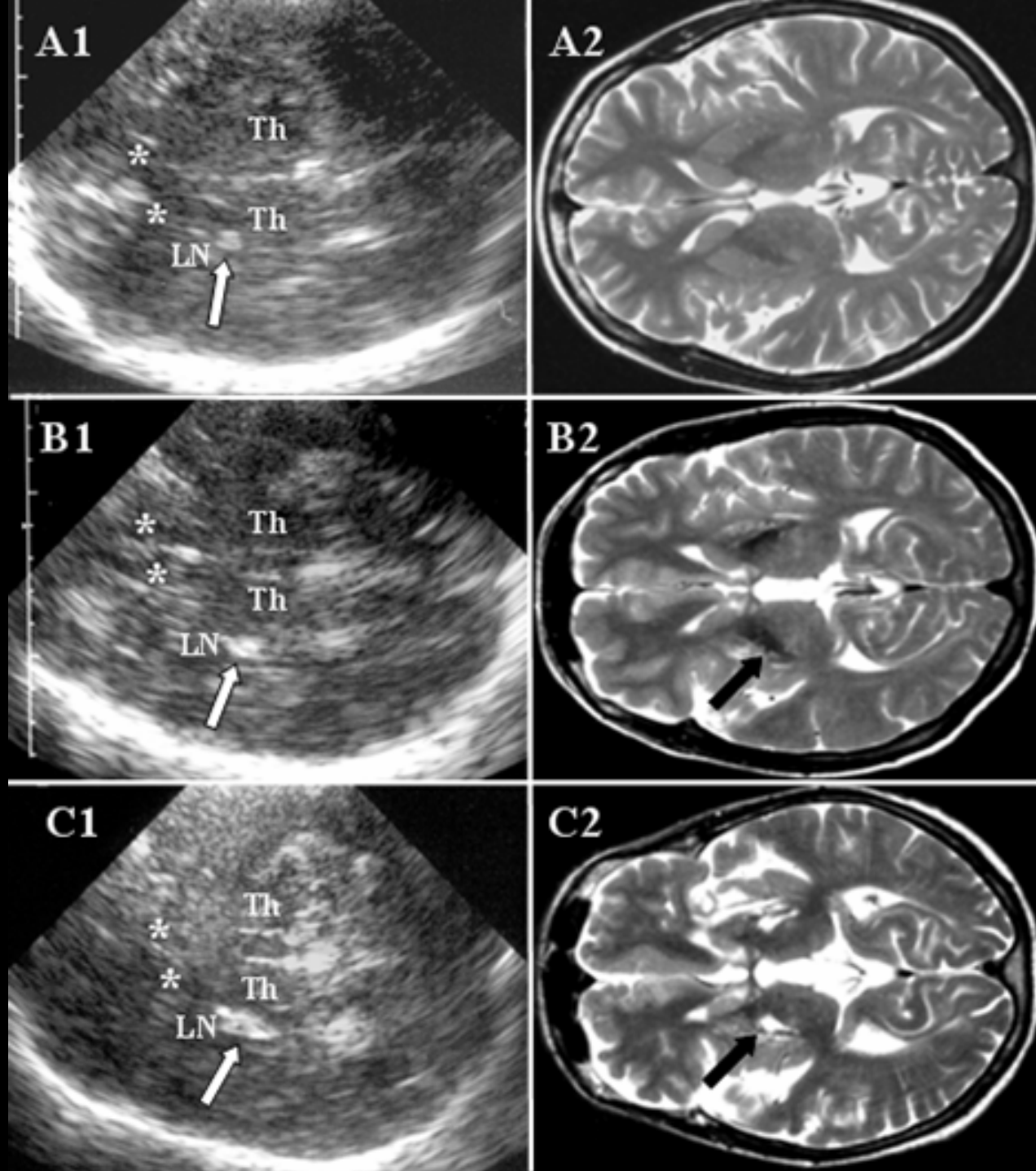


PD (n=138), probable MSA-P (n=21), probable PSP (n=22)

Walter et al. *Arch Neurology* 2007

Wilson's disease

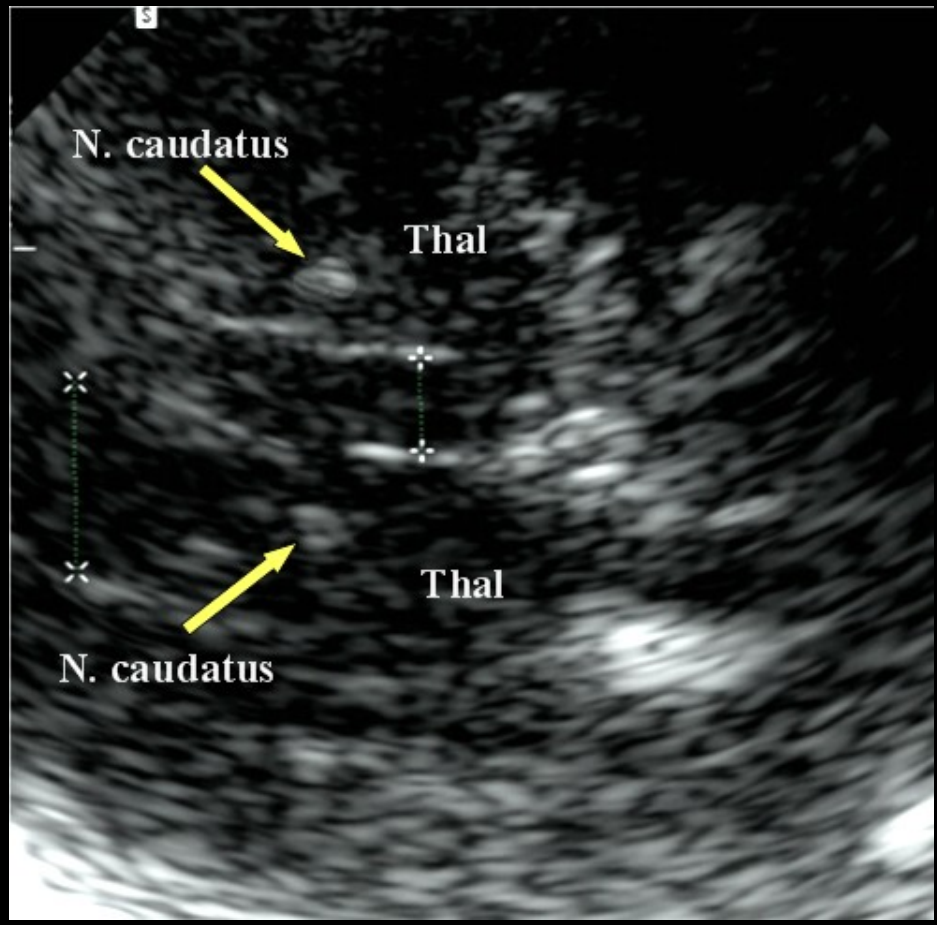
- Asymptomatic
- Moderate disease
- Severe disease



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

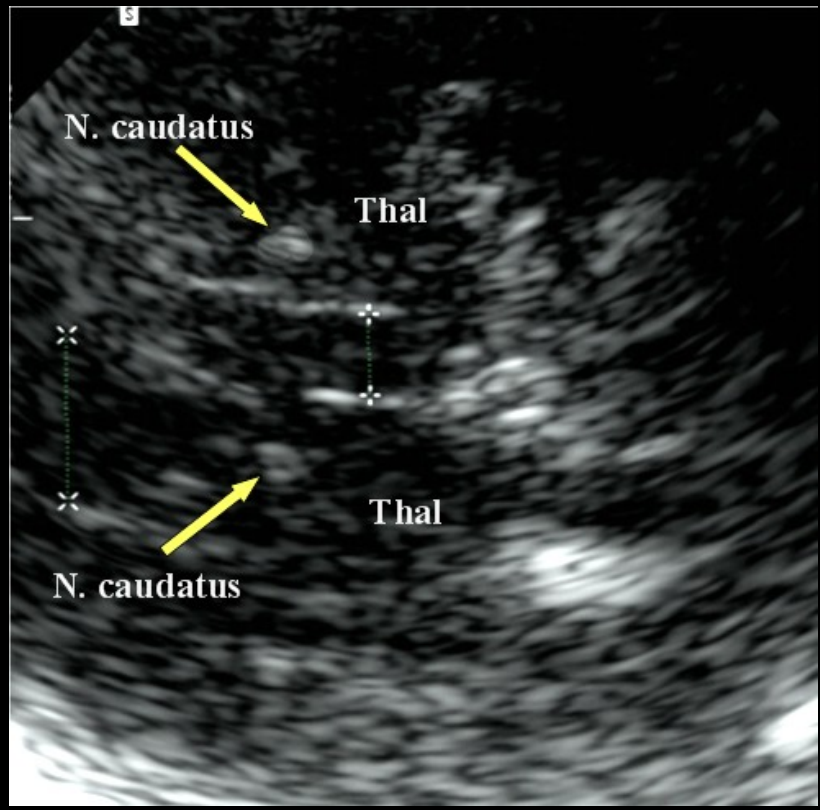
Caudate nucleus hyperechogenicity
Clinical relevance

- In Parkinson‘s disease:
  - correlates with occurence of levodopa-induced psychosis

    Walter et al. *Mov Disord* 2007

- In Huntington‘s disease:
  - discriminates HD from secondary forms of Chorea

    Postert et al. *JNNP* 1998
    Walter et al. (unpublished)

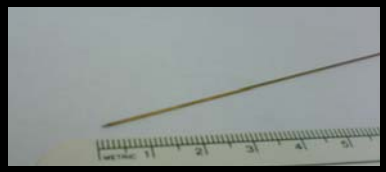


6. Clinical relevance of DBS electrode localization

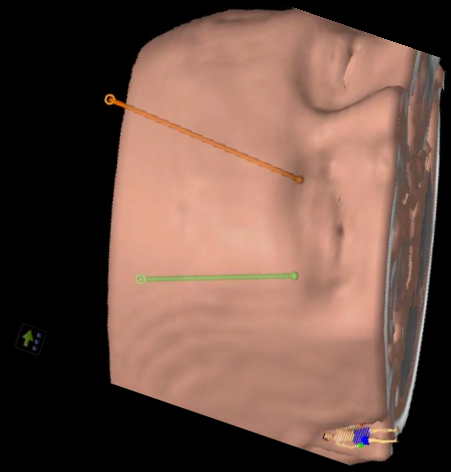
TCS in deep brain stimulation (DBS)

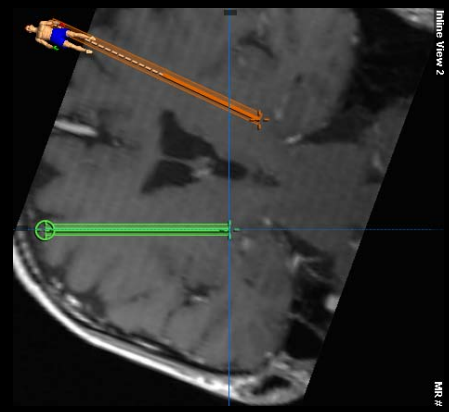
Perioperative monitoring of DBS electrode implantation

Microelectrode

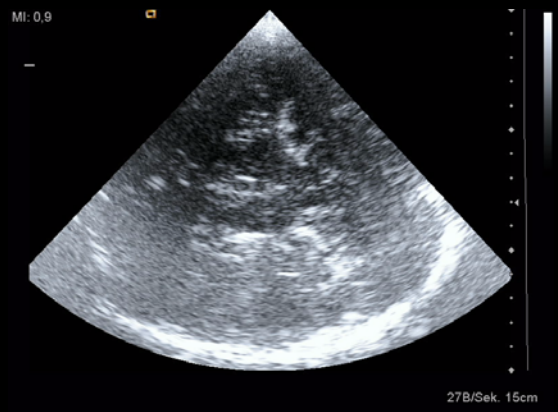


Macroelectrode

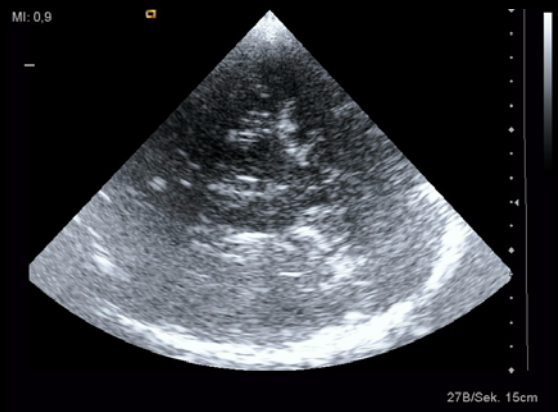




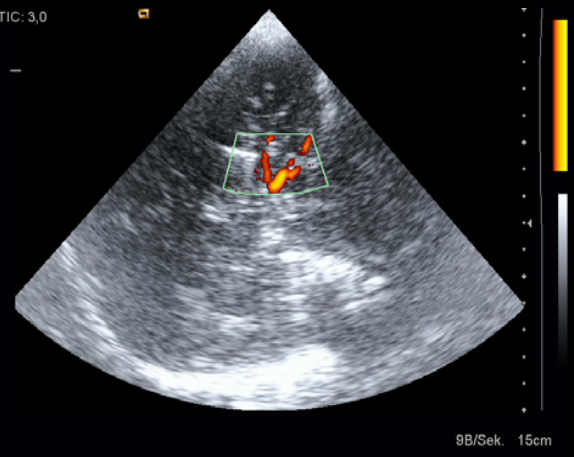
Microelectrode 2



Microelectrode 3



Macroelectrode

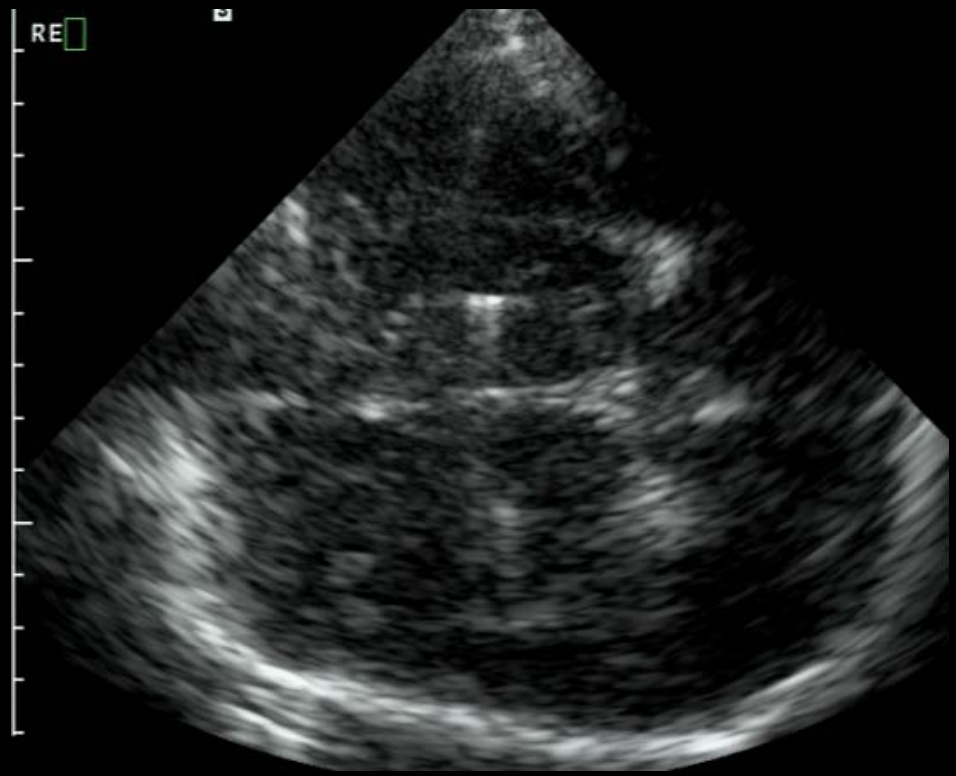


TCS in deep brain stimulation (DBS)
Electrode [ø 0.8 mm] artifacts in axial section

- Artifact in
  axial direction
  2.0-2.5 mm

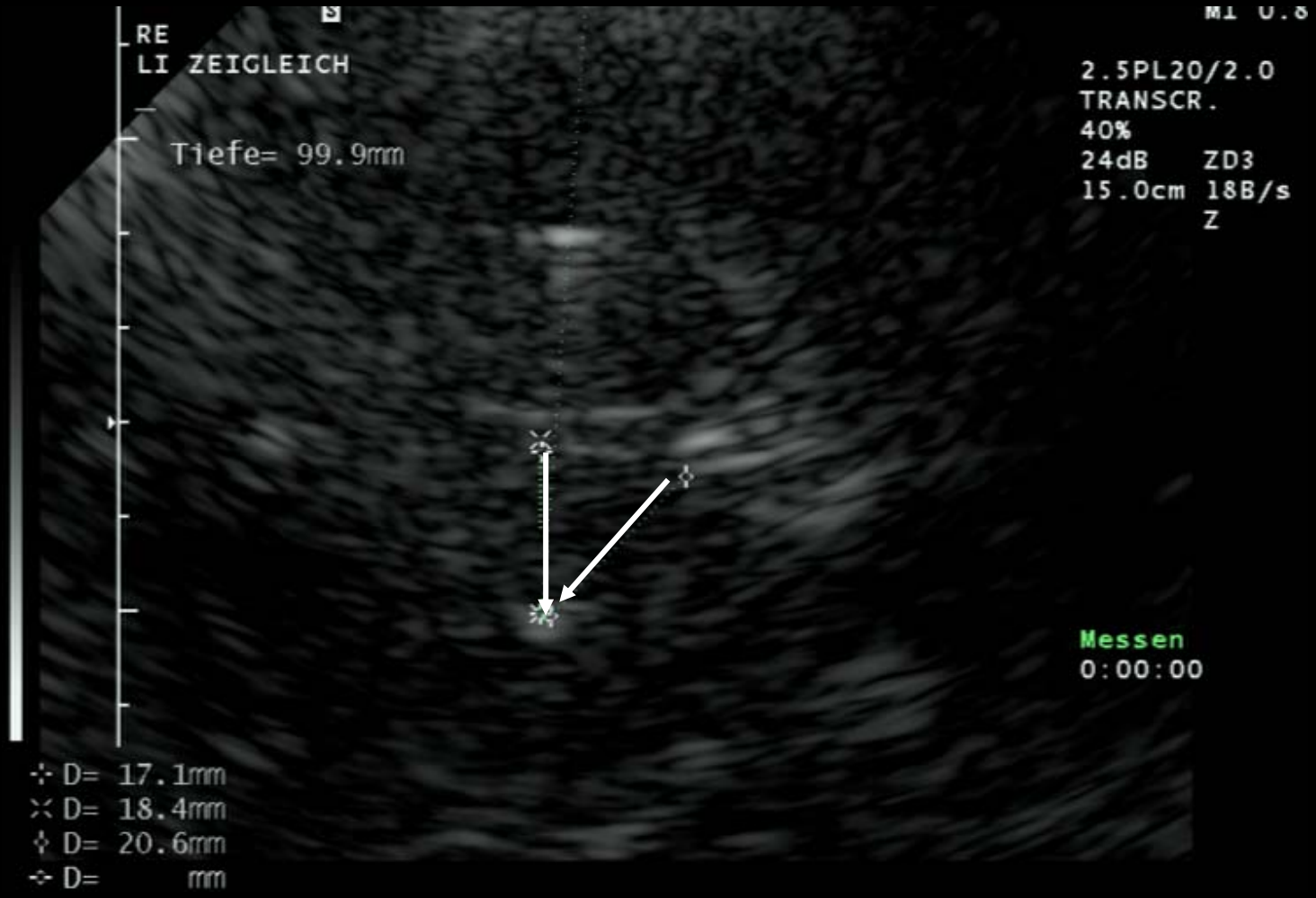
- Artifact in lateral
  direction
  4-5 mm

- 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 und slower progression of disease
- Midbrain raphe reduced echogenicity correlates:
  - in depressive disorders with better SSRI response
  - in PD patients with mit 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