

Neurologist-in-training

The aim of this section is to prepare the neurologist-in-training for the FMH examination, to confront her or him with specific problems of everyday neurological practice and to give him or her updates on recent controversies in clinical neurology.

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Neurological MCQ

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Select the one correct answer.

1 Which observation is not typical of a vertigo of peripheral origin?

- A Important autonomic signs (vomiting, paleness, transpiration)
- B Delayed saccades during the "head-thrust test" (Halmagyi manoeuvre)
- C Gaze dependent, direction-changing nystagmus
- D Absence of other neurological signs except for nystagmus on exam
- E Patient lying on one side to relieve symptoms

2 What is true with regard to an acute vestibular syndrome?

- A Bilateral loss of vestibular function may have no nystagmus and may resemble a psychogenic gait problem.
- B The patient usually deviates to the contralateral side.
- C A purely horizontal, vertical or rotatory nystagmus is most likely to be of peripheral origin.
- D A hypaesthesia ipsilateral to the vestibular deficit is acceptable as part of a vestibular neuritis.
- E A nystagmus of central origin can usually be inhibited by fixation.

3 Which work-up is recommended in typical vestibular neuritis?

- A Contrast head CT and Lyme serology
- B Posterior fossa MRI with Gadolinium and Lyme serology
- C Lyme serology in endemic areas, HIV serology if patient at risk
- D Contrast head CT and lumbar puncture
- E None of the above

4 All of the following nystagmi may occur in cerebellar lesions except

- A Upbeat
- B Dissociated
- C Gaze-evoked
- D Rebound
- E Periodic alternating

5 Which statement is wrong about cerebellar diseases?

- A Transient mutism may be seen after excision of cerebellar tumours.
- B The presence and extent of cognitive dysfunction after cerebellar lesions are controversial.
- C A kinetic ("intention") tremor is typical of dentate nucleus lesions.
- D Chronic alcoholism mainly affects the anterior and superior vermis.
- E A paraneoplastic cerebellar syndrome mainly affects the vestibulocerebellum.

6 What is incorrect regarding cerebellar strokes?

- A Stroke in any of the 3 cerebellar territories may cause ipsilateral hemiataxia.
- B Acute hemiataxia may be caused by a non-cerebellar lesion that is contralateral to the ataxia.
- C PICA lesions may cause ipsilateral gaze deviation.
- D Isolated vertigo resembling acute labyrinthitis cannot be caused by cerebellar strokes.
- E In PICA stroke nystagmus is usually contralateral, in SCA stroke it is usually ipsilateral.

(For correct answers, see page 80)

References

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Neuroradiology, neuroanatomy and EEG

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Figure 1

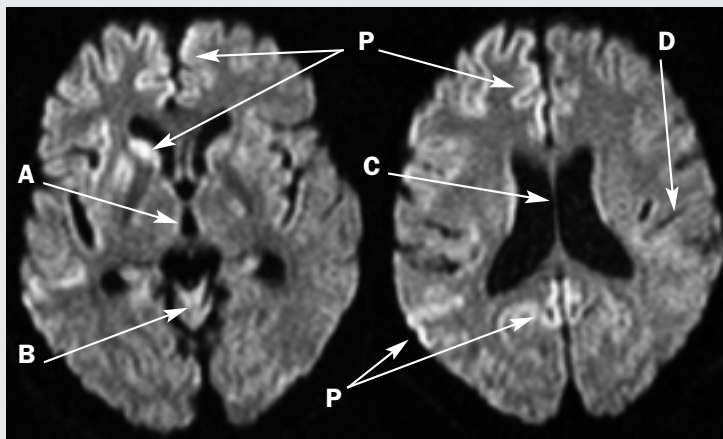
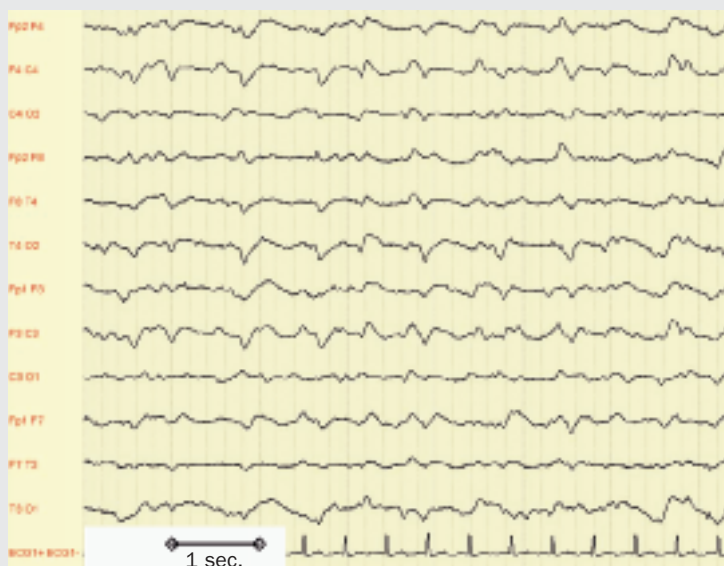


Figure 2



On figure 1 indicate the anatomical structures (A–D) and the pathology (P) on the diffusion-weighted images of this 41-year-old African patient, hospitalised in a psychiatric hospital for the subacute onset of vertigo, followed by visual hallucinations and progressive behavioural problems. Describe the findings on his EEG (fig. 2) while the patient is awake (upper half: right hemisphere, lower half: left hemisphere).

Figure 1 kindly provided by the Hôpital Cantonal de Fribourg.

EEG (fig. 2) kindly provided by the Centre d'Explorations Fonctionnelles, Service de Neurologie, CHUV, Lausanne.

(For correct answers, see page 80)

Read for you

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Update on Creutzfeldt-Jakob disease (CJD)

Prion diseases are considered as a family of degenerative diseases [1] that can occur sporadically, genetically (autosomal dominant mutations within the short arm of chromosome 20) or by infection. The prion is a physiologically occurring protein (PrPc) which is a constituent of the neuronal cell membrane. Its precise physiological role is unknown.

When PrPc comes into contact with the abnormal prion protein (PrPSc), the former changes its conformation into the pathological isoform and becomes proteinase resistant. It is hypothesised that this process may occur in *continuitatem* [2]. The abnormal prion protein aggregates to produce amyloid. There are five known major syndromes in humans: sporadic CJD (sCJD), Gerstmann-Sträussler-Scheinker syndrome (GSS), fatal familial insomnia (FFI), kuru and the new variant of CJD (vCJD). The main differential diagnoses of CJD are Alzheimer's disease, dementia with Lewy bodies and cerebrovascular dementia. The typical clinical triad comprises cognitive disturbances, ataxia and myoclonus and is present in about 60 to 70% of sCJD patients. Since 1998, sCJD is diagnosed according to the "Revised World Health Organization Criteria" (table 1) [3].

Among the additional exams, EEG was the first to be integrated in the current diagnostic criteria. The characteristic pattern of the EEG is one of bilateral (initially unilateral) periodic discharges of 0.5 to 2 Hz and is present in 60 to 70% of cases at some time during the illness (sensitivity 66% and specificity 74%) [4]. Additionally, CSF 14-3-3 protein measures (sensitivity 94% and specificity 84%) [5] and CSF neuron-specific enolase can contribute to the probable diagnosis but one has to keep in mind that false-positive results are found in diseases such as herpes simplex encephalitis, stroke, Hashimoto encephalopathy and paraneoplastic disorders [6].

So far, MRI is not an official criterion for the diagnosis of CJD. However, MRI abnormalities have now been described for more than 10 years.

Table 1

Revised World Health Organization Criteria of sporadic Creutzfeldt-Jakob disease (CJD).

Definite sporadic CJD:

- neuropathology (vacuolation of cortical grey matter, severe astrogliosis and neuronal loss) and/or resistant PrP and/or scrapie-associated fibrils

Probable sporadic CJD:

- progressive dementia and at least 2 of the following 4 clinical features: myoclonus / visual or cerebellar disturbance / pyramidal-extrapyramidal signs / akinetic mutism and
- periodic sharp wave complexes (PSWCs) on the EEG and/or
- a positive protein 14-3-3 CSF assay and a clinical duration to death <2 years and
- routine investigations should not suggest an alternative diagnosis

Possible sporadic CJD:

- progressive dementia and at least 2 of the following 4 clinical features: myoclonus / visual or cerebellar disturbance / pyramidal-extrapyramidal signs / akinetic mutism and
 - no EEG available or atypical EEG, and no 14-3-3 in CSF in a patient with clinical duration to death <2 years
-

They include hyperintensities in the basal ganglia (mainly caudate nucleus and putamen), thalamus (including the pulvinar) and in a multifocal distribution along the cortical ribbon (cerebral or cerebellar) in up to 80% of cases [7, 8]. Although T₂-weighted and fluid-attenuated inversion recovery (FLAIR) sequences show many of these lesions, diffusion-weighted (DWI) sequence seems to be the most sensitive to show cortical abnormalities [9]. The thalamic and cortical signals in sCJD are usually less intense than those in the putamen and caudate nucleus. These radiological findings are not completely specific, however, as they can also be seen in other neurological conditions such as encephalitis, hypoxia, CO poisoning,

hypoglycaemia, Wilson's disease, mitochondrial diseases and Huntington's disease. Patients with the new variant of CJD typically show bilateral DWI changes in the pulvinar thalami (sensitivity 78% and specificity 100%) [10].

There is hope of stopping the disease process in humans by using substances that limit PrPSc production in animals, such as derivatives of acridine and phenothiazine (for example chlorpromazine or quinacrine) [11] or pentosan polysulphate which is derived from beechwood [12]. Preliminary experience in humans with such substances against sCJD or vCJD has been rather disappointing, however.

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Answers to MCQ

1 C 2 A 3 E 4 B 5 E 6 D

Answers to neuroradiology, neuroanatomy and EEG

Figure 1

- A** Third ventricle
- B** Vermis cerebelli
- C** Septum pellucidum
- D** Central sulcus (Rolandii)
- P** Multifocal hyperintensities on DWI in the head of the caudate, anterior pallidum, putamen and in the cerebral cortex, as typically seen in sporadic Creutzfeldt-Jakob disease. The radiological differential diagnosis is discussed in the section “Read for you”. This patient died 6 months later and the diagnosis was confirmed histologically.

Figure 2

This EEG shows generalised slowing in the 4–6 Hz range (theta) with pseudoperiodic discharges of 0.5 to 2 Hz, compatible with but not specific for Creutzfeldt-Jakob disease.