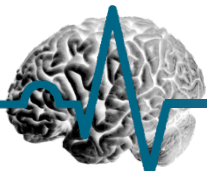


Neurologie im perioperativen Umfeld Pitfalls und Therapieoptionen

105 – na und?!
Anästhesie-, Intensiv- und Notfallmedizin im Alter

Bettina Pfausler
Universitätsklinik für Neurologie
Medizinische Universität innsbruck

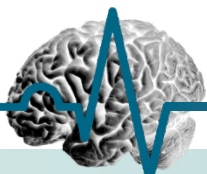


Konsiliaranforderung

- „bewegt nicht“
- „wacht nicht auf“
- „verwirrt“
- „bewegt zu viel (zuckt)“

Neurologische Erkrankungen mit höherer Prävalenz im Alter

- Neurodegenerative Erkrankung
 - Morbus Parkinson
 - Demenz
 - (- ALS)
- Neurovaskuläre Erkrankungen
- Epilepsie
- Schlafstörungen
 - Obstruktives Schlafapnoe Syndrom
 - Restless leg syndrome
- Polyneuropathie



~~Neurologische Erkrankungen des kritisch kranken Patienten als Folge der Intensivmedizin/therapie~~

~~Erworbene neuromuskuläre Erkrankungen (CIP/CIM)~~

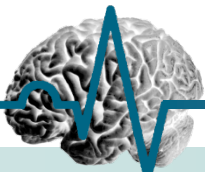
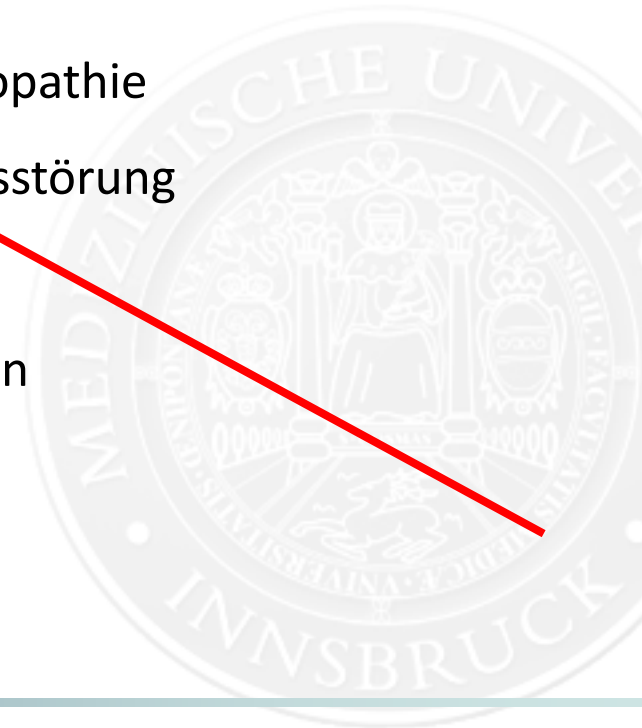
~~Pentane Myelinolyse~~

~~Reversible posteriore Leukenzephalopathie~~

~~Differentialdiagnose der Bewusstseinsstörung~~

~~Septische Enzephalopathie~~

~~Metabolische Enzephalopathien~~

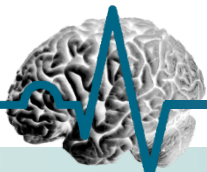


Epidemiologie

- Prävalenz 120-180/ 100 000
- Verteilung f > m (1,2:1)
- 2,5% > 65-jährigen, 3% >75-jährigen (10% vor dem 40. LJ) sind therapiebedürftig krank
- 15% > 65-jährigen haben klinische Zeichen eines Parkinson-Syndroms

Klinik

- Kombination aus **einseitiger** Bewegungsverlangsamung plus mindestens einem weiteren Symptom
 - > Rigor (Zahnradphänomen)
 - > Ruhetremor (Pillendrehtremor)
 - > Posturalen Reflexe (Haltungsstörung)



Pathogenese

- Degeneration der dopaminergen Zellen in der Substantia nigra
(symptomatische Schwelle bei 50% igem Zellverlust)

DA-Mangel im Striatum (Putamen)

- Sekundäre Überaktivität im Ncl. Subthalamicus und GPi
- vermehrte GABAerge Hemmung aus GPi auf den motorischen Thalamus
- Aktivitätsminderung thalamocorticaler motorischer Projektionen
- Unteraktivität prämotorischer kortikaler Areale und der SMA



Non motor symptoms

- Schluckfrequenz ↓
- oropharyngeale Dysphagie
- ösophagealer Transit ↓, air trapping, gastro-ösophagealer reflux
- Gastroparese
- Dünndarmatonie
- Megacolon, Volvulus
- Anorectale Dysfunktion
- neurogene Blasenstörung
- orthostatische Hypotonie
- psychiatrische Störungen
(Depressio, Halluzination, Demenz)

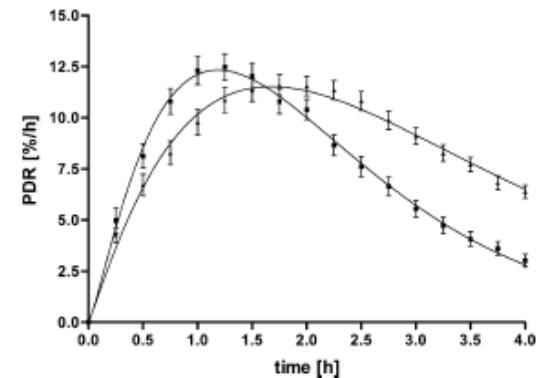
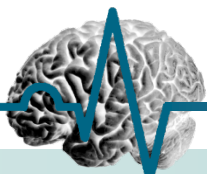


Fig. 1. Mean $^{13}\text{CO}_2$ excretion in function of time in 36 patients with Parkinson's disease (▲) and in 22 controls (■). Gastric emptying was determined from the measurement of $^{13}\text{CO}_2/^{12}\text{CO}_2$ -isotopic ratio in breath samples collected after ingestion of a solid test meal (241 kcal) labelled with 100 mg ^{13}C -sodium octanoate using isotope selective infrared spectroscopy. Data is given as mean \pm S.E.M. and fitted curves are interpolated.



Dopamin-Mangelsyndrom

Prevention and treatment of malignant syndrome in Parkinson's disease: a consensus statement of the malignant syndrome research group

Parkinsonism &
Related Disorders

Shin-ichiro Ikebe^a, Toshiaki Harada^b, Takao Hashimoto^c, Ichiro Kanazawa^d, Sadako Kuno^e, Yoshikuni Mizuno^{a,*}, Eiji Mizuta^e, Miho Murata^f, Toshiharu Nagatsu^g, Shigenobu Nakamura^b, Hideki Takubo^h, Nobuo Yanagisawaⁱ, Hirotarō Narabayashi^j

Events triggering MS in PD

Discontinuation of anti-parkinsonian drugs
Abrupt decrease of anti-parkinsonian drugs

Poor drug compliance

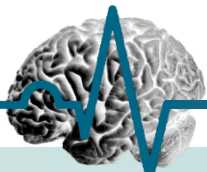
Intercurrent infections

Hot weather

Dehydration

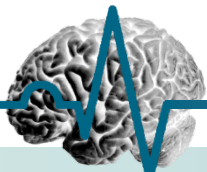
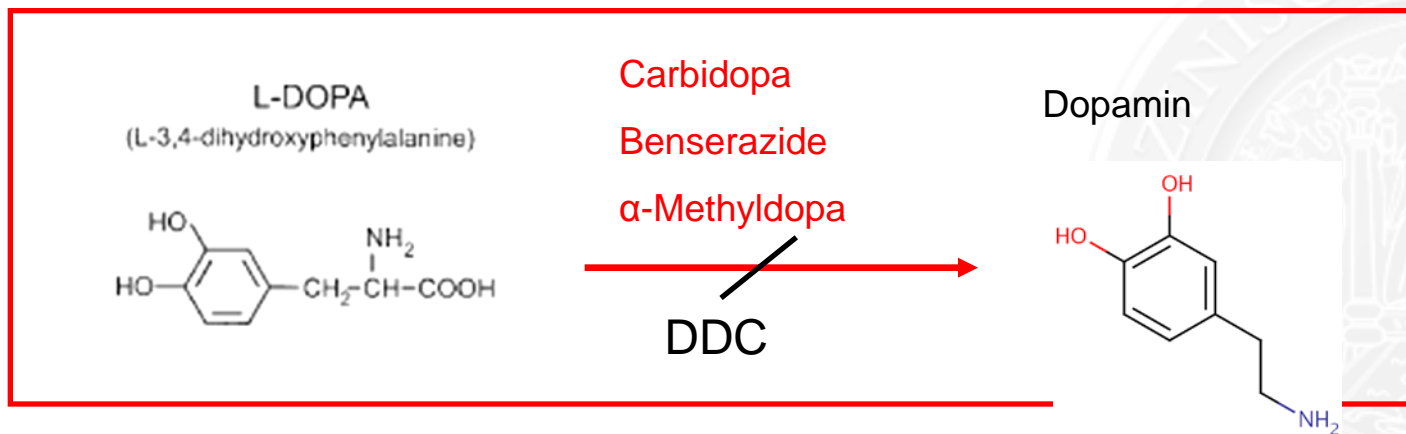
Motor fluctuations

Ileus



Therapie

- Prinzip: Dopaminsubstitution
- L-Dopa + Carbidopa oder Benserazide
- Carbidopa und Benserazide verhindern die periphere Umwandlung von L-Dopa zu Dopamin



Therapie

Dopaminerge Therapie

L-Dopa + Decarboxylase-Hemmer (Madopar, Sinemet)
L-Dopa + DDC Inhibitor + COMT-Hemmer (Stalevo)

Dopaminagonisten

Pramipexol (Sifrol)
Ropirinol (Requip)

Rotigotin (als Pflaster erhältlich)
Apomorphin (nur sc.)

Bromocriptin, Cabergolin, Pergolid

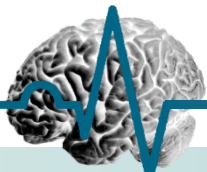
Nur
po.
Gabe
möglich

Nicht dopaminerge Therapie

Amantadin (iv. Gabe möglich)

MAO-B Hemmer (Cave: Interaktionen mit SSRI)

Agonisten 2.Wahl



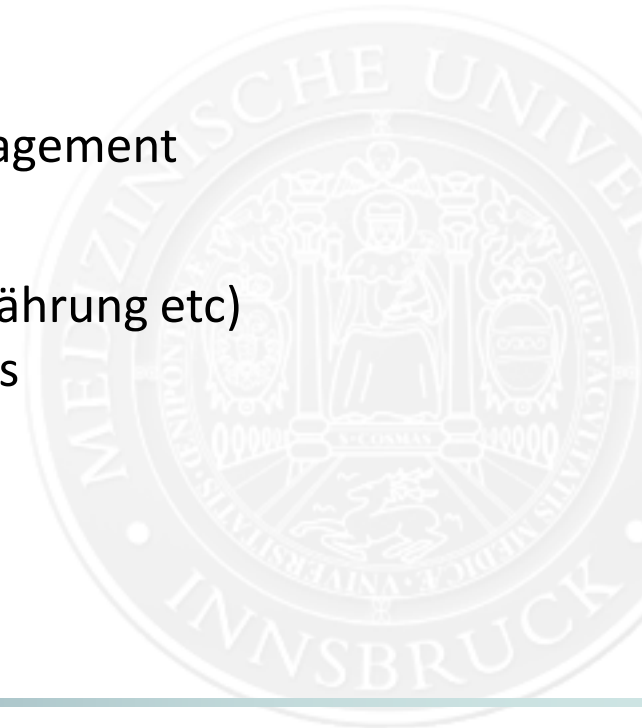
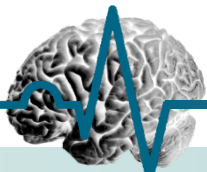
Parkinson – Risikoeinstufung

- Krankheitsdauer > 5 Jahre
- L-Dopa Substitution > 600mg/die
- L-Dopa Langzeitsyndrom (on-off Fluktuationen)
- 2-3 fach Kombinationen der Parkinsontherapie
- Demenz
- Kreislaufdysregulation

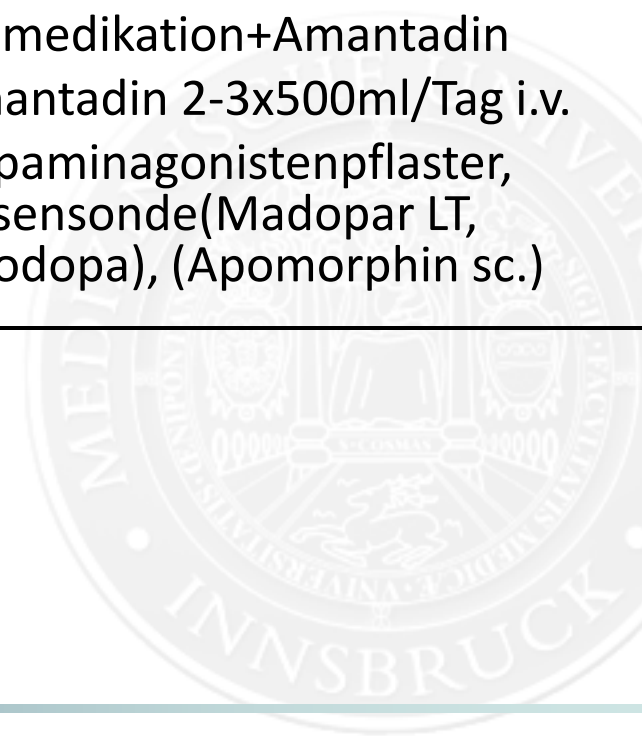
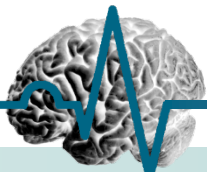
Adaptierte Risikoabschätzung im perioperativen Management

- Dauer und Schwere des Eingriffs
- Art und Ort des Eingriffs (GI Trakt, orale Ernährung etc)
- OP Dauer und postoperative Rekonvaleszenz

Interdisziplinäres Wahrnehmen des Problems/Risikos



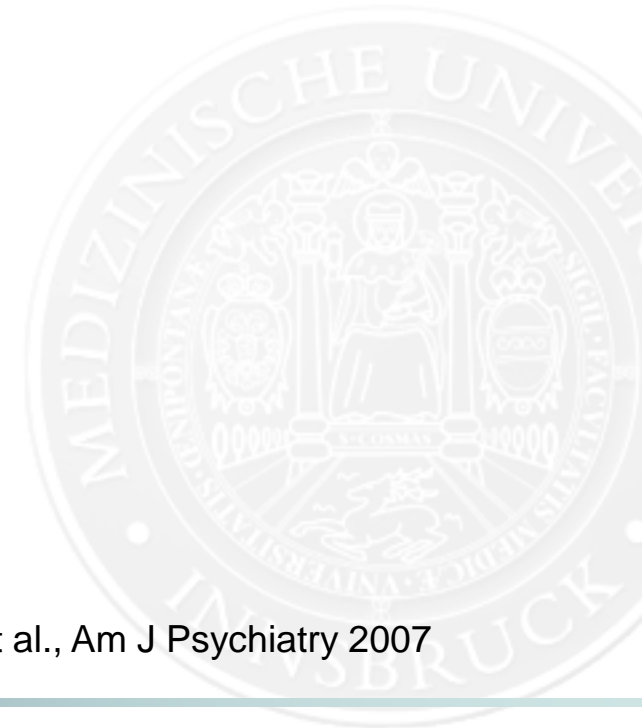
PD Stadium	OP Dauer	postOP	Parkinson Medikation
Frühstadium	< 3 Stunden	kurz, kein GI	Beibehalten der Medikation
Frühstadium	> 3 Stunden	lang, GI	Prämedikation+Amantadin
Spätstadium	< 3 Stunden	kurz	Prämedikation+Amantadin
Spätstadium	> 3 Stunden	lang, GI	Amantadin 2-3x500ml/Tag i.v. Dopaminagonistenpflaster, Nasensonde(Madopar LT, Duodopa), (Apomorphin sc.)



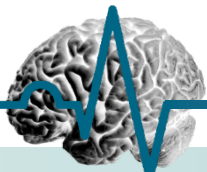
Pathophysiologie des Dopaminmangelsyndroms

-

Dopamine
deficiency
DA Antagonists



Adapted, Strawn et al., Am J Psychiatry 2007



Klinik des Dopaminmangelsyndroms

Clinical features of levodopa withdrawal malignant syndrome

Elevation of body temperature (up to 40 °C)

Marked rigidity

Altered consciousness

Autonomic disturbance

 Tachycardia

 Perspiration

 Anhidrosis

 Non-obstructive ileus

 Fluctuation of the blood pressure

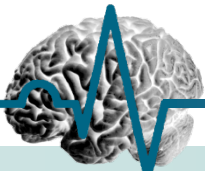
 Vocal cord paralysis

Elevation in serum creatine kinase

Rhabdomyolysis

DIC

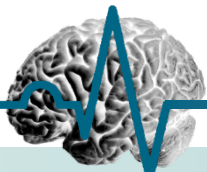
Acute renal failure (myoglobin plugging)



Differentialdiagnose des Dopaminmangelsyndroms

Clinical features of levodopa withdrawal malignant syndrome, neuroleptic malignant syndrome, and malignant hyperthermia

	Levodopa withdrawal malignant syndrome	Neuroleptic malignant syndrome	Malignant hyperthermia
Underlying disease	Parkinson's disease Secondary parkinsonism	Schizophrenia Manic depressive psychosis	Central core disease in some cases
Genetics	Sporadic	Sporadic	Autosomal dominant and sporadic
Triggering event	Withdrawal of anti-parkinsonian drugs, particularly levodopa	Neuroleptic drugs	Inhalation anesthesia
Muscle rigidity	Marked	Marked	Marked
Body temperature	Marked elevation	Marked elevation	Marked elevation
Consciousness	May be disturbed	May be disturbed	May be disturbed
Autonomic dysfunction	Present	Present	
Serum CK	Marked elevation	Marked elevation	Marked elevation
Rhabdomyolysis	May occur	May occur	May occur



Therapie des Dopaminentzugsyndroms (akinetische Krise)

- Guidelines 2003, Ikebe et al, Parkinsonism & related Disorders nicht mehr aktuell, Neuentwicklungen nicht berücksichtigt!!

Empfehlung

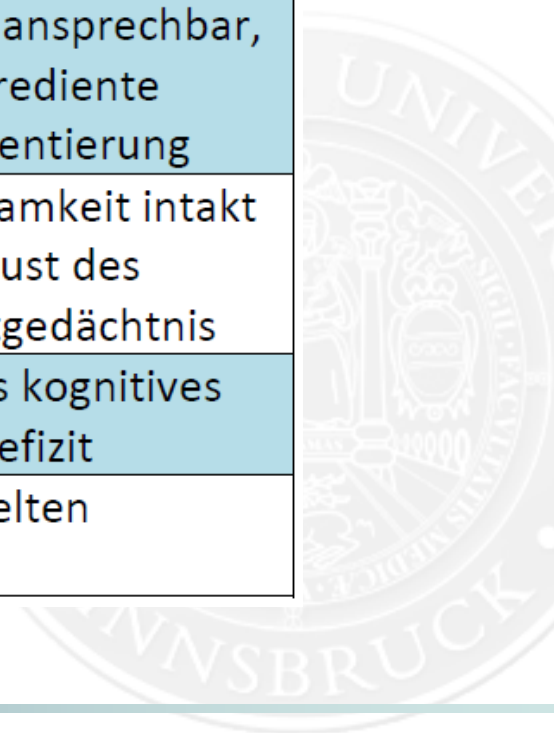
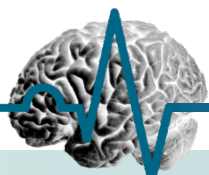
- Amantadin iv (max 600mg/die)
- L-Dopa Substitution über Nasensonde (Löstabletten, Pharmakokinetik beachten)

alternativ Apomorphin sc
 Rotigotin-Pflaster

- Normothermie mittels Kühlkatheter
- Hämofiltration bei Niereninsuffizienz
(- Dantrolen)



	Delirium	Demenz
Auftreten	akut	schleichend
Reversibilität	fluktuierend rasch	langsam fortschreitend
Bewusstsein und Orientierung	fluktuierende Vigilanz desorientiert	wach und ansprechbar, progrediente Desorientierung
Aufmerksamkeit und Gedächtnis	Aufmerksamkeitsdefizit Kurzzeitgedächtnis reduziert	Aufmerksamkeit intakt Verlust des Kurzzeitgedächtnis
Kognition	Teilleistungsstörungen	Globales kognitives Defizit
Psychotische Symptome	häufig, visuell	selten

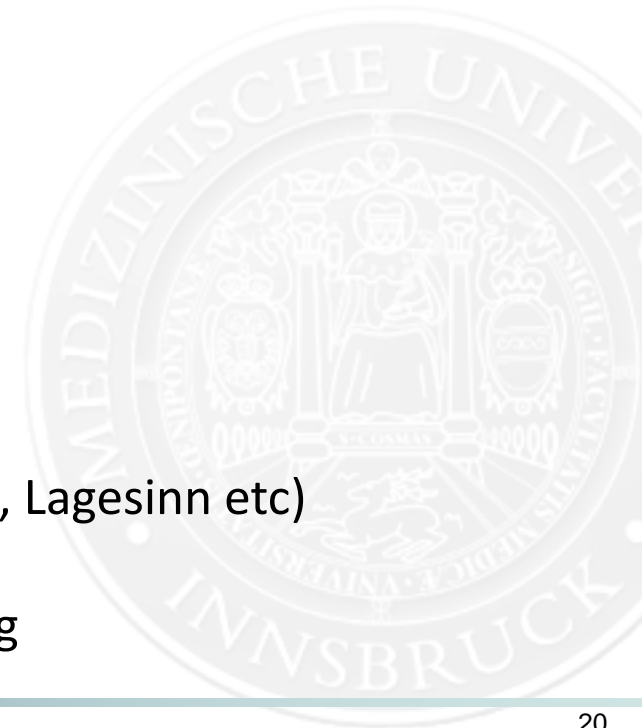
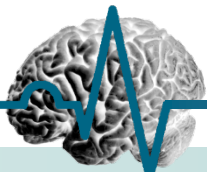


Risikofaktor Demenz

- 25% der deliranten Patienten sind dement /mild cognitive impairment
- 40% der dementen Patienten entwickeln im Krankenhaus ein Delir
- 30-40% der älteren Patienten haben ein Mild Cognitive Impairment bei Krankenhausaufnahme

Andere Faktoren

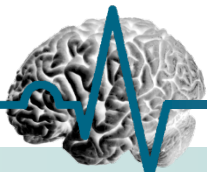
- Alter
- Komorbidität
- Operativen (Notfallsoperationen)
- Infekte/SIRS/Sepsis
- Hypotension
- Gestörter sensorischer Input (Hören, Sehen, Lagesinn etc)
- Kombination mehrerer Medikamente
- Neue Medikamente bzw Medikamentenentzug



Delir und Outcome

- Längerer Krankenhausaufenthalt
- Höhere Komplikationsrate
- Höhere Mortalität (20-70%)
- Schlechteres Rehabilitations-Outcome
- Höhere Pflegebedürftigkeit mit Transfer in Pflgeeinrichtungen
- Dauerhafte Verschlechterung der kognitiven Funktion im Lanagzeitverlauf (30-70%)

Marcantonio, Olofsson, Inoye, Ely



Epidemiologie des dementiellen Syndroms

	Age-group (years)					
	60-64	65-69	70-74	75-79	80-84	≥85
EURO A	0.9 (0.1)	1.5 (0.2)	3.6 (0.2)	6.0 (0.2)	12.2 (0.8)	24.8 (1.0)
EURO B	0.9 (0.1)	1.3 (0.1)	3.2 (0.3)	5.8 (0.3)	12.2 (0.3)	24.7 (2.3)
EURO C	0.9 (0.1)	1.3 (0.1)	3.2 (0.2)	5.8 (0.2)	11.8 (0.5)	24.5 (1.8)
AMRO A	0.8 (0.1)	1.7 (0.1)	3.3 (0.3)	6.5 (0.5)	12.8 (0.5)	30.1 (1.1)
AMRO B	0.8 (0.1)	1.7 (0.1)	3.4 (0.2)	7.6 (0.4)	14.8 (0.6)	33.2 (3.5)
AMRO D	0.7 (0.1)	1.5 (0.3)	2.8 (0.4)	6.2 (1.1)	11.1 (2.0)	28.1 (5.2)
EMRO B	0.9 (0.3)	1.8 (0.1)	3.5 (0.3)	6.6 (0.2)	13.6 (0.8)	25.5 (2.3)
EMRO D	1.2 (0.3)	1.9 (0.2)	3.9 (0.3)	6.6 (0.4)	13.9 (1.3)	23.5 (2.3)
WPRO A	0.6 (0.1)	1.4 (0.1)	2.6 (0.3)	4.7 (0.6)	10.4 (1.2)	22.1 (3.5)
WPRO B	0.6 (0.1)	1.8 (0.2)	3.7 (0.4)	7.0 (0.9)	14.4 (1.9)	26.2 (3.9)
SEARO B	1.0 (0.1)	1.7 (0.2)	3.4 (0.2)	5.7 (0.5)	10.8 (1.2)	17.6 (2.7)
SEARO D	0.4 (0.1)	0.9 (0.1)	1.8 (0.2)	3.7 (0.4)	7.2 (1.2)	14.4 (2.7)
AFRO D	0.3 (0.1)	0.6 (0.1)	1.3 (0.2)	2.3 (0.5)	4.3 (1.0)	9.7 (1.9)
AFRO E	0.5 (0.3)	1.0 (0.4)	1.9 (0.9)	3.8 (1.7)	7.0 (3.6)	14.9 (7.2)

Table 1: Group mean consensus estimates (SD) for prevalence of dementia (%) for each region and age-group

Lancet 2005; 366: 2112-17



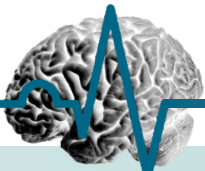
Pathophysiologie des Delirs (viele Hypothesen, multifaktoriell)

Neuro-Transmitter

- **Dopaminerge** Hyperaktivität und Depletion der cerebralen **cholinergen** Speicher
- **Serotonin** Imbalanz und **noradrenerge** Hyperaktivität

+

- Sepsis und Inflammation (-> Endotoxine, Cytokine etc)
- inadequate zerebrale Perfuion (-> Hypoxämie)
- Metabolische Störungen (-> Hyperglykämie, LFP, NFP)
- Medikamente (-> Sedativa, Analgetika [Acetylcholin, Dopamin, Serotonin, GABA, Glutamat, Norepinephrin], H₂-Blocker, Antibiotika etc.)



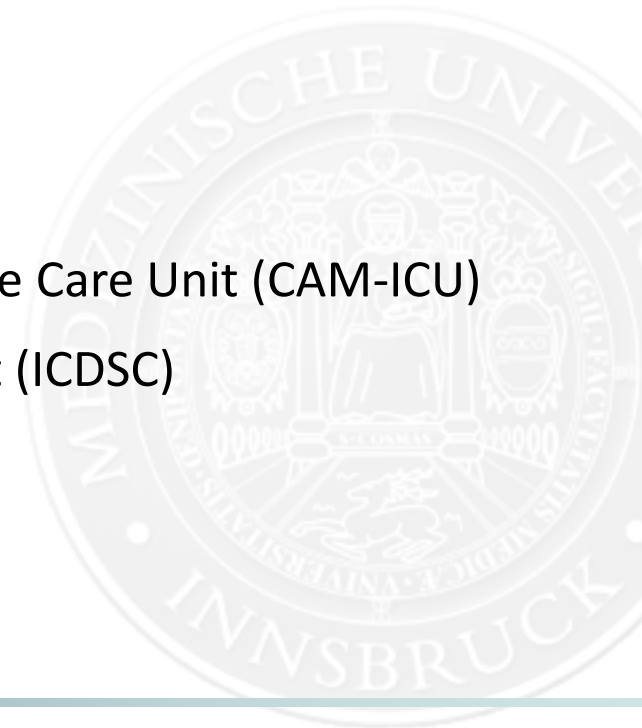
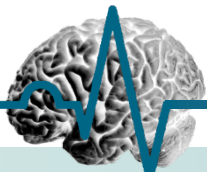
Screening und Assessment-Instrumente

Sedierung und Agitation

- Sedation Agitation Scale (SAS)
- Richmond Agitation Sedation Scale (RASS)
- Motor Activity Assessment Scale (MAAS)

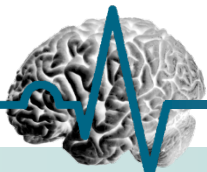
Delirium

- Confusion Assessment Method for Intensive Care Unit (CAM-ICU)
- Intensive Care Delirium Screening Checklist (ICDSC)
- Delirium Detection Score (DDS)



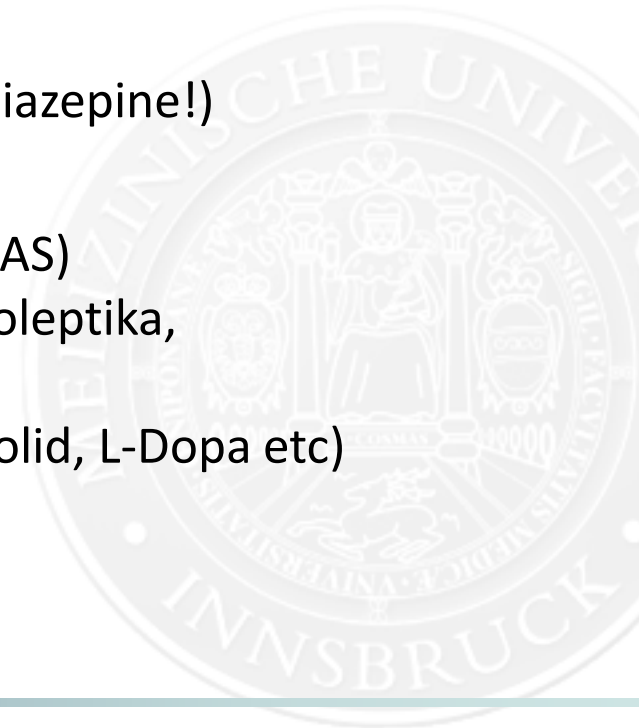
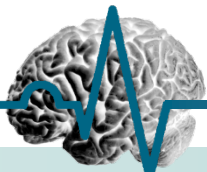
Therapie

- Vermeidung der möglichen auslösenden Faktoren
- Symptomatische Therapie
 - Neuroleptika -> typische Neuroleptika
(Haloperidol –Zulassungsänderung 2010)
-> atypische Neuroleptika
(Clozapin, Risperidon, Quetiapin, Olanzapin, Ziprasidon[im])
 - Benzodiazepine -> paradoxer Effekt
-> schlechteres kognitives Outcome
 - Propofol (-> Hypotonie)
 - Ketamin
- Physiostigmin (Anticholinium®) bei ZAS



Differentialdiagnose

- Septische Enzephalopathie
- Metabolische Enzephalopathie (Leber, Niere, Hypovitaminose etc)
- Fokale intracranielle Prozesse
- Meningitis / Encephalitis
- Substanzmissbrauch / Entzug (Cave: Benzodiazepine!)
- Medikamente
 - Zentral anticholinerges Syndrom (ZAS)
(-> H₂ Rezeptor- Blocker, SSRI, Neuroleptika, Benzodiazepine etc)
 - Serotonerges Syndrom (SSRI, Linezolid, L-Dopa etc)



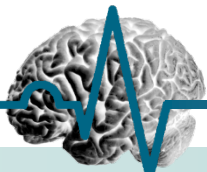
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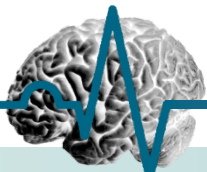
Impact of aging on cerebral vasoregulation and parenchymal integrity

Tomáš Peisker ^{a,*}, Aleš Bartoš ^a, Ondřej Škoda ^b, Ibrahim Ibrahim ^c, Pavel Kalvach ^a

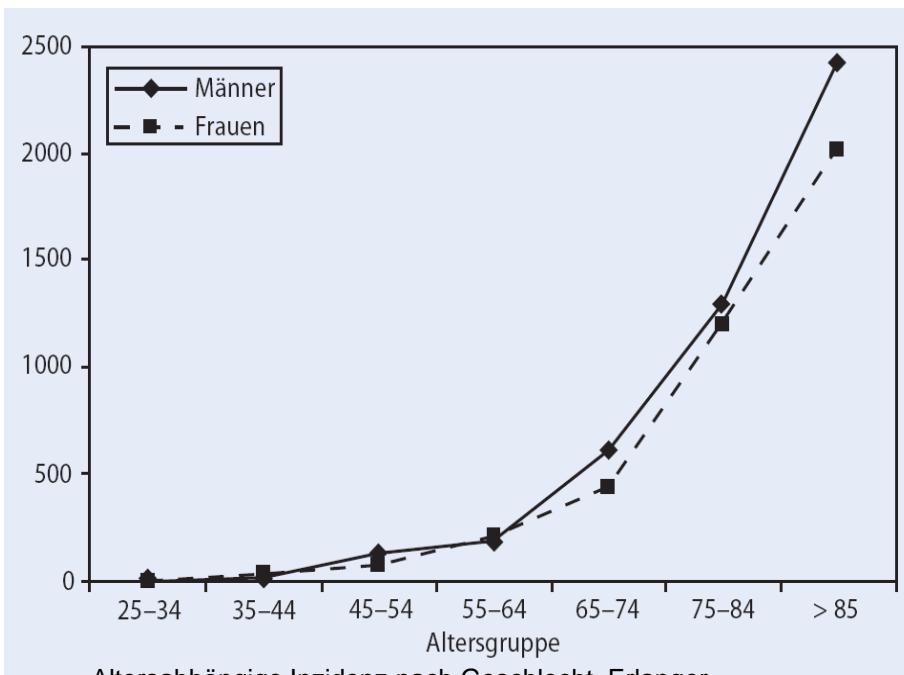
^a Department of Neurology, Charles University, 3rd Medical Faculty, FNKV, Šrobárova 50, 100 34 Prague 10, Czech Republic

^b Department of Neurology, District hospital, Jihlava, Czech Republic

^c Department of Radiology, Institute of Experimental Medicine, Vídeňská 800, 140 00 Prague 4, Czech Republic



Epidemiologie im Alter



Altersabhängige Inzidenz nach Geschlecht. Erlanger Schlaganfall-Register bezogen auf 100.000 EW

Silent stroke

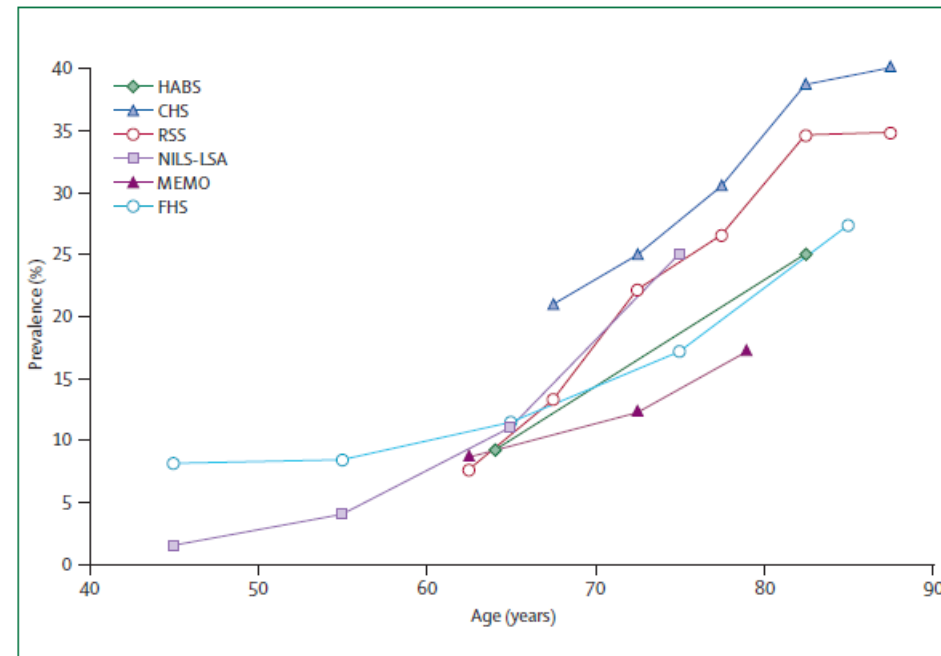
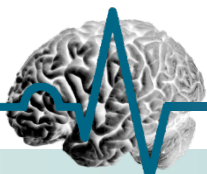


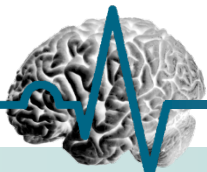
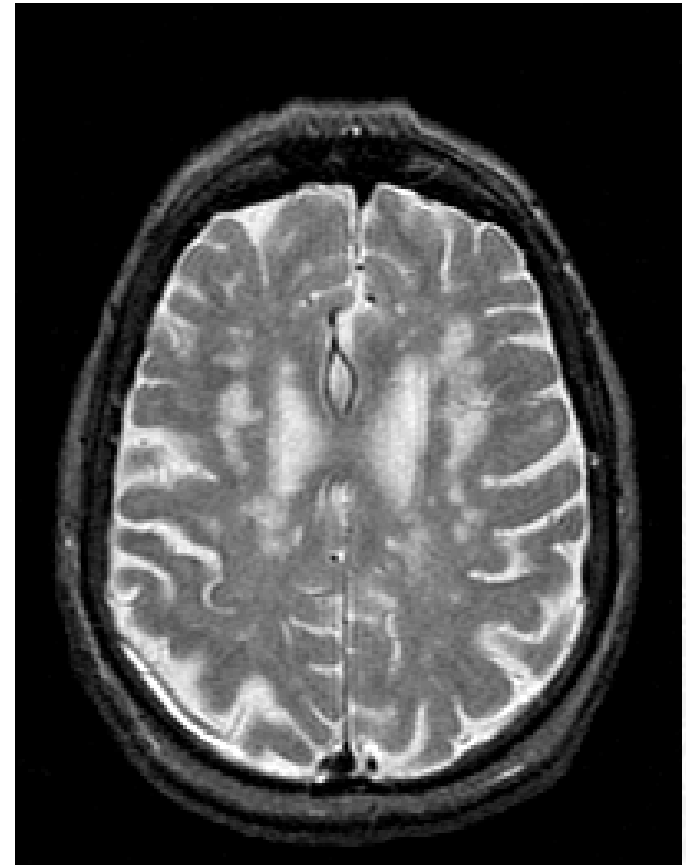
Figure 2: Prevalence of silent brain infarcts with increasing age, as reported in six population-based studies HABS, Helsinki (Finland) Aging Brain Study;⁹ CHS, Cardiovascular Health Study;¹⁰ RSS, Rotterdam Scan Study;¹¹ NILS-LSA, National Institute for Longevity Sciences-Longitudinal Study of Aging;¹² MEMO, Memory and Morbidity in Augsburg Elderly study;¹⁴ and FHS, Framingham Heart Study.¹⁵

Lancet Neurol 2007; 6: 611-19

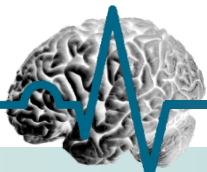
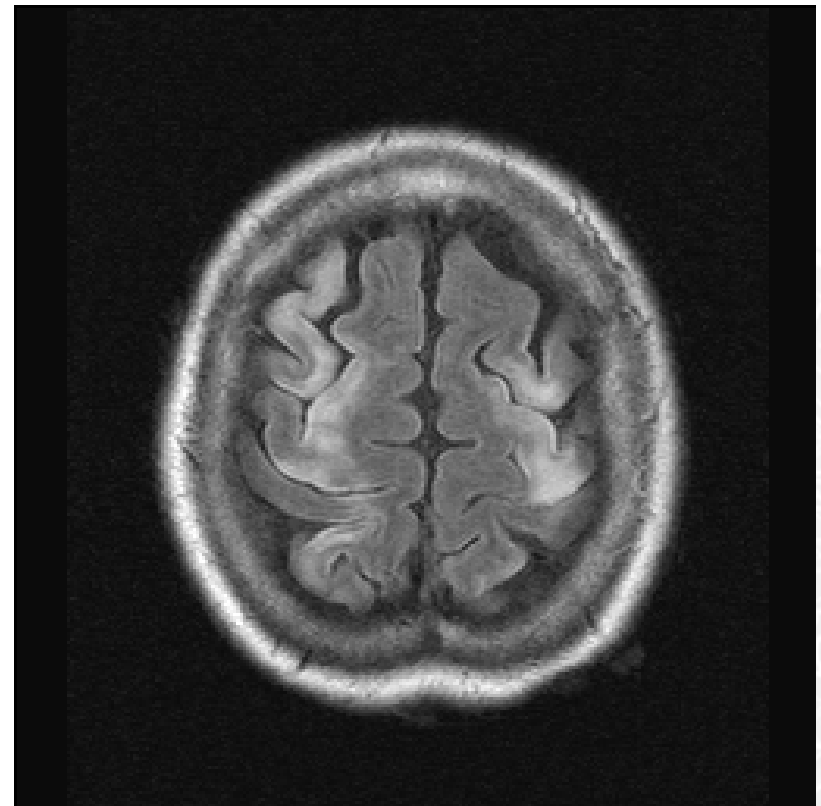


Silent Stroke

- häufig
- Small vessel disease
- Hypertonus
- keineswegs still
- Risikofaktor für manifesten Schlaganfall und Demenz



Hämodynamische Infarkte („low flow“ Infarkte, "letzte Wiese")



Blutdruckmanagement bei chronisch neurovaskulären Veränderungen

Recommendations

1. BP reduction is recommended for both prevention of recurrent stroke and prevention of other vascular events in persons who have had an ischemic stroke or TIA and are beyond the first 24 hours (*Class I; Level of Evidence A*).
2. Because this benefit extends to persons with and without a documented history of hypertension, this recommendation is reasonable for all patients with ischemic stroke or TIA who are considered appropriate for BP reduction (*Class IIa; Level of Evidence B*).
3. An absolute target BP level and reduction are uncertain and should be individualized, but benefit has been associated with an average reduction of approximately 10/5 mm Hg, and normal BP levels have been defined as <120/80 mm Hg by JNC 7 (*Class IIa; Level of Evidence B*).
4. Several lifestyle modifications have been associated with BP reduction and are a reasonable part of a comprehensive antihypertensive therapy (*Class IIa; Level of Evidence C*). These modifications include salt restriction; weight loss; consumption of a diet rich in fruits, vegetables, and low-fat dairy products; regular

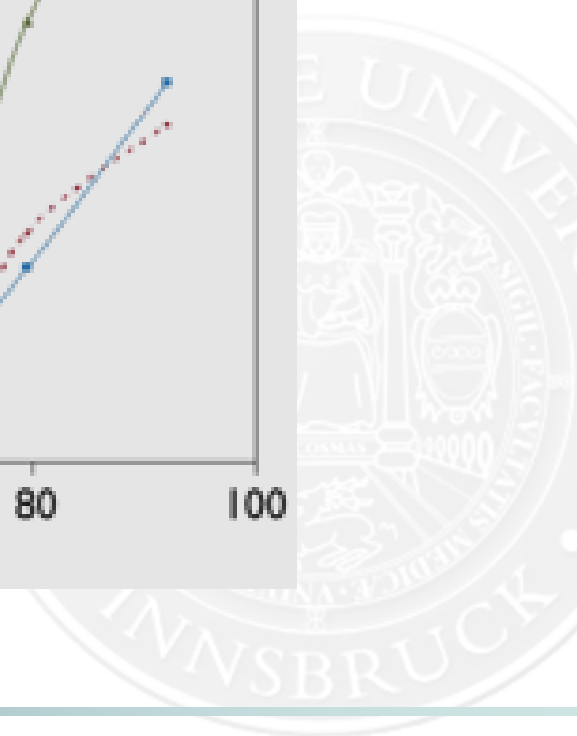
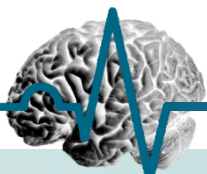
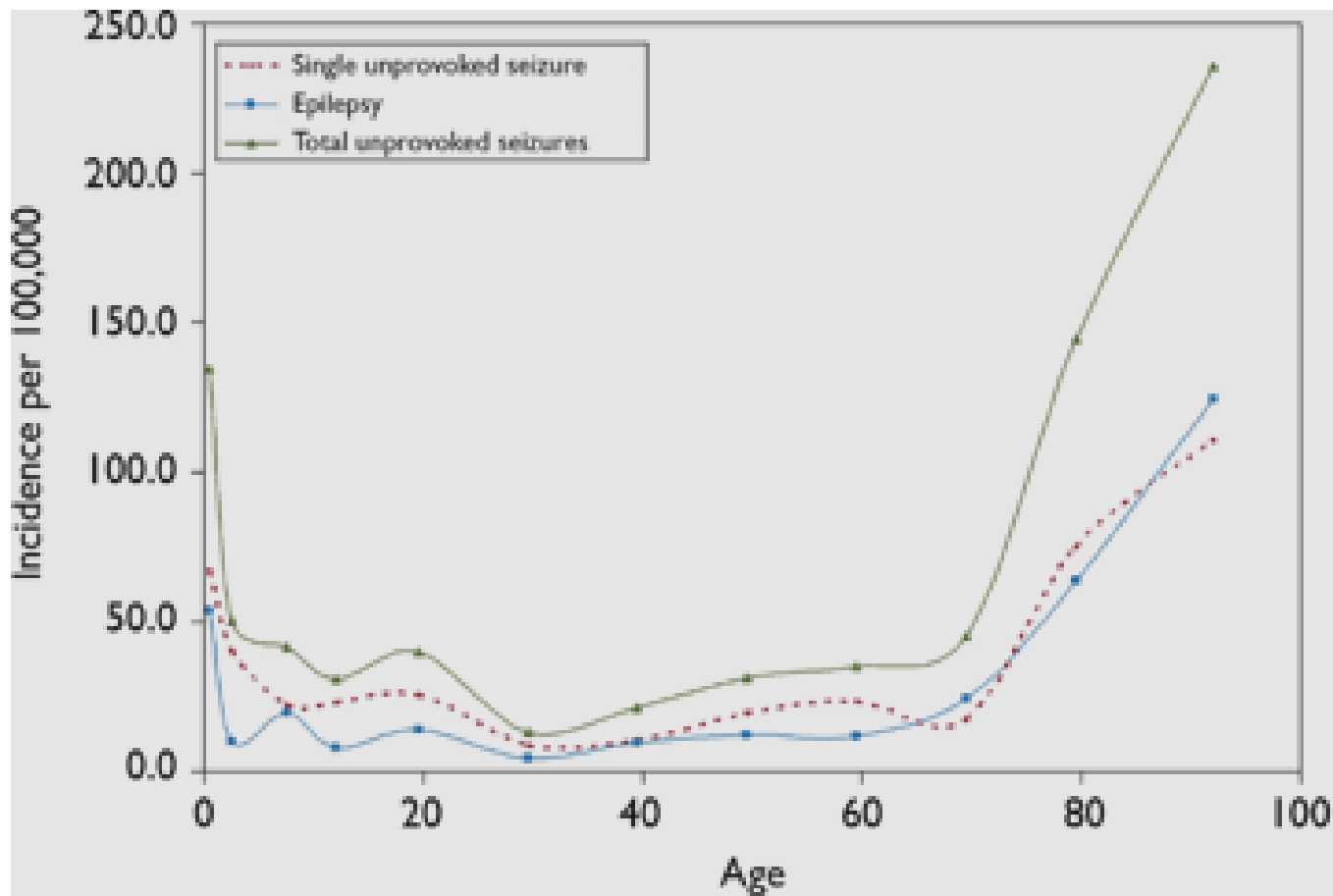
aerobic physical activity; and limited alcohol consumption.

5. The optimal drug regimen to achieve the recommended level of reduction is uncertain because direct comparisons between regimens are limited. The available data indicate that diuretics or the combination of diuretics and an ACEI are useful (*Class I; Level of Evidence A*). The choice of specific drugs and targets should be individualized on the basis of pharmacological properties, mechanism of action, and consideration of specific patient characteristics for which specific agents are probably indicated (eg, extracranial cerebrovascular occlusive disease, renal impairment, cardiac disease, and diabetes) (*Class IIa; Level of Evidence B*). (New recommendation; Table 3)

(*Stroke*. 2011;42:227-276.)



Epidemiologie



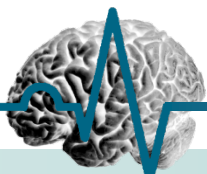
New-Onset Epilepsy Risk Factors in Older Veterans

Mary Jo V. Pugh, PhD, RN,^{*†} Janice E. Knoefel, MD,[‡] Eric M. Mortensen, MD, MSc,^{*†}
Megan E. Amuan, MPH,[§] Dan R. Berlowitz, MD, MPH,^{§||} and Anne C. Van Cott, MD^{||#**}

JAGS 57:237–242, 2009

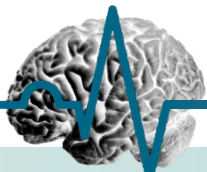
CNS risk factors		
Stroke*	700 (37.9)	151,971 (14.9)
Dementia*	308 (16.7)	67,236 (6.6)
Brain tumor*	29 (1.6)	5,833 (0.6)
Head injury	26 (1.4)	3,805 (0.4)
Other CNS disorders*	160 (8.7)	36,842 (3.6)
Systemic cerebrovascular risk factors		
Cardiovascular disease*	674 (36.6)	312,334 (30.5)
Peripheral vascular disorders*	363 (19.7)	164,150(16.0)
Hypertension*	1,389 (75.4)	734,477 (71.8)
Diabetes mellitus	566 (30.7)	301,487 (29.5)
Obesity*	181 (9.9)	137,542 (13.4)
Hypercholesterolemia*	638 (34.6)	434,628 (42.5)
Alcohol abuse or dependence*	130 (7.1)	42,470 (4.2)

*p < 0,001

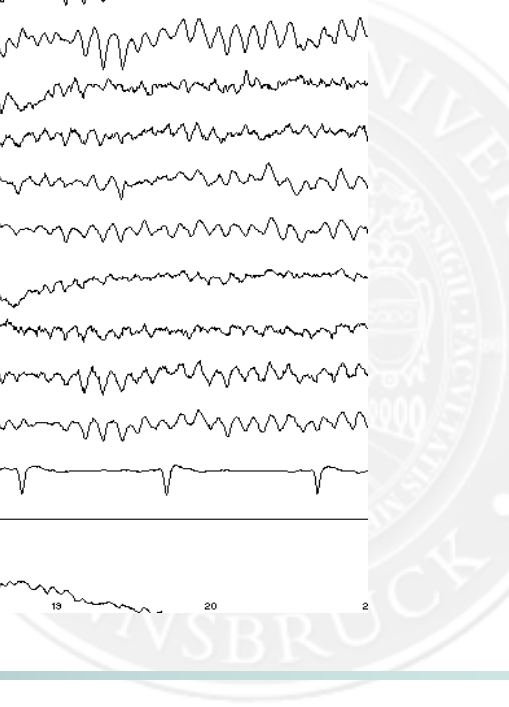
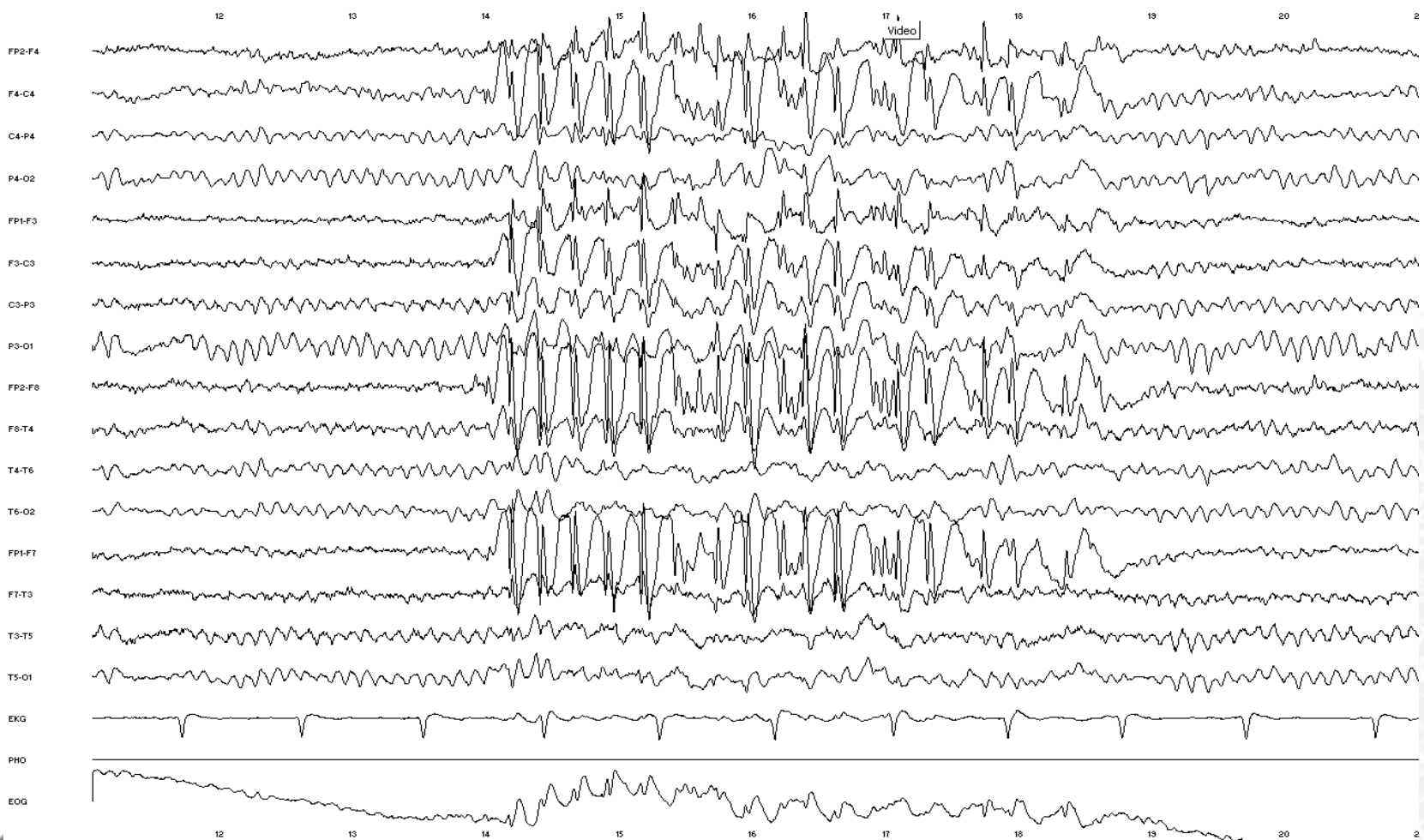


Klassifikation

- fokale Anfälle
 - fokal einfache Anfälle (normales Bewusstsein)
 - fokal komplexe Anfälle (**gestörtes Bewusstsein**)
-> EEG
- generalisierte Anfälle
 - **tonisch-klonische**
 - tonisch (DD Strecksynergismen)
 - klonisch (Hypoxie?)
 - myoklonische (Hypoxie?)
 - atonische
 - Absencen



Content

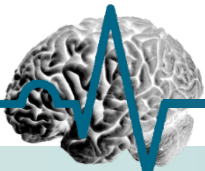


Therapie

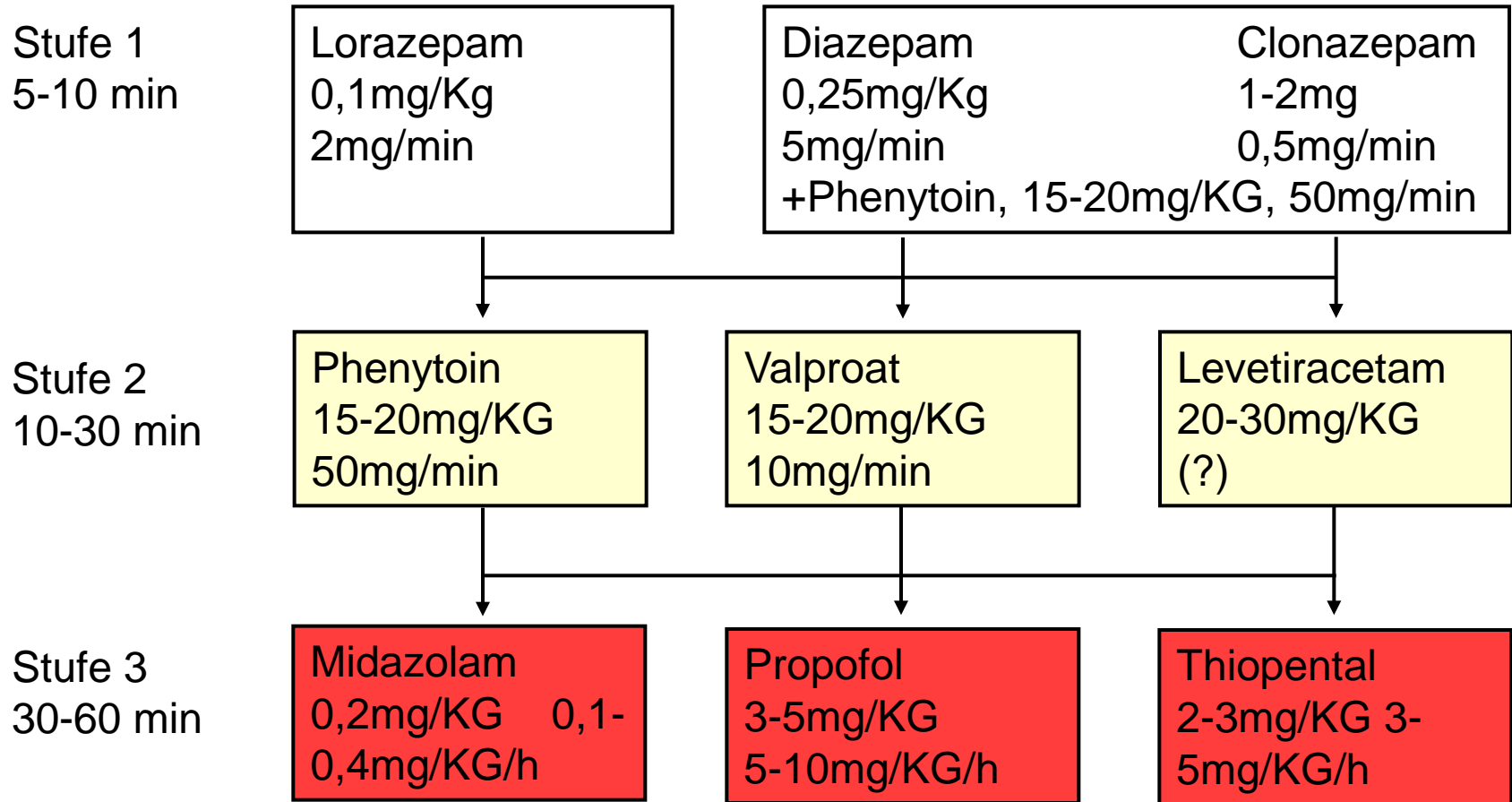
- 1. Anfall prinzipiell nicht zu therapieren
- bei V.a symptomatische Ursache (Stroke, Demenz) Anfallstherapie indiziert

spezifische Anfallsmedikation

- | | | |
|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| iv/po | Levitiracetam (Keppra®) | -> NW Albträume, Aggressivität |
| | Valproat (Convulex®) | -> NW Enzephalopathie |
| | Phenytoin (Epanutin®) | |
| | Lacosamid (Vimpat®) | |
| oral | Carbamzepin (Tegretol®), Lamotrigin (Lamictal®),
Gabapentin (Neurontin®), Oxcarbazepin (Trileptal®),
Topiramamat (Topamax®), Zonesamid (Zonegran®) | |



Therapierefrakterärer Status epilepticus - Stufenplan





Danke für die Aufmerksamkeit

