5th Congress of the European Academy of Neurology

Oslo, Norway, June 29 - July 2, 2019

Teaching Course 15

Eye movements and vestibular function in critical care, emergency, and ambulatory neurology (Level 2)

Eye movements and vestibular function in critical care and emergency neurology

Alexander Tarnutzer
Baden, Switzerland

Email: alexander.tarnutzer@ksb.ch

Kantonsspital Baden

KSB

Eye movements and vestibular function in critical care and emergency neurology

5th EAN Congress Oslo, Norway June 29 - July 2, 2019
TC 15, July 2nd 2019

PD Dr. med. Alexander Tarnutzer
Senior leading physician
Neurology
Cantonal Hospital of Baden
Switzerland

Alexander.Tarnutzer@ksb.ch

Disclosures

- Royalties from books (Oxford University Press, Verlagshaus der Aerzte).
- I do not have any financial interest in commercial products presented in this talk.
- I do not have any stock holdings in commercial products presented in this talk.

Topics covered

- Focused clinical examination of eye movements and vestibular function at the bedside → which key tests to obtain?
- Neuro-otological assessment of the comatouse patient in the ICU → how to get the maximum out of a limited examination.
- Differential diagnosis of eye movement abnormalities in the ED / ICU setting.

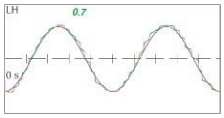
Kantonsspital Baden KSB

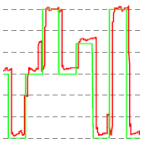
Bedside clinical neuro-otological examination in the ED / ICU

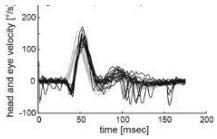
Kantonsspital Baden KSB

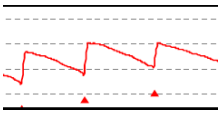
Principal types of eye movements

- Smooth pursuit eye movements → following a moving target
- Saccadic eye movements → shifting gaze
- Vestibulo-ocular reflex (VOR) → stabilizing gaze despite moving
- Nystagmus (spontaneous, gaze-dependent, optokinetic etc...) → stabilize gaze
- Vergence eye movements → binocular control









Ramboldt et al. 2004

Kantonsspital Baden KSB

5

Key domains to assess at the bedside

- Ocular stability for (I) nystagmus and (II) skew deviation & gaze deviation
- (III) the head-impulse test
- (IV) postural stability (including malleolar vibration sense)
- (V) ocular motor deficits (of saccades, smooth pursuit eye movements and optokinetic nystagmus).

Kantonsspital Baden KSB

6

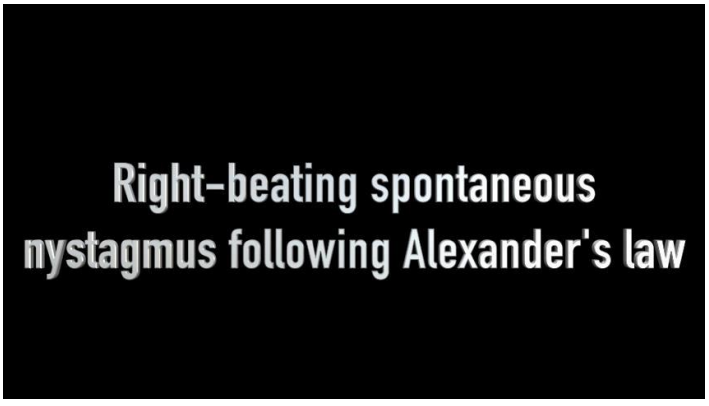
Ocular stability (I)
– spontaneous or gaze-evoked nystagmus?

- Primary gaze (spontaneous) nystagmus
  - Along one axis (horizontal, vertical, torsional)
  - Combined (e.g. vertical-torsional)
- Gaze-dependent nystagmus
- Positional nystagmus (peripheral vs. central)
- Other (head shaking nystagmus, vibration-induced nystagmus, periodic alternating nystagmus etc...)

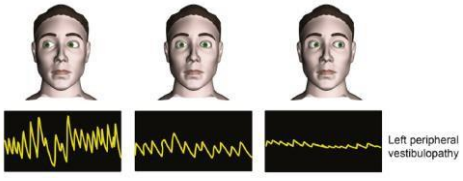
Kantonsspital Baden KSB

7

Acute peripheral vestibulopathy – right beating spontaneous nystagmus



- Nystagmus beating away from the lesioned (left) side
- Following Alexander's law
- Mostly horizontal
- Suppressed/reduced with fixation → stronger on fixation suppression

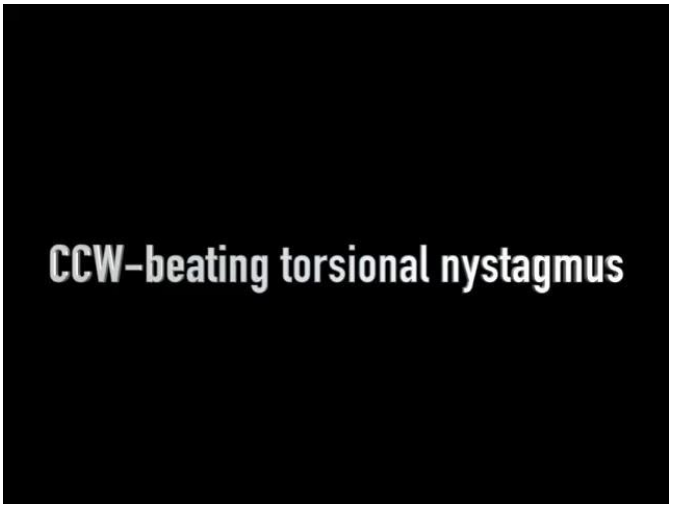


Welgampola et al. Neurol Clin. 2015; 33:551–564

Kantonsspital Baden KSB

8

Torsional spontaneous nystagmus



Clinical features

- Predominantly torsional nystagmus in straight-ahead position → usually central origin.
- Associated with lesions of the medulla (Wallenberg Syndrome) or cerebellar peduncles (stroke, MS, tumor etc..).
- Can be part of an ocular tilt reaction or INO.
- Varies with eye position in the orbita
- Poorly suppressed by fixation of distant target, but may be suppressed on convergence.

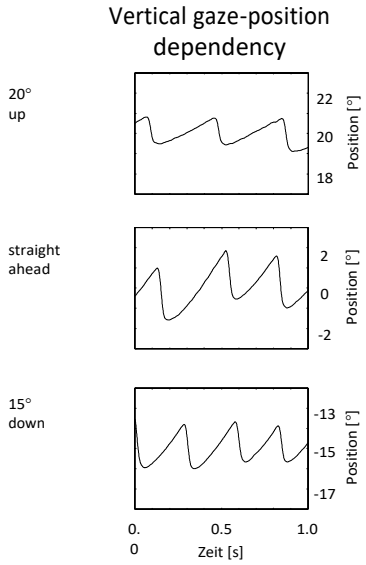
Leigh and Zee. Neurology of eye movements, 5th ed. Oxford University Press 2015

Kantonsspital Baden KSB

9

Vertical spontaneous nystagmus: downbeat nystagmus (DBN)

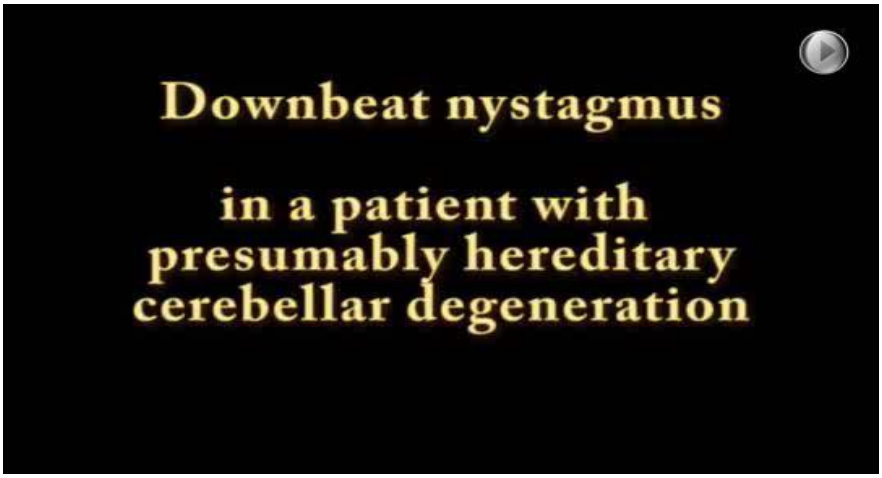
- Present in gaze straight-ahead (= „spontaneous“ nystagmus)
- Increase in downgaze
- Increase in lateral gaze
- Increase in prone and ear-down position
- Accompanied by impaired smooth pursuit eye movements and impaired visual cancellation of the VOR
- Poorly suppressed by fixation



Kantonsspital Baden KSB

10

Vertical (downbeat) spontaneous nystagmus



Kantonsspital Baden KSB

11

Downbeat nystagmus: main clinical characteristics

- Most typical: cerebellar degeneration (hereditary, sporadic, acquired)
- Structural cerebellar lesions: Chiari, tumors, vascular or inflammatory lesions
- Episodic ataxia Type II
- Drugs: anticonvulsant therapy, lithium intoxication, opioids, amiodarone.
- Alcohol intoxication (and alcoholic cerebellar degeneration)
- Nutritional deprivation: thiamine (B1), vitamin B12, magnesium depletion
- In isolation: ‚idiopathic' DBN (Wagner et al. 2007)

Leigh and Zee. Neurology of eye movements, 5th ed. Oxford University Press 2015

Kantonsspital Baden KSB

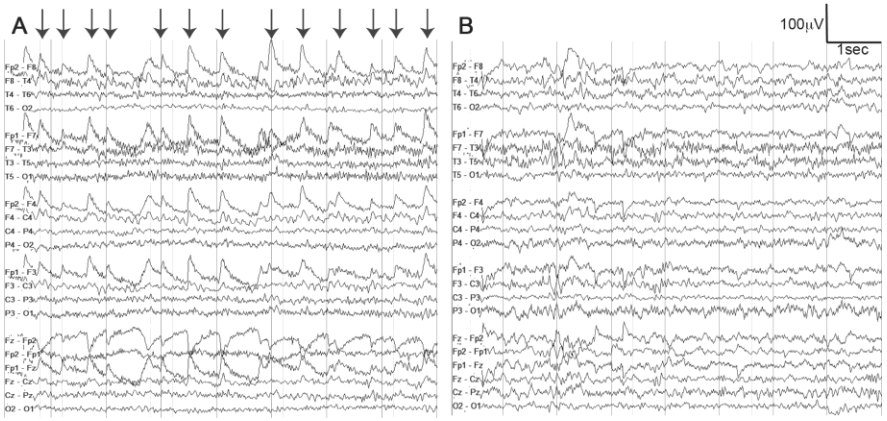
12

Downbeat nystagmus due to carbamazepine intoxication (76µmol/l, range: 17-50)

Kantonsspital Baden KSB

13

Oxcarbazepine intoxication recorded on video-EEG monitoring



A.A. Tarnutzer, L.L. Imbach / Seizure 45 (2017) 100–101

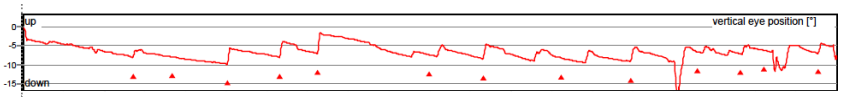
Kantonsspital Baden KSB

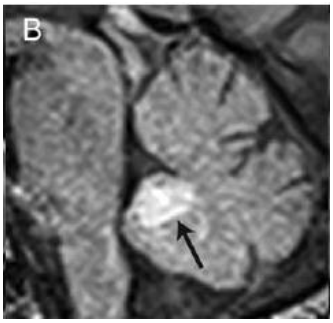
14

Upbeat nystagmus → Usually transient

Caused by acute brainstem lesions

- Vertebrobasilar ischemia (medulla, ponto-mesencephalic, cerebellar)
  - Focal demyelination („plaque“) in multiple sclerosis
- Wernicke encephalopathy (acute thiamine deficiency)
- Brainstem encephalitis, paraneoplastic (anti-Ma2 antibodies)
- Tumors of the medulla
- Often associated with other brainstem signs (internuclear ophthalmoplegia, dissociated sensory disturbances etc...)
- Poorly suppressed by fixation of a distant target.





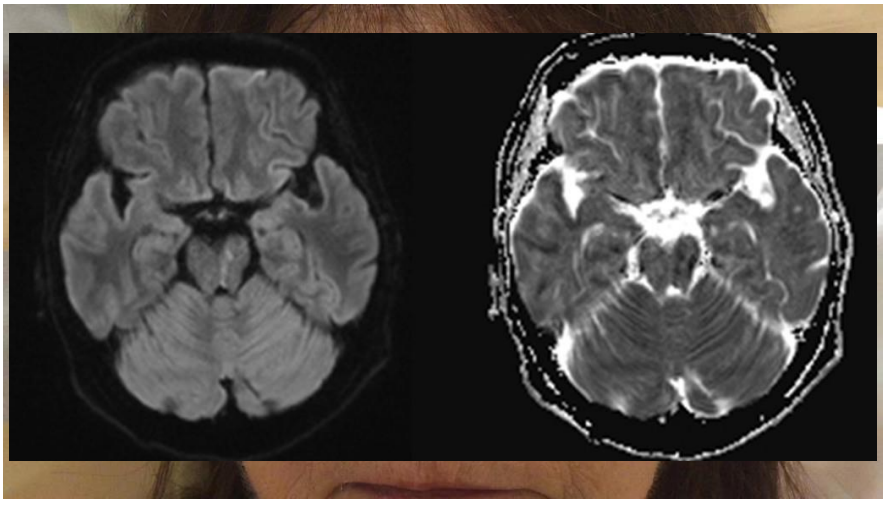
Tarnutzer et al. Ann Neurol 2014

Leigh and Zee. Neurology of eye movements, 5th ed. Oxford University Press 2015

Kantonsspital Baden KSB

15

Upbeat nystagmus due to pontomesencephalic stroke



Courtesy of Alexander Tarnutzer, M.D.

Kantonsspital Baden KSB

16

Other less common types of spontaneous nystagmus

Pendular nystagmus

- No slow / fast phase
- etiology: focal brainstem lesions (ischemic, MS), sometimes accompanied by palatal tremor

Periodic-alternating nystagmus (PAN) (congenital, acquired)

- Periodic change of beating direction
- etiology: lesions at the craniocervial junction or the cerebellar nodulus, cerebellar atrophy

Seesaw nystagmus

- Changing elevation and intorsion of one eye and (at the same time) depression and extorsion of the other eye
- Very rare, e.g. in case of lesions at the mesodiencephalic junction.

Kantonsspital Baden KSB

17

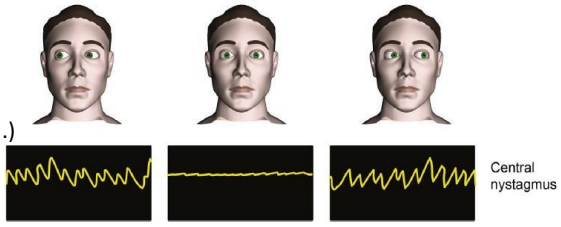
Periodic-alternating nystagmus

Kantonsspital Baden KSB

18

Gaze-evoked nystagmus

- Beating direction is gaze-dependent → left beating on left gaze and right beating on right gaze
- "central" sign pointing to deficient velocity-to-position integrator
- Most frequent **acute/subacute causes**:
  - Vertebrobasilar stroke (brainstem, cerebellum)
  - Drug intoxication (phenytoin, carbamazepin, oxcarbazepin..)
  - Alcohol intoxication
  - Thiamine deficiency (Wernicke encephalopathy)
- Most frequent **chronic causes**
  - Cerebellar degeneration (sporadic, acquired, hereditary)

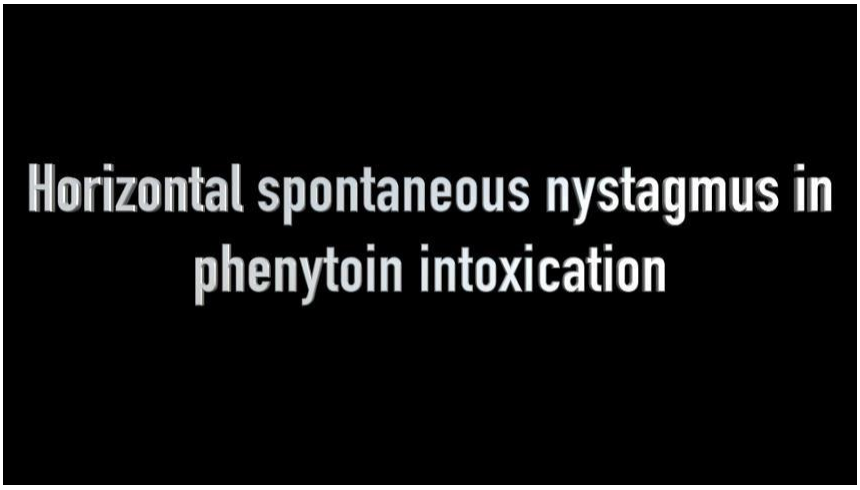


Welgampola et al. Neurol Clin. 2015; 33:551–564

Kantonsspital Baden KSB

19

Gaze-evoked nystagmus due to phenytoin intoxication (174µmol/l; range: 40-80)



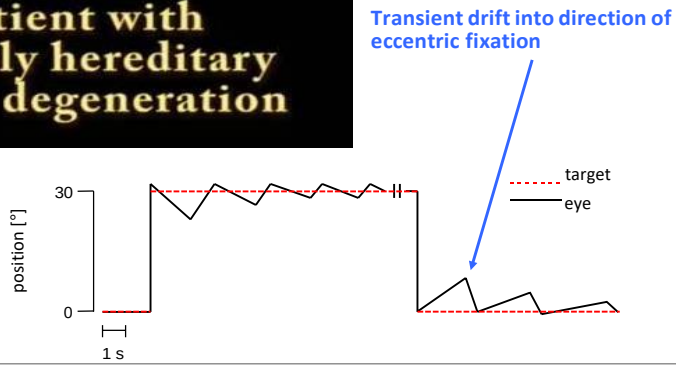
Kantonsspital Baden KSB

20

Gaze holding and rebound nystagmus

Rebound nystagmus after prolonged eccentric fixation

in a patient with presumably hereditary cerebellar degeneration

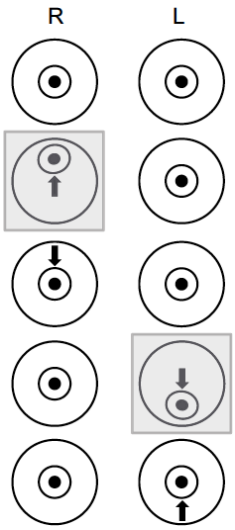


Kantonsspital Baden KSB

21

Ocular stability (IIa) – skew deviation?

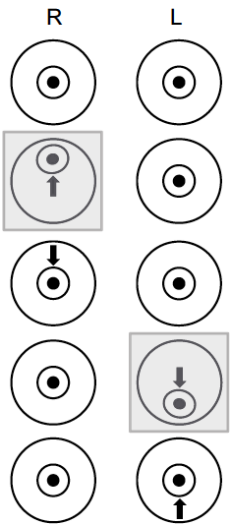
- Vertical divergence of the eyes on alternating cover test
- Part of the ocular tilt reaction (OTR → ocular tosion, head tilt, skew deviation)
- Rarely seen in peripheral-vestibular disorders → usually a central sign
- The amount of skew deviation modulates with head position relative to gravity → minimal in supine position (allows differentiation from 4th nerve palsy)



Kantonsspital Baden KSB

22

Skew deviation

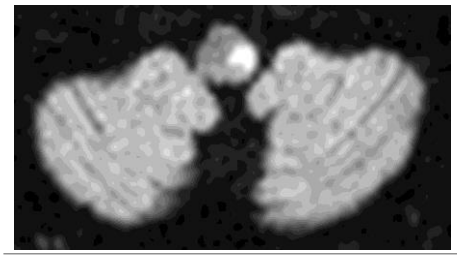


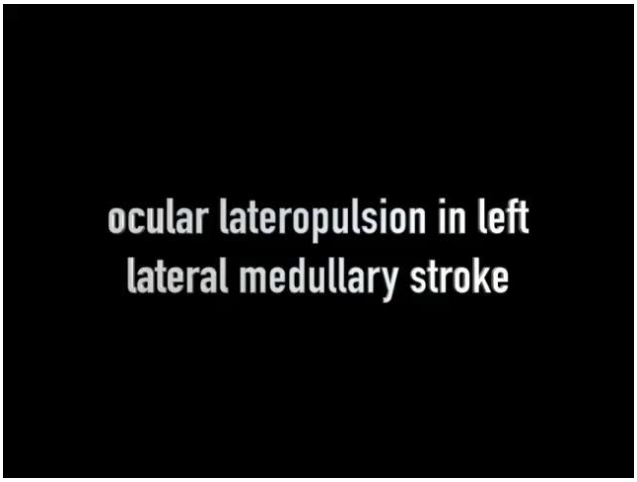
Leigh and Zee. Neurology of eye movements, 4th ed. Oxford University Press 2006

Kantonsspital Baden KSB

Ocular stability (IIb) – ocular lateropulsion

- Strong ipsilesional horizontal conjugate gaze deviation upon brief (3-5sec) eye closure
- Associated with lateral medullary stroke[1]
- Low sensitivity, but very high specificity for predicting central origin



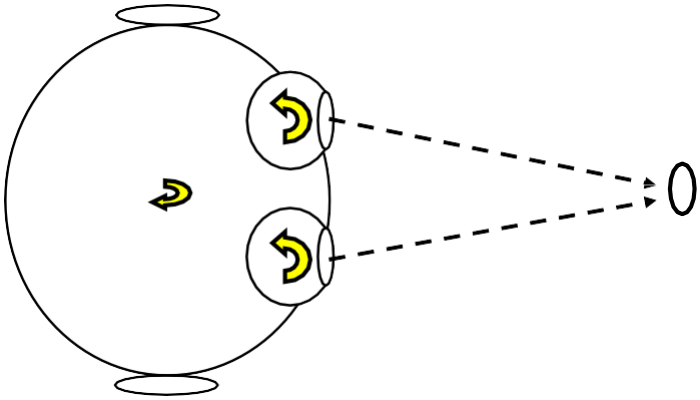


[1] Kattah et al. (2011) ANAS;1233:249-55. d

Kantonsspital Baden KSB

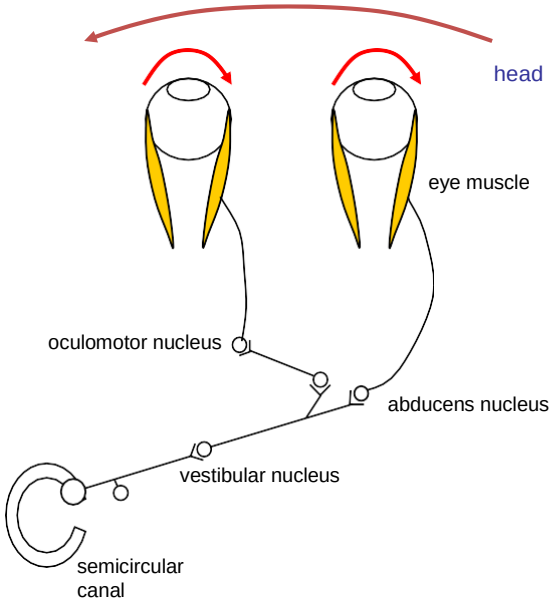
The head-impulse test (HIT) (III)

Angular vestibulo-ocular reflex (aVOR)
→ gaze stabilization



Kantonsspital Baden KSB

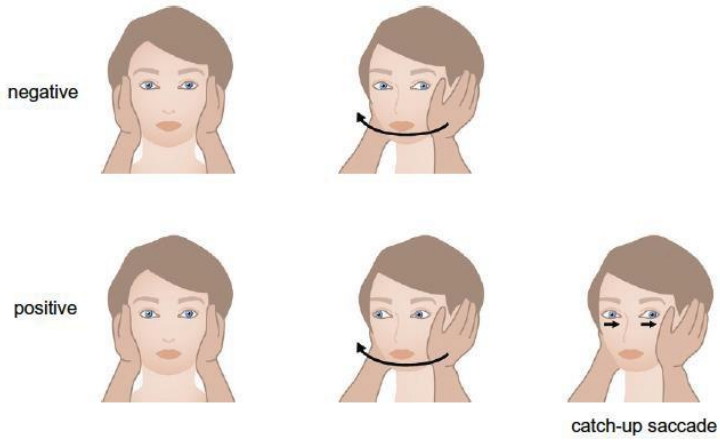
25



Kantonsspital Baden KSB

26

Normal head-impulse test*

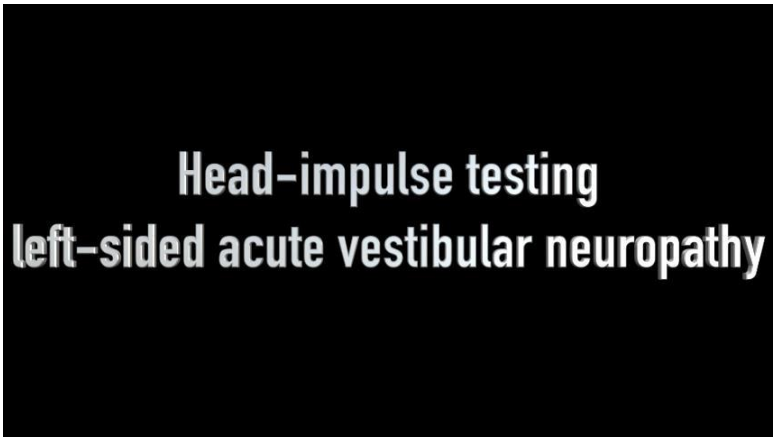


*Halmagyi G.M., Curthoys I.S (1988) Archives of Neurology

Kantonsspital Baden KSB

27

Acute peripheral vestibulopathy → impaired angular VOR



Kantonsspital Baden KSB

28

Postural stability (IV): increased sway?

Stance

- Romberg test
- Romberg test on foam
- Truncal ataxia

Gait

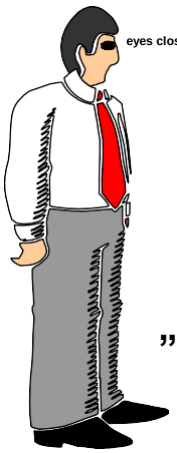
- Normal walking
- 180° turns
- Tandem gait

Freddy Nock, Corvatschbahn (Keystone)

Kantonsspital Baden KSB

29

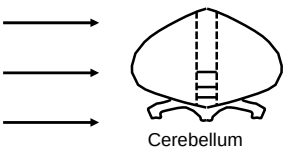
Redundancy of sensory inputs



visual

proprioceptive

vestibular



„Romberg Test“

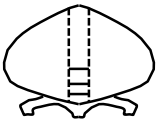
*Moritz Heinrich Romberg 1795-1873

Kantonsspital Baden KSB

30

Redundancy of sensory inputs II

visual
proprioceptive
vestibular



„Fromberg Test“ (Romberg test on Foam)

*Moritz Heinrich Romberg 1795-1873

Kantonsspital Baden KSB

Ocular motor deficits (V)

Domains

- Saccadic eye movements
- Smooth pursuit eye movements
- Optokinetic nystagmus.
- Gaze deviations (→ next section)
- Gaze palsies (→ next section)

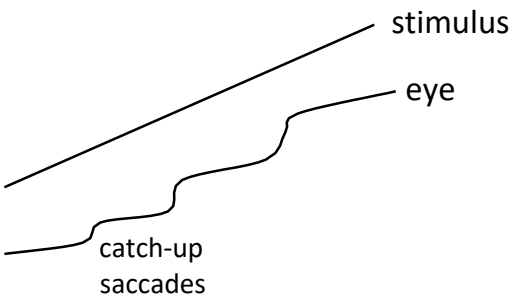
From left: Andyworks, Ralf Hettler, vicmicallef/iStockPhoto

Kantonsspital Baden KSB

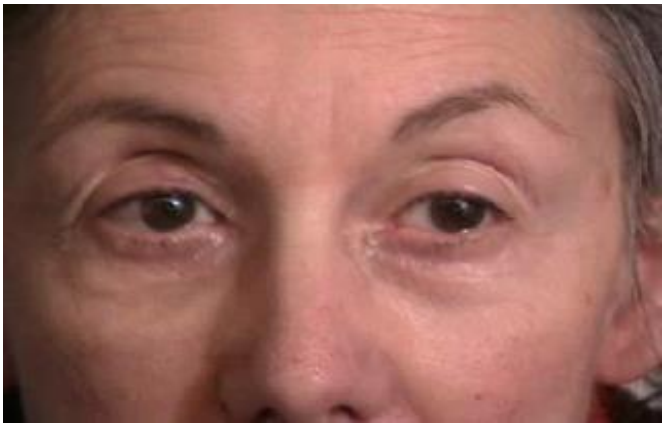
Smooth pursuit eye movements

- Follow a moving target along either the vertical or horizontal plane (with constant velocity at about 20°/sec).
- If other eye movements interfere (e.g. gaze-evoked nystagmus), visual suppression of the VOR (also termed VOR-cancellation) can be used to assess the integrity of the smooth pursuit system while the eyes remain centered and are not moving.
- Therefore, the patient is asked to look at a head-fixed target (e.g. his/her thumb that is rotating at the same speed as the patient's head).
- Assuming an intact VOR, the inability to suppress nystagmus during head oscillations and simultaneous fixation of a head-fixed target suggests an impaired smooth pursuit system.
- Only of minor diagnostic utility as nonspecific and observed in many different disorders including visual loss, cerebellar disorders, advanced age, inattention etc…

Smooth pursuit eye movements: IMPAIRED SMOOTH PURSUIT



Smooth pursuit eye movements: IMPAIRED SMOOTH PURSUIT



Courtesy of Prof. D. Straumann

Kantonsspital Baden KSB

35

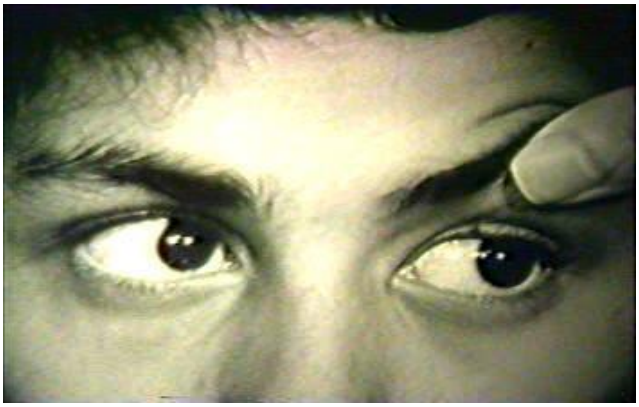
Saccadic eye movements

- **Fast** eye movements for shifting gaze
- Triggered by brainstem nuclei and under cerebellar control
- Disorders of
  - Velocity (slow)
  - Metrics (hypometric, hypermetric)
  - Latency (increased)

Kantonsspital Baden KSB

36

Saccadic eye movements: SLOW SACCADES (patient with spino-cerebellar ataxia 2)

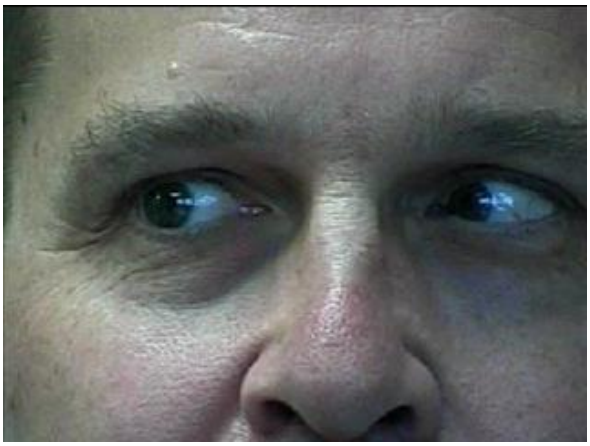


Leigh and Zee. Neurology of eye movements, 4th ed. Oxford University Press 2006

Kantonsspital Baden KSB

37

Saccadic eye movements: HYPERMETRIC SACCADES (patient with spino-cerebellar ataxia 8)



Leigh and Zee. Neurology of eye movements, 4th ed. Oxford University Press 2006

Kantonsspital Baden KSB

38

Saccadic intrusions (SI)

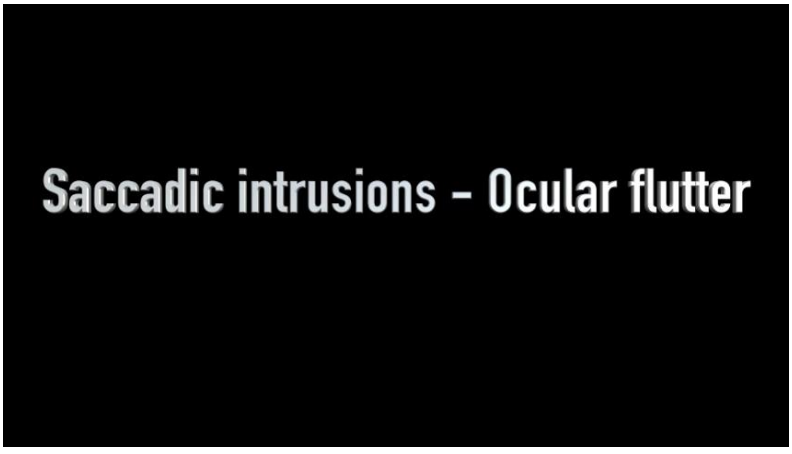
- Two main categories of saccadic intrusions (i.e., back-to-back conjugate saccades)
  - SI **with** intersaccadic interval → e.g. square-wave jerks
  - SI **without** intersaccadic interval → e.g. ocular flutter or opsoclonus
- Asymptomatic saccadic intrusions can be found in healthy normals.

➢ If symptomatic (e.g. causining oscillopsia and blurred vision) → indicate neurologic dysfunction.

- Occular flutter (limited to one plane) and opsoclonus (multidirectional) associated with parainfectious brainstem encephalitis, metabolic-toxic states, demyelinating disorders, paraneoplastic syndromes (SCLC, ovarian cancer, breast cancer).

Lemos and Eggenberger. Curr Opin Neurol 2013, 26:59–66

Ocular flutter in a patient with a migraine attack



Opsoclonus

Leigh and Zee. Neurology of eye movements, 4th ed. Oxford University Press 2006

Kantonsspital Baden KSB

41

Optokinetic nystagmus

- Optokinetic nystagmus can be triggered by a moving visual pattern or a hand-held rotating drum. It allows an assessment of the conjugacy of pursuit eye movements (slow phase of nystagmus) and saccades (fast phase of nystagmus).
- Only of minor diagnostic utility as potentially impaired in various disorders (visual loss, deficits in smooth pursuit, cerebellar disease etc...)

www.smelltest.eu

www.bernell.com

Kantonsspital Baden KSB

42

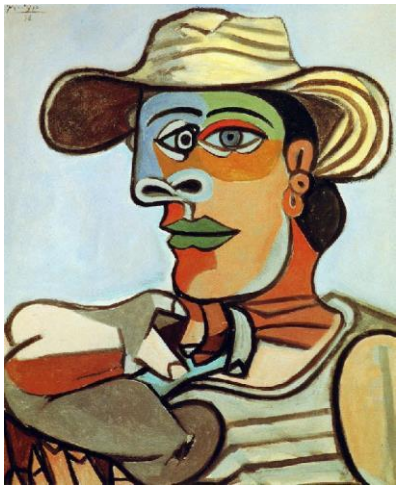
Supratentorial and infratentorial lesions – evaluation of eye movements in the ED / ICU

Kantonsspital Baden KSB

Eye movement testing – key findings

Domains

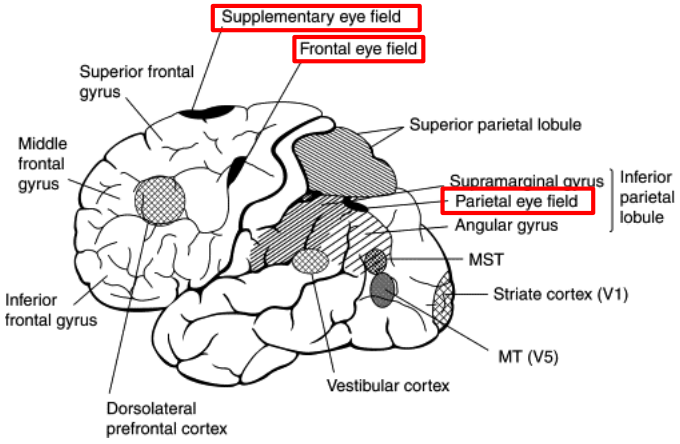
- Saccadic eye movements
- Smooth pursuit eye movements
- Optokinetic nystagmus.
- Gaze deviations
- Gaze palsies
  - Nuclear gaze palsies
  - Supranuclear gaze palsies



Pablo Picasso, 1938

Kantonsspital Baden KSB

Supratentorial (supranuclear) lesions



Leigh and Zee. Neurology of eye movements, 4th ed. Oxford University Press 2006

Kantonsspital Baden KSB

45

TABLE 9-1 Localization of Eye Movement Disorders

Brain Level	Ocular Motor Structure	Disorders Caused by Lesions	Other Neurologic Deficits
Cerebral cortex	Cortical gaze centers (eye fields)	Ipsilateral gaze deviation Hypometric saccades Impaired smooth pursuit	Contralateral weakness Hemisensory loss
Basal ganglia	Descending gaze control pathways	Saccadic intrusions Impaired smooth pursuit Hypometric saccades	Axial rigidity Dyskinesias
Thalamus	Descending gaze control pathways ? Vergence pathways	Wrong-way deviation Thalamic esotropia	Hemisensory loss Visual field defect
Midbrain	Vertical gaze centers (rostral interstitial nucleus of medial longitudinal fasciculus, interstitial nucleus of Cajal) Trochlear nucleus and fascicle Oculomotor nucleus and fascicle	Vertical gaze palsy Superior oblique palsy Convergence-retraction nystagmus Third nerve palsy	Contralateral hemiparesis Light-near dissociation Contralateral tremor
Pons	Abducens nucleus and fascicle Paramedian pontine reticular formation Medial longitudinal fasciculus	Internuclear ophthalmoplegia Horizontal gaze palsy Sixth nerve palsy Skew deviation	Facial nerve palsy Trigeminal neuropathy Hearing loss Contralateral weakness

Van Stavern. Continuum Lifelong Learning Neurol 2009;15(4):128–149.

Kantonsspital Baden KSB

46

Gaze deviation

- To the side of the lesion for inhibition/loss of function → **away from the side with clinical findings**
- Away from the lesioned side for excitation (epileptogenic, before generalization) → **towards the side with clinical findings**[1]
- More frequently found for right-hemispheric lesions.

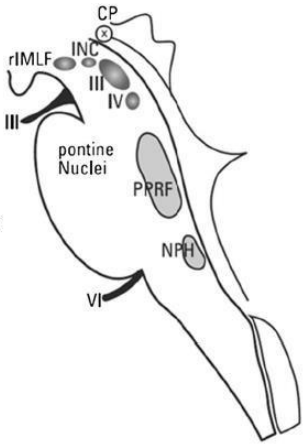
[1] Kernan et al. Lateralizing significance of head and eye deviation in secondary generalized tonic-clonic seizures. Neurology. 1993 Jul;43(7):1308-10.

Infratentorial lesions

- Nuclear eye muscle palsies (Oculomotor nerve palsy (N. III), trochlear nerve palsy (N. IV), abducens nerve palsy (N. VI))
- Supranuclear palsies (Internuclear ophthalmoplegia (INO))
- Pathologic nystagmus (Downbeat, Upbeat, periodic-alternating nystagmus, oculopalatal tremor, etc...)
- Impaired gaze holding (gaze-evoked nystagmus, rebound nystagmus)

The infratentorial supranuclear centers of eye movement control

CP	Posterior commisure
INC	Interstitial nucleus of Cajal
NPH	Nucleus prepositus hypoglossi
PPRF	Paramedian pontine reticular formation
rIMLF	Rostral interstitial nucleus of the medial longitudinal fasiculus
III	Nucleus or oculomotor nerve
IV	Nucleus of trochlear nerve
VI	Nucleus of abducent nerve or abducent nerve



rIMLF lesion: vertical saccadic paresis

INC lesion: vertical gaze deviation nystagmus

CP lesion: convergence retraction nystagmus

MLF lesion: internuclear ophthalmoplegia

PPRF lesion: horizontal saccadic paresis (ipsiversive)

NPH lesion: horizontal gaze deviation nystagmus

Bilateral flocular lesion or pontomedullar lesion: downbeat nystagmus

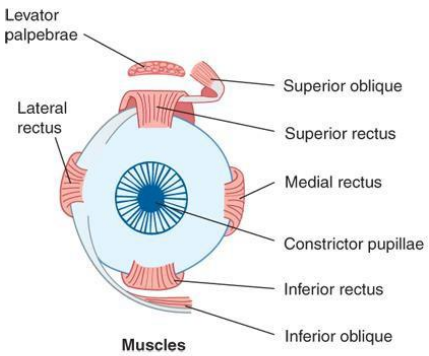
Medullary or pontomesencaphallic lesion: upbeat nystagmus

Strupp et al. J Neurol (2014) 261 (Suppl 2):S542–S558

Kantonsspital Baden KSB

49

Eye muscle palsies



Muscles

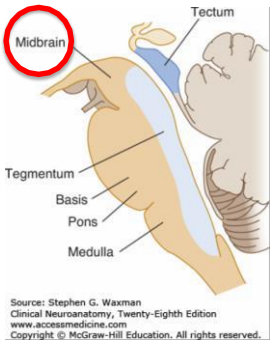
Source: Stephen G. Waxman
Clinical Neuroanatomy, Twenty-Eighth Edition
www.accessmedicine.com

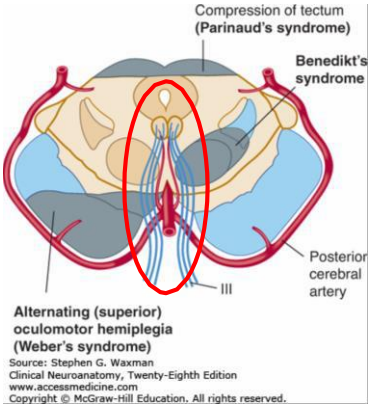
Muscle	Effect	Nerve
Medial rectus muscle	Adduction	III
Superior rectus muscle	Elevation	III
Inferior rectus muscle	Depression	III
Inferior oblique muscle	Elevation, extorsion	III
Superior oblique muscle	Depression, intorsion	IV
Lateral rectus muscle	Abduction	VI

Kantonsspital Baden KSB

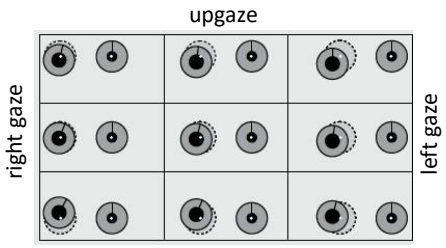
50

3rd nerve (oculomotor) palsy





Right-sided 3rd nerve palsy



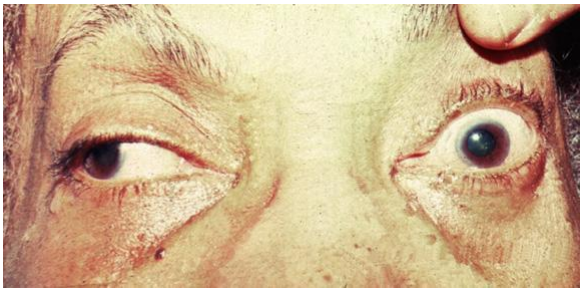
Staubach and Lagrèze. Ophthalmologe 2007 · 104:733–746

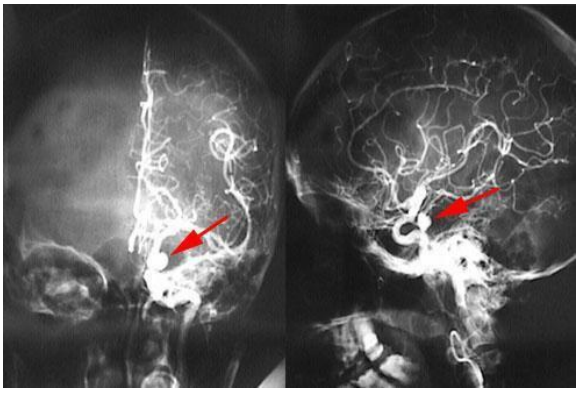
Eye deviating "down and out"

Kantonsspital Baden KSB

51

Left-sided 3rd nerve palsy due anterior communicating artery aneurysm





Courtesy of James Goodwin, MD (retrieved from emedicine.medscape.com)

Kantonsspital Baden KSB

52

3rd nerve (oculomotor) palsy - case

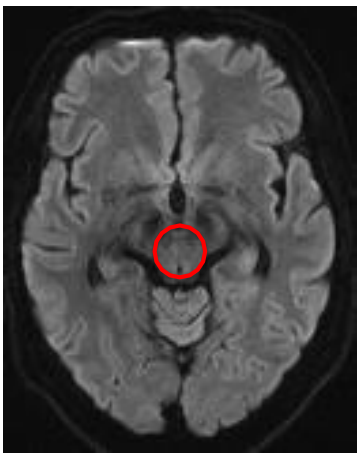
Courtesy of Alexander Tarnutzer, M.D.

Kantonsspital Baden KSB

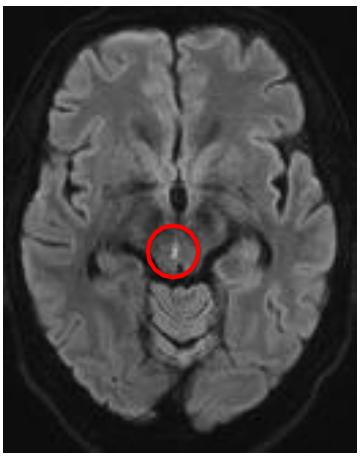
53

Progressive 3rd nerve palsy

cMRI **5h** after symptom onset



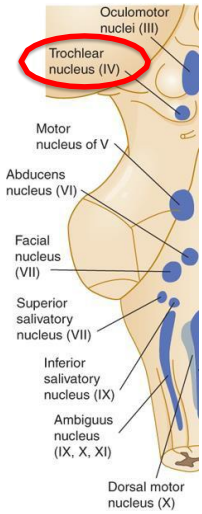
cMRI **24h** after symptom onset

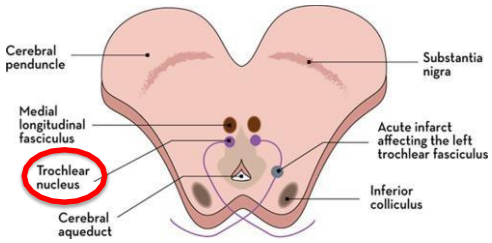


Kantonsspital Baden KSB

54

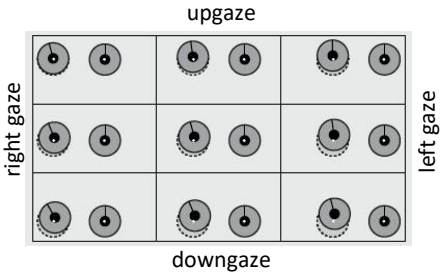
4th nerve (trochlear) palsy





Abkur. Practical Neurology 2017;17:474-475.

Right-sided 4th nerve palsy



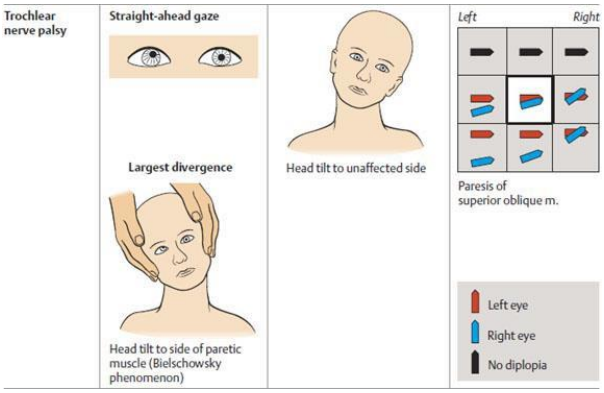
Eye showing "upward deviation and extorsion"

Staubach and Lagrèze. Ophthalmologe 2007 · 104:733–746

Kantonsspital Baden KSB

55

4th nerve palsy- Bielschowsky phenomenon

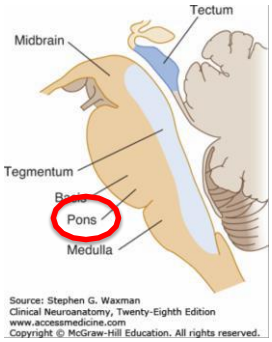


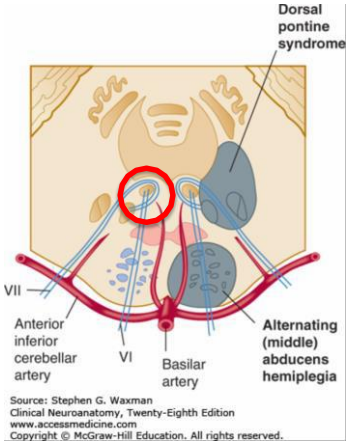
www.jingjingz.com

Kantonsspital Baden KSB

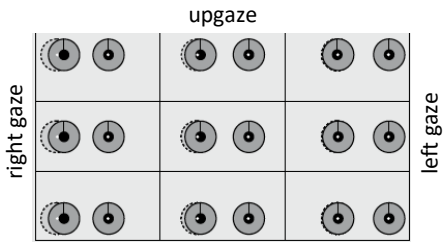
56

6th nerve (abducens) palsy





Right-sided 6th nerve palsy



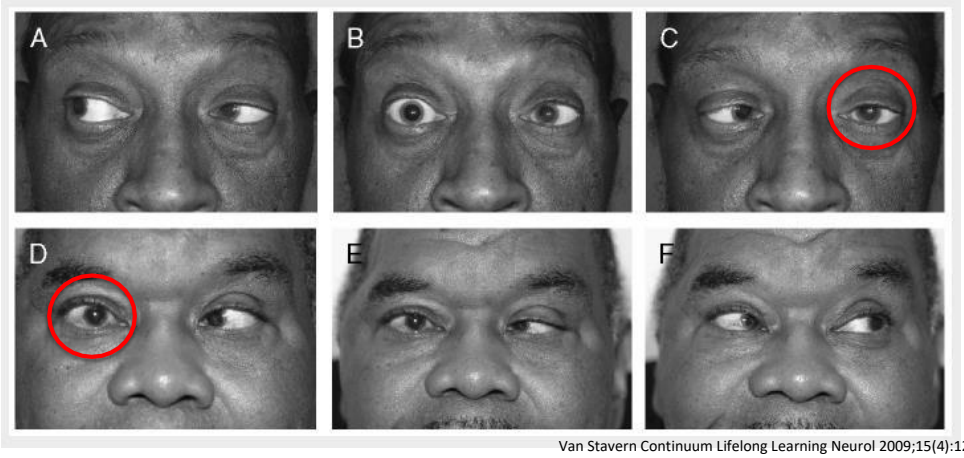
Staubach and Lagrèze. Ophthalmologe 2007 · 104:733–746

Eye deviating "in"

Kantonsspital Baden KSB

57

6th nerve (abducens) palsy - case



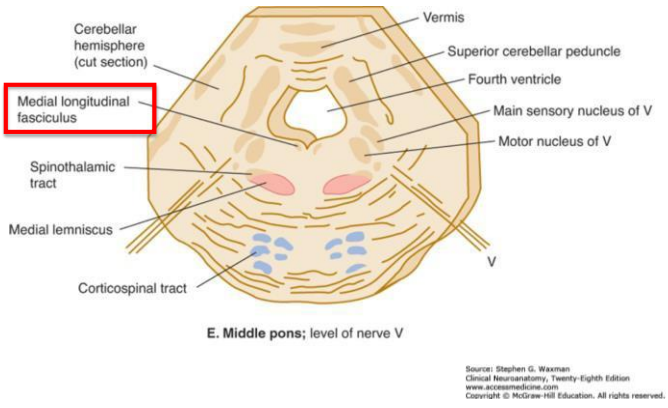
Van Stavern Continuum Lifelong Learning Neurol 2009;15(4):128–149.

Kantonsspital Baden KSB

58

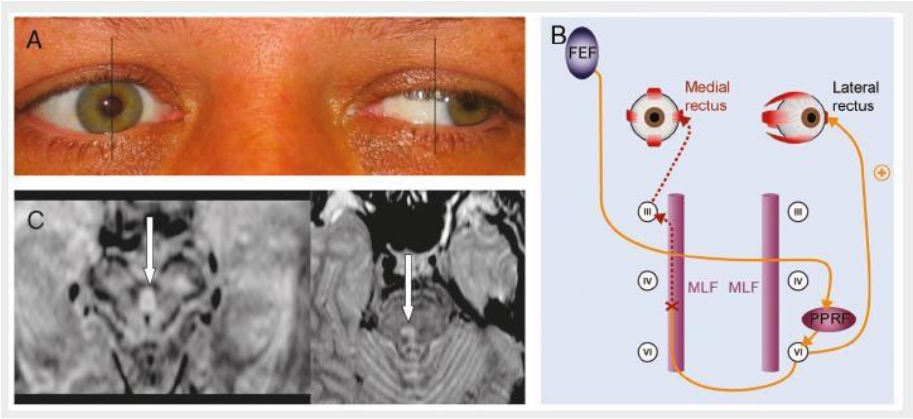
Supranuclear gaze palsy - Internuclear ophthalmoplegia (INO)

- Patients may report transient diplopia on gaze away from the lesioned side
- Causes: demyelination (MS), stroke
- Slowing of the adducting eye (ipsilesional), usually range of ocular motion little / not affected → use saccades for testing
- Dissociated nystagmus of the abducting eye
- Supranuclear lesion → affecting the MLF
- Thus, convergence is preserved!



Kantonsspital Baden KSB

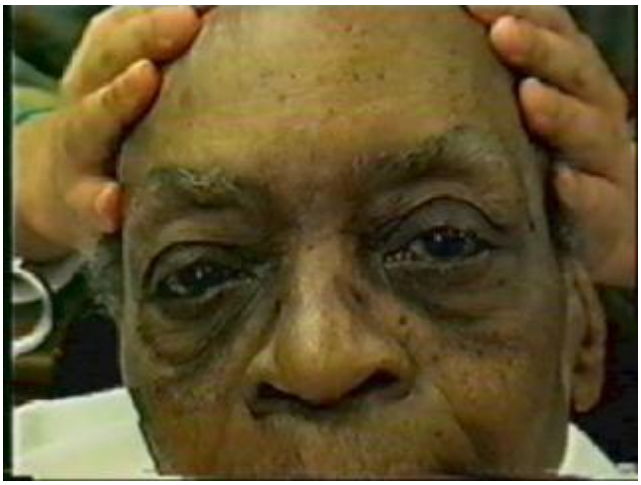
Internuclear ophthalmoplegia (INO)



Frohman et al. Continuum Lifelong Learning Neurol 2010;16(5)

Kantonsspital Baden KSB

Unilateral left-sided INO (ischemic) with convergence preserved



Leigh and Zee. Neurology of eye movements, 4th ed. Oxford University Press 2006

Kantonsspital Baden KSB

61

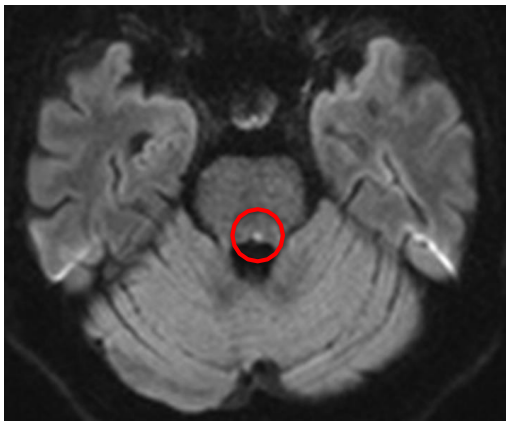
Bilateral INO

Courtesy of Alexander Tarnutzer, M.D.

Kantonsspital Baden KSB

62

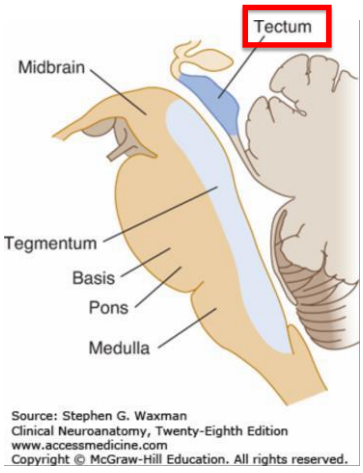
Bilateral INO - MRI



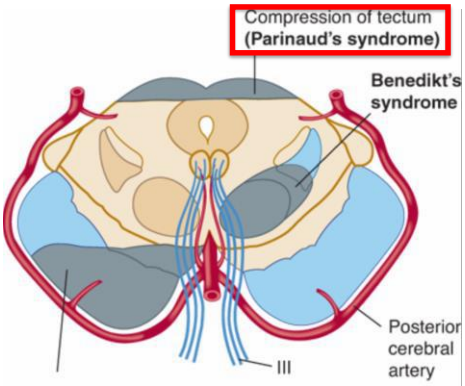
Left-sided paramedian dorsal pontine stroke

Kantonsspital Baden KSB

Parinaud Syndrom



Source: Stephen G. Waxman
Clinical Neuroanatomy, Twenty-Eighth Edition
www.accessmedicine.com



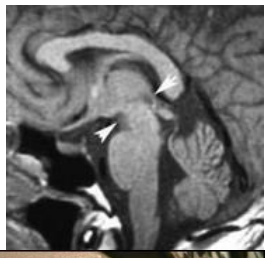
Alternating (superior) oculomotor hemiplegia (Weber's syndrome)

Source: Stephen G. Waxman
Clinical Neuroanatomy, Twenty-Eighth Edition
www.accessmedicine.com

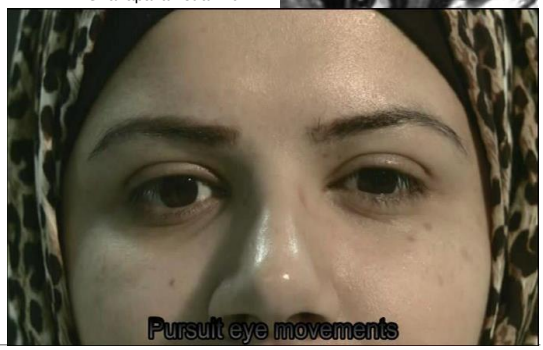
Kantonsspital Baden KSB

Parinaud syndrome

- Dorsal midbrain syndrome
  - Vertical gaze palsy (upgaze >> downgaze)
  - Convergence spasm or palsy
  - Light-near dissociation of the pupils
  - Lid retraction
  - Square-wave jerks
  - Konvergence-retraction nystagmus
  - Skew deviation
- Etiology:
  - Pineal gland tumors
  - MS
  - Mesencephalic stroke



Gnanapavan et al. 2014



Kantonsspital Baden KSB

65

Bedside diagnostic approach in acute and persistent vertigo or dizziness – peripheral or central?

Kantonsspital Baden KSB

66

Acute vestibular syndrome (AVS)[1]

Vertigo or dizziness for more than 24 hours accompanied by

- Nausea / Vomitus
- (head) motion intolerance
- Nystagmus
- Gait imbalance

~250'000 – 500'000 patients with AVS per year in US emergency departments

Vertebrobasilar ischemia in ~25 ±15%.

[1] Tarnutzer et al. Does my dizzy patient have a stroke? A systematic review of bedside diagnosis in acute vestibular syndrome. CMAJ 2011;183(9):E571-92

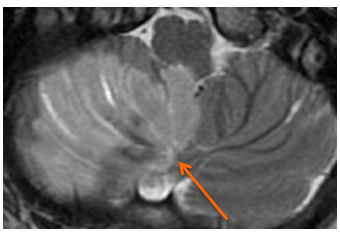
Kantonsspital Baden KSB

67

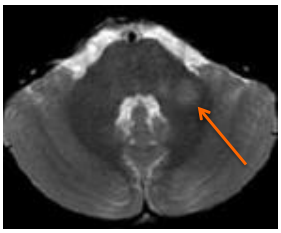
AVS – differentiation peripheral vs. central

Most important central causes*

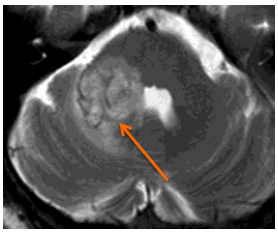
Vertebrobasilar ischemia (79%)



Multiple sclerosis (11%)



Cerebellar bleeding (4%)



* Tarnutzer et al. CMAJ 2011;183(9):E571-92

Kantonsspital Baden KSB

68

Clinical examination for suspected AVS

- Obvious focal-neurological findings (including examination of gait and eye movements)

-Vertical or torsional nystagmus
- eye muscle palsies (3-4-6, INO, gaze-paretic)

Only **64% sensitivity** for stroke

- Subtle ocular motor signs: **H.I.N.T.S.**

98% sensitivity for stroke

Kattah et al. (2009) Stroke. 40, 3504-3510
Tarnutzer et al. (2011) CMAJ;183(9):E571-92

Kantonsspital Baden KSB

69

Subtle ocular motor signs: H.I.N.T.S. to I.N.F.A.R.C.T.

- 3 components "H.I.N.T.S." battery
  - horizontal Head Impulse Test (h-HIT)
  - Nystagmus
  - Test of Skew
- Dangerous H.I.N.T.S. to "I.N.F.A.R.C.T."
  - Impulse Normal
  - Fast-phase Alternating
  - Refixation on Cover Test

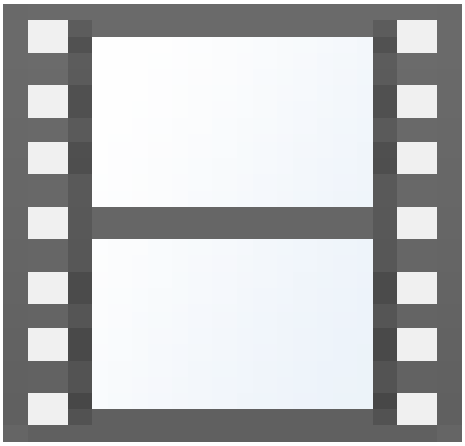
Any of these signs suggests a central (ischemic) origin in AVS!

Kattah et al. Stroke. 2009;40:3504-3510

Kantonsspital Baden KSB

70

H.I.N.T.S: **head-impulse test**



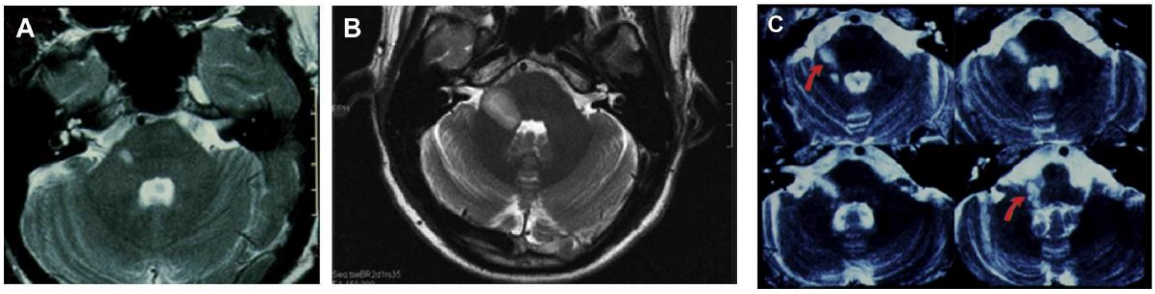
Dangerous H.I.N.T.S. to "I.N.F.A.R.C.T.":
Impulse **N**ormal

Courtesy of Prof. D. Straumann

Kantonsspital Baden KSB

71

Fascicular and nuclear lesions of the vestibular nerve

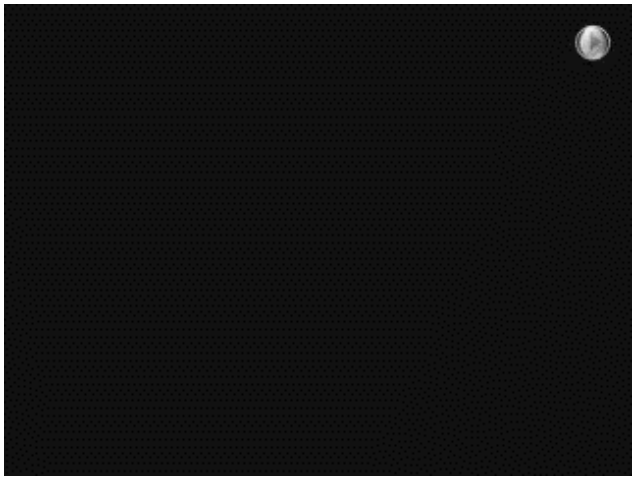


Strupp und Magnusson Neurol Clin. 2015; 33:669–685

Kantonsspital Baden KSB

72

H.I.N.T.S: **gaze-evoked nystagmus**

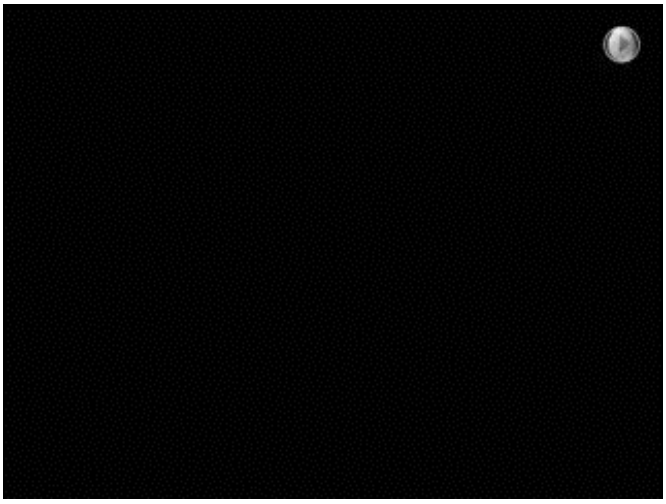


Dangerous H.I.N.T.S. to "I.N.F.A.R.C.T.":
Fast-phase **A**lternating

Kantonsspital Baden KSB

73

H.I.N.T.S: **Skew deviation**



Courtesy of Dr. J. Kattah

Dangerous H.I.N.T.S. to "I.N.F.A.R.C.T.":
Refixation on **C**over **T**est

Kantonsspital Baden KSB

74

Quantification of ataxia – a valuable alternative to the H.I.N.T.S.?

- Grading truncal ataxia (n=114, 72 pAVS, 42 cAVS)
  - Grade 1 → mild to moderate imbalance with walking independently
  - Grade 2 → severe imbalance with standing, but cannot walk without support
  - Grade 3 → falling at upright posture / while sitting unassisted
- Grade 3 found only with central AVS
- ➢ Grade 2 or 3 → 92.9% sensitivity and 61.1% specificity for AICA/PICAstroke

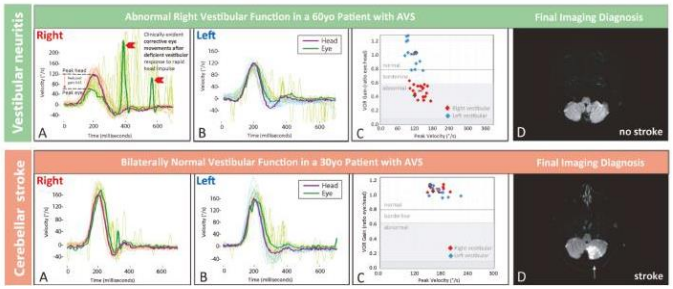
Carmona et al. (2016) Front. Neurol.; 7:125

Kantonsspital Baden KSB

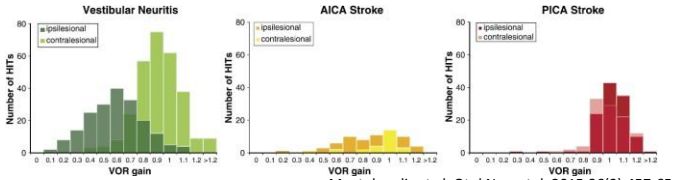
75

The video-head-impulse test: useful in the ED?

Büki and Tarnutzer 2013. Vertigo and dizziness. ONL, Oxford University Press



Newman-Toker et al. Stroke. 2013;44:1158-1161



Mantokoudis et al. Otol Neurotol. 2015;36(3):457-65

Kantonsspital Baden KSB

76

Summary AVS

predictors for central origin

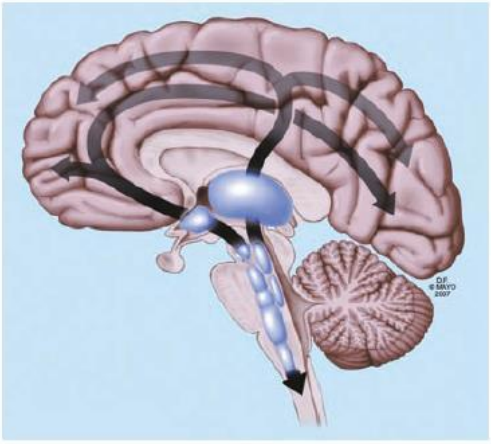
- Normal head-impulse test (HIT)
  - → central (ischemic) origin (PICA, less often AICA)
  - → CAVE: HIT "false" positive in AICA / lateral pontine stroke
- ➢ Testing for gaze-evoked nystagmus and skew deviation → increases sensitivity of the HIT to 98%.
- H.I.N.T.S. have higher sensitivity to exclude stroke than early (first 24-48h) MRI with diffusion weighted imaging (DWI)
- MRI (including DWI) may be negative in first 24-48h in up to 20% and up to 50% for small (lacunar) strokes.

Kantonsspital Baden KSB

77

Eye movement testing in the critically ill patient

- ➢ Limitations in bedside testing due to
  - reduced consciousness of the patients
  - Many installations
  - Sedative drugs
- ➢ Brain death diagnostics



Wijdick (2010) JNNP;10:51–60.

Kantonsspital Baden KSB

78

Types of eye movements seen in critically ill (unconscious) patients

- Resting position of the eyes → Gaze deviations?
- Spontaneous eye movements (nystagmus, pendular eye movements)
- Reflexive eye movements → aVOR-testing ("Dolls head maneuver“) or ice-water caloric irrigation
- NO fast eye movements, NO voluntary eye movements
- Pupillary changes and eye muscle palsies as signs of increased intracranial pressure

Bateman. J Neurol Neurosurg Psychiatry 2001;71(suppl I):i13–i17
Wijdicks. Critical Care (2016) 20:193
Wijdick. JNNP (2010);10:51–60.

79

Kantonsspital Baden KSB

Deviations of the eye(s)

- Conjugate gaze deviations
  - Sustained horizontal **ipsilateral** → destructive (ischemic, hemorrhagic) hemispheric lesions (including frontal eye fields and posterior (right-sided) location
  - Sustained horizontal **contralateral** („looks toward the hemiparesis“) → pontine lesions (parapontine reticular formation (PPRF)), thalamic lesions
  - Intermittent horizontal → epileptic (deviating contralateral to seizure focus)
  - Sustained upward → following hypoxic ischemic insult (early stages), drug effects (including oculogyric crisis)
  - Sustained downward → thalamic hemorrhage, lesions compressing / involving the midbrain, following hypoxic ischemic insult (late stages)
- Disconjugate → 3rd or 6th nerve palsy or intrinsic brainstem lesions
- Downward / upward deviations → often seen in post CPR (cardiopulmonary resuscitation) coma, but are of poor localizing value

Leigh and Zee. Neurology of eye movements,5th ed. Oxford University Press 2015
Bateman. J Neurol Neurosurg Psychiatry 2001;71(suppl I):i13–i17
Wijdicks. Critical Care (2016) 20:193
Wijdick. JNNP (2010);10:51–60.

80

Kantonsspital Baden KSB

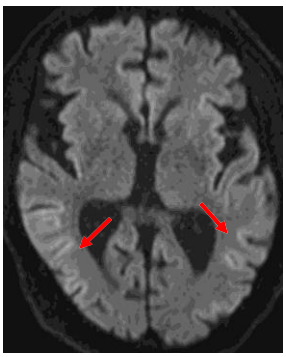
Spontaneous eye movements

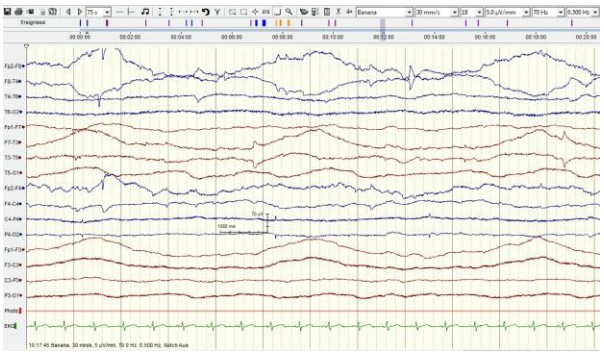
- If purposeful eye movements are present in an otherwhise unresponsive patient → consider locked-in syndrome (**vertical** eye movements), catatonia and pseudo coma.
- Roving eye movements (slow, conjugate, lateral, to-and-fro excursions („ping-pong gaze")) → 3rd/6th nerve nuclei and connections are intact → toxic, metabolic or bilaterally hemispheric cause of coma.
- Ocular bobbing → rapid conjugate downward jerk of both eyes with slow returning to mid-position → specific for acute pontine lesions (or cerebellar lesions compressing the pons).

Bateman. J Neurol Neurosurg Psychiatry 2001;71(suppl I):i13–i17
Wijdicks. Critical Care (2016) 20:193
Wijdick. JNNP (2010);10:51–60.

Pendular („ping-pong gaze") eye movements

Hypoxia as most likely cause → bihemispheric dysfunction





Reflexive eye movements → angular VOR testing (1-2Hz, sinusoidal)[1] *

Questions asked	Indicative of
Is there a VOR slow phase and is it fully compensatory?	• Presence of a vestibular response.
Is there a resetting quick phase?	• Structurally intact pontine or mesencephalic reticular formation (and thus excludes a significant depression of the level of consciousness). • If unilateraly absent → focal infratentorial lesion.
If there are no quick phases, can both eyes be driven into extreme contraversive positions in the orbita?	• Intact abducens and oculomotor nuclei as well as a functionally preserved medial longitudinal fascicle (INO).
Can the eyes be held in an eccentric position in the orbita if rotation of the head is stopped when the eyes are fully deviated in the orbita?	• Intact brainstem/cerebellar gaze-holding network (and it's absence indicative ofdepressive brainstem function)

* Response depends on the instructions given and on the state of concsiousness!

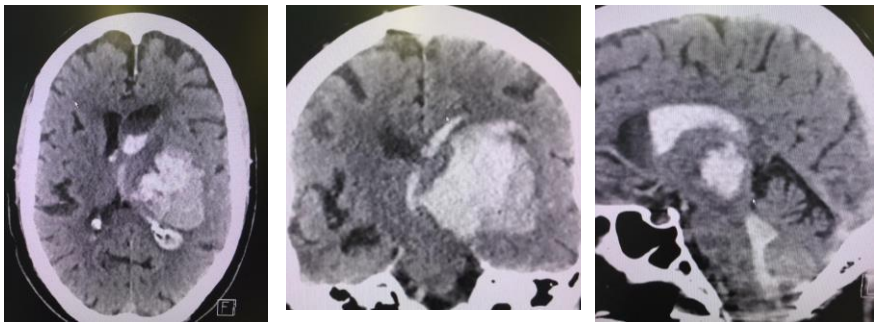
[1] Buettner and Zee. Arch Neurol (1989) 46:561-3

Kantonsspital Baden KSB

83

Increased intracranial pressure

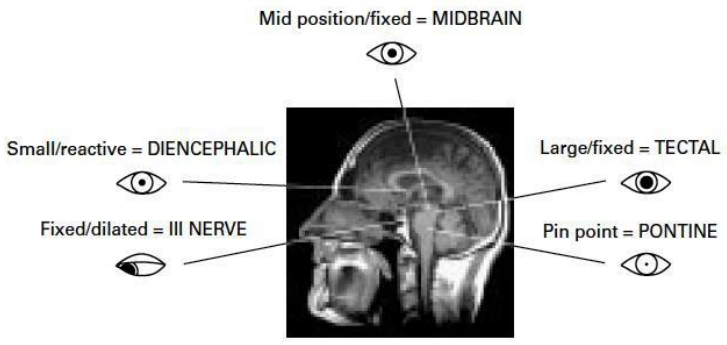
compression of midbrain ocular motor complex



Kantonsspital Baden KSB

84

Pupillary findings in comatose patients



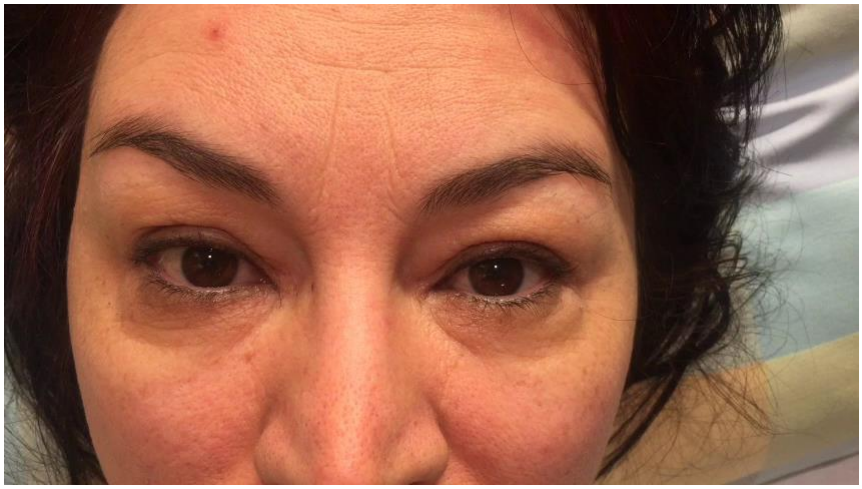
Patients with non-structural (metabolic) coma have small reactive pupils

Figure 4 Pupillary findings in comatose patients

Bateman. J Neurol Neurosurg Psychiatry 2001;71(suppl I):i13–i17

Clinical cases

Case 1 – what is the key finding here?



Dangerous H.I.N.T.S. to "I.N.F.A.R.C.T.":
Fast-phase **A**lternating

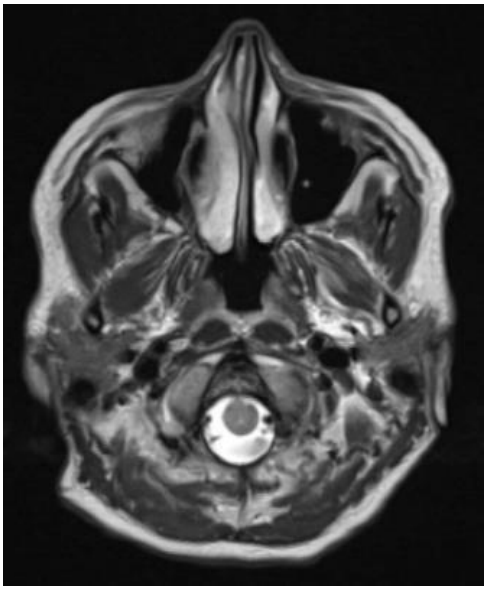
Courtesy of Alexander Tarnutzer, MD

Kantonsspital Baden KSB

87

Case 1 - brain MRI 24h after symptom onset

Large right sided PICA stroke with modarate infolvement of the left hemisphere as well



Kantonsspital Baden KSB

88

Case 2 – is it a stroke?

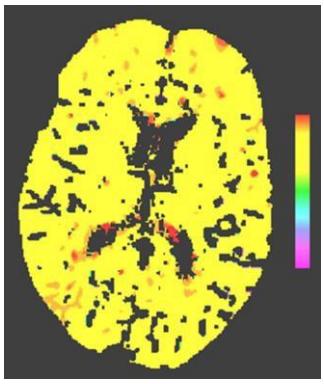
- 64-year-old male patient
- Presented with sudden-onset right sided hemiparesis and global aphasia since 15 minutes.
- Initially he noted only dysarthria and then felt weak on the right leg.
- On clinical examination:
  - non-responsive
  - did not follow instructions
  - no response to pain on both sides.
  - Both the right arm and the right foot showed some effort against gravity.
  - NIHSS was 21/42 points

Kantonsspital Baden KSB

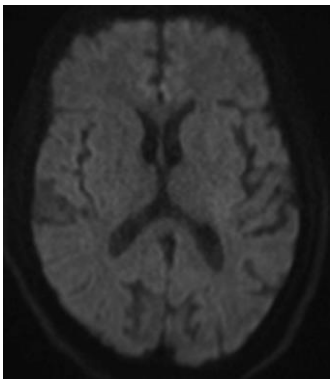
89

Case 2 - perfusion CT and MRI DWI

Normal perfusion



Normal DWI

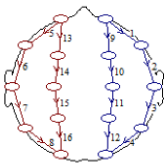


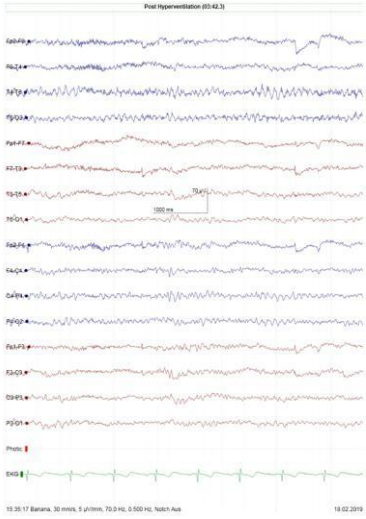
Kantonsspital Baden KSB

90

Case 2 - EEG findings

→ Epileptic nystagmus beating away from the affected side





Diffuse slowing on left hemisphere

Kantonsspital Baden KSB

91

Epileptic nystagmus – key facts

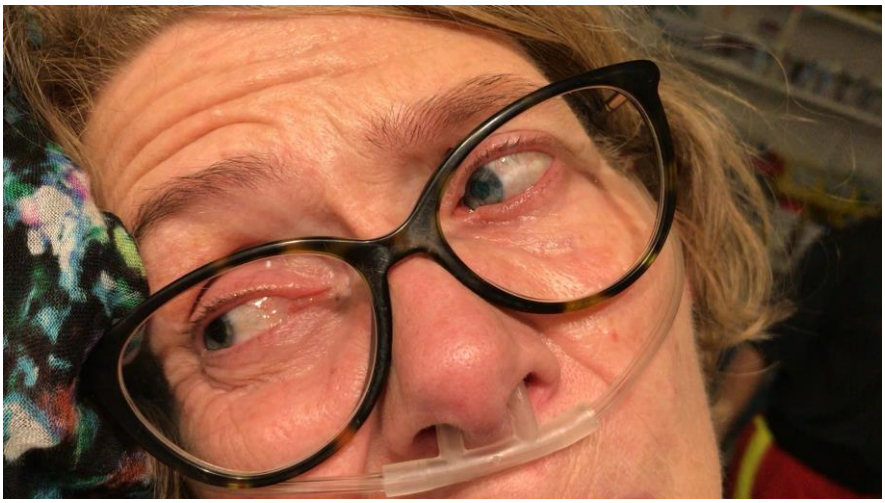
- Epileptic nystagmus → disruption of cortical control over saccades or smooth pursuit.
- Infrequent clinical finding (present in 0.5% in an epilepsy monitoring unit).[1]
- Usually accompanied by other signs as unresponsiveness, muscle twitches, increased muscle tone etc... → part of symptomatic seizurs in most cases.
- Rarely accompanied by epileptic vertigo or dizziness as different cortical areas are involved.[2]
- Predominantly horizontal nystagmus.
- Fast phase usually beating away from the side of ictal discharges → of lateralizing value.[3]
- Originating from occipital>parietal>temporo-occipital>frontal>temporal areas.

[1] Kellinghaus et al. Epilepsy Behav 2008;13:700–2.
[2] Tarnutzer et al. Neurology. 2015;84(15):1595-604
[3] Lee et al. Epilepsy & Behavior Case Reports 2 (2014) 156–160

Kantonsspital Baden KSB

92

Case 3 - Another case with epileptic nystagmus



Kantonsspital Baden KSB

93

Case 4 - New-onset persistent dizziness, gait imbalance and oscillopsia

- A 73-year-old male presenting to the ED
- One-week history of worsening dizziness, gait imbalance and blurred vision on lateral gaze.
- He also had lost interest in daily activities recently. He had received daily intravenous antibiotics for 2.5 months due to infected liver cysts.
- Due to persistent nausea his food intake was very limited, resulting in a weight loss of 22kg.

→ **Marked horizontal gaze-evoked nystagmus**

Kantonsspital Baden KSB

94

Case 4 - horizontal head-impulse testing

→ **Horizontal HIT bilatarlly impaired**

Kantonsspital Baden KSB

Case 4 - what is the most likely diagnosis?

a) Acute vertebrobasilar stroke

b) Thiamine deficiency (Wernicke‘s encephalopathy)

c) Drug-induced cerebellar loss-of-function

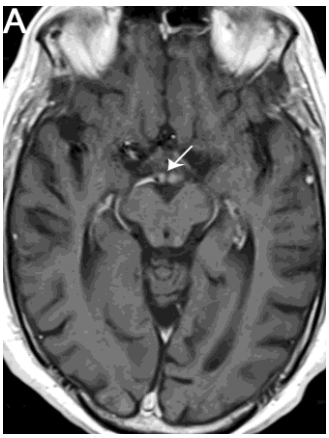
d) Gastroenteritis

e) Acute peripheral vestibulopathy („vestibular neuritis“)

Kantonsspital Baden KSB

Case 4 - diagnostic testing

Contrast-enhanced T1-weighted MRI



Blood testing

Material vom: 20.03.2019 11:55:00
Eingang am: 20.03.2019 12:17:20

Untersuchungen		Resultat	Einheit	Referenzbereich
CHEMIE				
Natrium		141	mmol/l	135-145
Kalium		3.6	mmol/l	3.5-4.8
Kreatinin	*	55	µmol/l	62-106
eGFR (MDRD)		>60 (1)	ml/min/1.73m2	
eGFR (CKD-EPI)		98 (2)	ml/min/1.73m2	
Alk.Phosphatase (Liquid)		44	U/l	40-130
g-GT		50	U/l	10-71
ALAT (GPT)		15	U/l	10-50
Thiaminpyrophosphat*	*	23 (3)	nmol/l	67-200

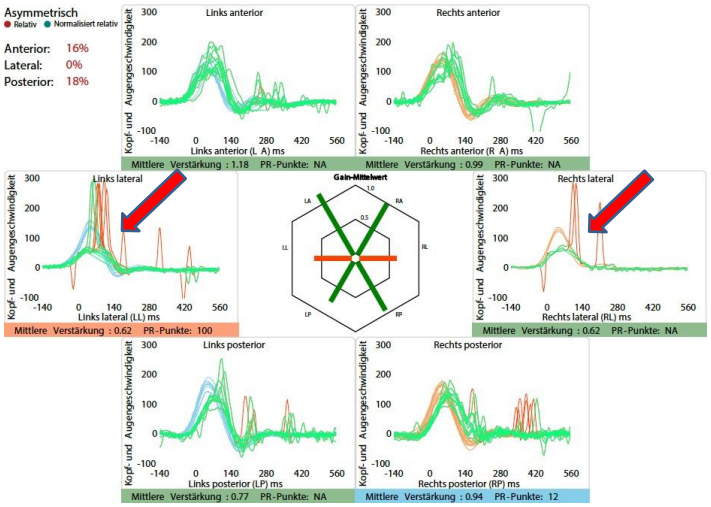
→ Disrupted blood-brain-barrier of the mamillarian bodies due to thiamine deficiency

Kantonsspital Baden KSB

97

Case 4 - Videl-head impulse testing (obtained 4 weeks after symptom onset)

Büki and Tarnutzer 2013. Vertigo and dizziness. ONL, Oxford University Press



Kantonsspital Baden KSB

98

Clinical findings – Wernicke‘s enzephalopathy (WE)

- **Thiamin deficiency → storage only for up to 18 days!**
- Chronic alcohol abuse, gastrointestinal surgery, persistent vomiting (e.g. due to chemotherapeutics), magnesium deficiency...
- **Classic trias[1]**
  - Subacute cognitive decline (esp. memory) (82%)
  - Eye movement abnormalities (29%)[2] – BUT likely much more prevalent![3]
  - Ataxia (23%)
- This trias is incomplete in most cases (3/3 in only 16-19%)!
- Old data (from the 60s/70s), before the head-impulse test was first described.

Carl Wernicke

En.wikipedia.org

First description 1881

[1] Sechi und Serra. Lancet Neurol 2007; 6: 442–55
[2] Victor M. The Wernicke-Korsakoff syndrome. In: Vinken PJ, Bruyn GW, eds. Handbook of clinical neurology, vol 28, part II. Amsterdam: North-Holland Publishing Company, 1976: 243–70.
[3] Ghez. JNNP. 1969;32:134–9.

Kantonsspital Baden KSB

Thiamine supplementation in Wernicke‘s encephalopathy

Start as early as possible and also if diagnosis is only suspected!

Treatment schemes:

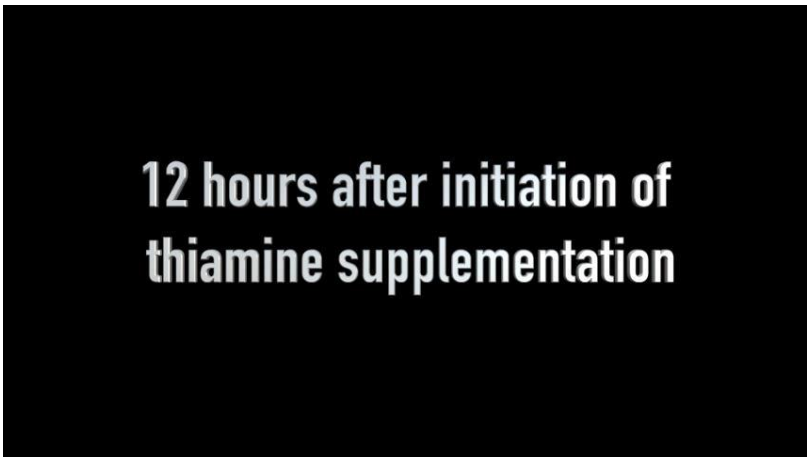
- **Secchi et al. 2007[1]**
  - First 2-3 days: 3x 500mg i.v. over 30min
  - Next 3-5 days: 3x 250mg i.v. over 30min
- **EFNS-guidelines[2]**
  - 3x 200mg i.v. per day

CAVE: Application of 100mg to 250mg thiamine per day may not be sufficient to reduce morbidity and mortality!

[1] Sechi und Serra. Lancet Neurol 2007; 6: 442–55
[2] Galvin et al. (2010) European Journal of Neurology 17, 1408–1418

Kantonsspital Baden KSB

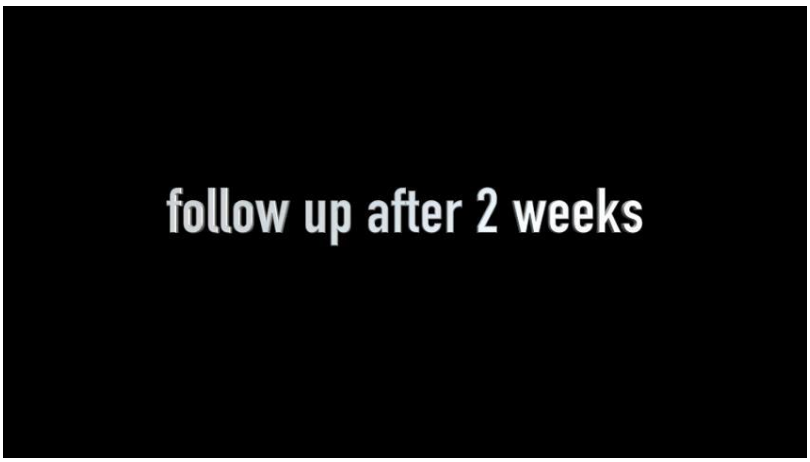
Case 4 - follow-up (GEN) after 12 hours



Kantonsspital Baden KSB

101

Case 4 - follow-up (GEN) after 2 weeks

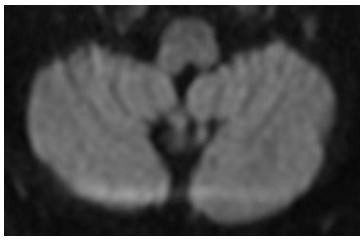


Kantonsspital Baden KSB

102

Case 5 - new-onset torsional nystagmus

- 87-year-old patient with sudden-onset ataxia of stance and gait (grade 2)
- Initial assessment (day 1) without focal neurologic changes except for ataxia.
- Brain MRI day 1 → negative
- On day 3 sudden speech disturbance and difficulties swallowing.



Kantonsspital Baden KSB

Case 5- day 4

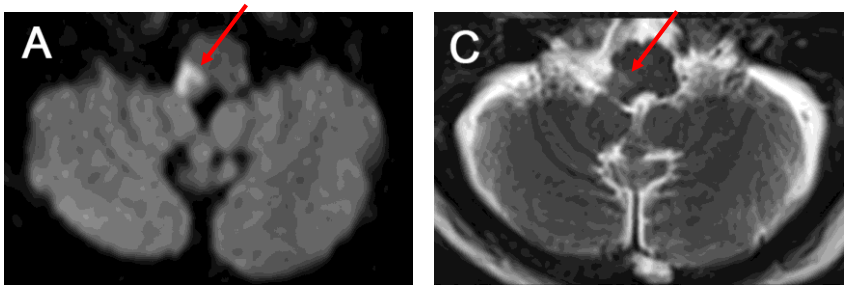
- Persistent ataxia of stance, dizziness only with head movements
- Clinical findings:
  - Purely torsional spontaneous nystagmus (beating clockwise)
  - Reduced pain sensation on the right side of the face and on the left leg
  - Hypophonia and dysarthria
  - Pathologic head-impulse test to the right

Kantonsspital Baden KSB

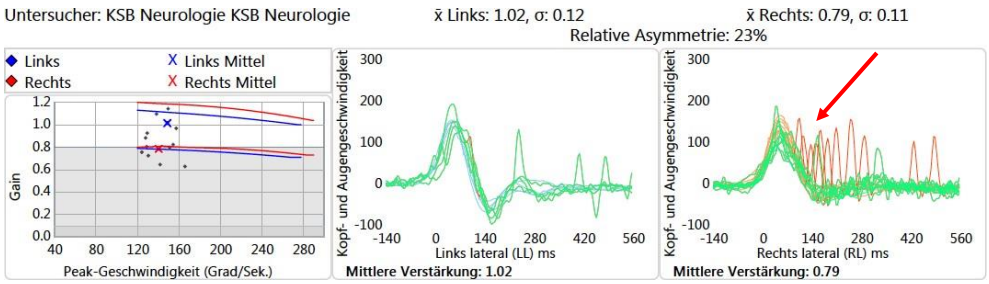
Case 5 – day 4

Right-sided dorsolateral medullary stroke

Case 5 – brain MRI (day 4)



Case 5 – video-head-impulse test



Kantonsspital Baden KSB

Case 6 - 44-year-old male patient with new-onset vertigo

Current medical history:

- Acute vertigo accompanied by nausea, vomiting, gait imbalance and intense sweating since this morning.

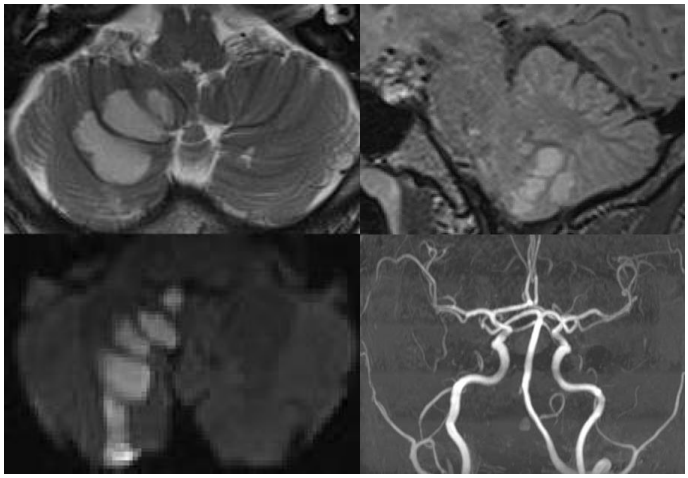
Relevant findings from clinical examination:

- Neurologic examination:
  - No obvious focal neurologic deficits (no eye muscle palsies, no limb palsies, no sensory loss, no aphasia)

- Targeted neuro-otolotic examination:
  - Torsional-horizontal spontaneous nystagmus to the left (Alexander grade II) without increase during fixation suppression
  - Bedside head impulse test to the right with very few catch-up saccades, normal on repetition.
  - No skew deviation, no gaze-evoked nystagmus, no hearing loss
  - Examination of stance and gait not possible due to his overall medical condition.

Kantonsspital Baden KSB

Case 6 - brain MRI

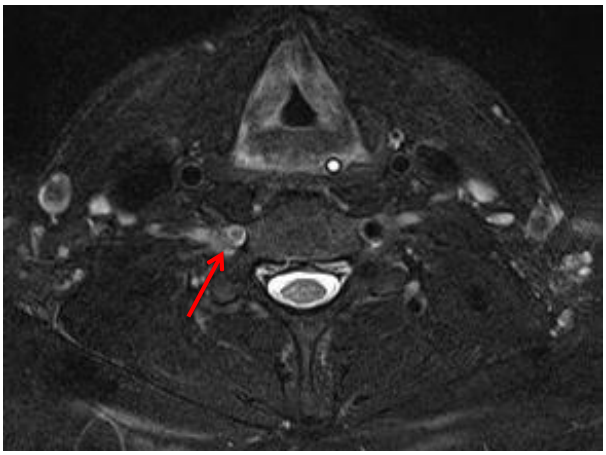


→ **Acute ischemic stroke in the right PICA territory**

Kantonsspital Baden KSB

109

Case 6 - cervical spine MRI with fat suppression



Dissection of the right vertebral artery

Kantonsspital Baden KSB

110

Case 7 – subacute AVS

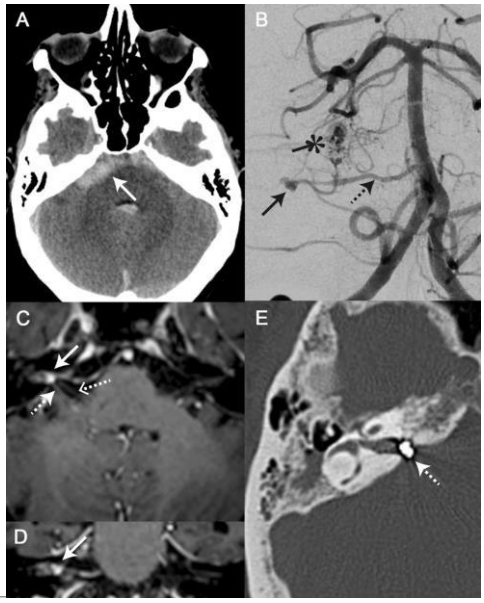
- 81-year old female patient with vertigo, gait imbalance, headache and nausea since three days.
- On exam: periphal facial palsy on the right side and adnormal head-impulse test to the right.
- Diagnostic work-up: brain MRI „normal“ → diagnosed and treated as acute peripheral vestibulopathy
- Disease course: Increase in headache, drop in GCS from 15 to 7.

Kantonsspital Baden KSB

Case 7 – dangerous peripheral AVS

A: head CT → SAH prepontine right side
B: DSA → AICA aneurysm (arrow) with accompanying AVM (arrow with star)
C/D: brain MRI before rupture → aneurysm (arrow) detectable
E: head CT → after coiling of the aneurysm. Arrow points to the coils.

→ **Distal AICA aneurysm!**



Willms et al. (2016) J Stroke Cerebrovasc Dis.

Kantonsspital Baden KSB

Case 7 – dangerous peripheral AVS

- Additional cranial nerve deficits besides the vestibulocochlear nerve is a red flag!
- Without clear signs for zoster oticus (VZV → Ramsey Hunt syndrome → Vesicles in the external auditory canal/at the ear) → incompatible with the diagnosis vestibular neuropathy!
- Imaging (focus on the cerebello-pontine angle) and joint evaluation with neuroradiology.
- Up to 50% of all AICA aneurysms become symptomatic BEFORE rupture!

Conclusions – vestibular and eye movement testing on the ED / ICU

- Targeted clinical neuro-otological examination is essential
- **Never forget** to test at the bedside
  - **H.I.N.T.S.** (gaze-evoked nystagmus, head-impulse test, skew deviation)
  - **Spontaneous nystagmus** → especially torsional / vertical nystagmus are helpful (peripheral vs. central)
  - **Truncal ataxia** → severe (grade 3) truncal ataxia is highly predictive for a central cause
- Obtain video-documentation whenever possible
- Select neuroimaging appropriately (no CCT in BPPV…)

Thank you very much for your attention

alexander.tarnutzer@ksb.ch

Kantonsspital Baden KSB

Structured history taking in the ED / ICU

Kantonsspital Baden KSB

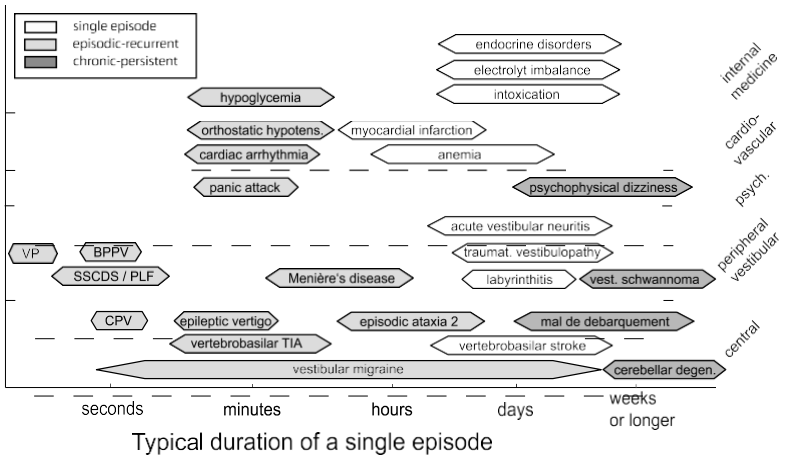
Structured history taking for acute vertigo / dizziness

- **Duration** and **frequency** of the single attacks?

Kantonsspital Baden KSB

117

Duration and frequency of attacks



abbreviations: BPPV = benign paroxysmal positional vertigo; CPV = central positional vertigo; PFL = perilymph fistula; SSCDS = superior semicircular canal dehiscence syndrome; VP = vestibular paroxysmia.

Kantonsspital Baden KSB

118

Structured history taking for acute vertigo / dizziness

- Duration and frequency of the single attacks?
- **Onset** of the attacks (abrupt vs. slowly)?

Structured history taking for acute vertigo / dizziness

- Duration and frequency of the single attacks?
- Onset of the attacks (abrupt vs. slowly)?
- **Provocation factors**?

Provocation factors

Head inclination/reclination, turning over in bed, standing up / lying down

→ **benign paroxysmal postional vertigo (BPPV)**

(fast) standing up

→ **orthostatic hypotension**

Valsalva maneuver, acoustic stimuli

→ **superior canal dehiscence syndrome**

Busy places (shopping centers, railway stations...)

→ **functional dizziness** („psychogenic dizziness“)

None

→ **Menière‘s disease, cardiac arrhythmia, epileptogenic vertigo, (migraine)**

Structured history taking for acute vertigo / dizziness

- Duration and frequency of the single attacks?
- Onset of the attacks (abrupt vs. slowly)?
- Provocation factors?
- **Focal-neurologic signs, hearing loss, tinnitus?**

Structured history taking for acute vertigo / dizziness

- Duration and frequency of the single attacks?
- Onset of the attacks (abrupt vs. slowly)?
- Provocation factors?
- Focal-neurologic signs, hearing loss, tinnitus?
- **Prodromi** and **accompanying symptoms**?

Structured history taking for acute vertigo / dizziness

- Duration and frequency of the single attacks?
- Onset of the attacks (abrupt vs. slowly)?
- Provocation factors?
- Focal-neurologic signs, hearing loss, tinnitus?
- Prodromi and accompanying symptoms?
- **Drug history** (antidepressants, AED, sedatives, diuretics, antihypertensive drugs)?

Structured history taking for acute vertigo / dizziness

- Duration and frequency of the single attacks?
- Onset of the attacks (abrupt vs. slowly)?
- Provocation factors?
- Focal-neurologic signs, hearing loss, tinnitus?
- Prodromi and accompanying symptoms?
- Drug history?
- **Accompanying diseases** (z.B. neoplasms, multiple sclerosis, diabetes mellitus, depression)?

Structured history taking for acute vertigo / dizziness

- Duration and frequency of the single attacks?
- Onset of the attacks (abrupt vs. slowly)?
- Provocation factors?
- Focal-neurologic signs, hearing loss, tinnitus?
- Prodromi and accompanying symptoms?
- Drug history?
- Accompanying diseases?
- **head** or **neck trauma**?

Six categories of vestibular syndromes

Table 1
Timing-and-trigger–based vestibular[a] syndromes

Timing	Obligate Triggers[b] Present	No Obligate Triggers[b]
New, episodic	t-EVS (eg, BPPV)	s-EVS (eg, cardiac arrhythmia)
New, continuous	t-AVS (eg, post gentamicin)	s-AVS (eg, posterior fossa stroke)
Chronic, persistent	Context-specific chronic vestibular syndrome (eg, uncompensated unilateral vestibular loss, present only with head movement)	Spontaneous chronic vestibular syndrome (eg, chronic, persistent dizziness associated with cerebellar degeneration)

Abbreviations: t-EVS, triggered episodic vestibular syndrome; s-EVS, spontaneous episodic vestibular syndrome; t-AVS, traumatic/toxic acute vestibular syndrome; s-AVS, spontaneous acute vestibular syndrome.

Newman-Toker and Edlow, Neurol Clin 33 (2015) 577–599

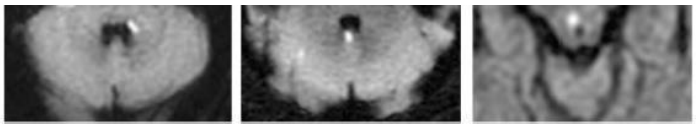
HINTS – additional slides

Lacunar strokes – H.I.N.T.S. vs. MRI

Table 2 Neuroimaging and oculomotor assessment in small vs large strokes presenting AVS

	Small strokes (≤10 mm), % (n of 15)	Large strokes (>10 mm), % (n of 90)	*p* Value
False-negative initial MRI[a]	53.3 (8)	7.8 (7)	<0.001
False-negative HINTS examination	6.7 (1)	3.3 (3)	0.46
False-negative HINTS "plus" hearing examination[9]	0 (0)	1.1 (1)	1

Abbreviations: AVS = acute vestibular syndrome; HINTS = head impulse, nystagmus, test of skew.
[a] All strokes were confirmed by MRI/diffusion-weighted imaging neuroimaging. For false-negative initial MRIs, confirmatory scans were obtained several days after the initial false-negative scan.



Saber Tehrani et al. (2014) Neurology; 83:169-173

Kantonsspital Baden KSB

129

ABCD2-risk statification for patients with acute dizziness/vertigo

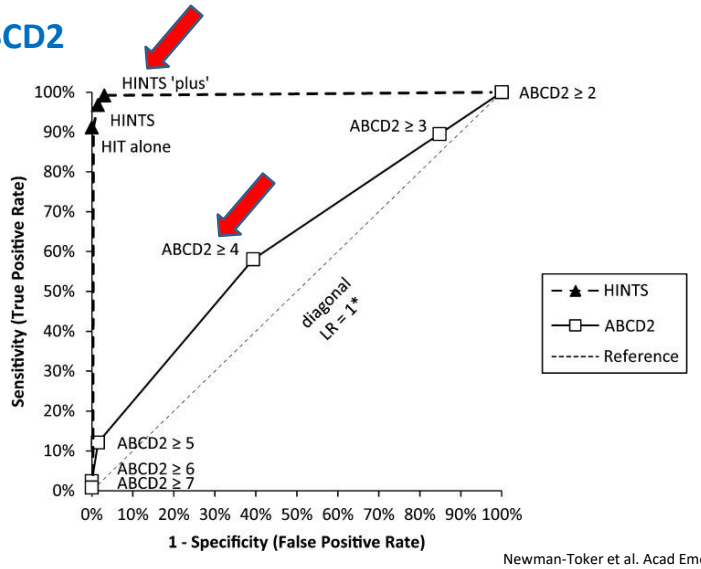
Five-item ABCD2 risk score	Stroke findings: risk score ≥ 4
• Age	• A ≥60 years = 1
• Blood pressure	• B systolic ≥140 or diastolic ≥/90 = 1
• Clinical features	• C unilateral weakness = 2, speech disturbance without weakness = 1, any other symptom = 0
• Duration of symptoms	• D <10 min = 0; 10–59 min = 1; ≥60 min = 2
• Diabetes	• D present = 1

Navi et al. Stroke. 2012; 43:1484–9.
Kerber et al. Neurology. 2015;85(21):1869-78.

Kantonsspital Baden KSB

130

H.I.N.T.S. vs. ABCD2



Newman-Toker et al. Acad Emerg Med. 2013;20(10):986-96

Kantonsspital Baden KSB

131