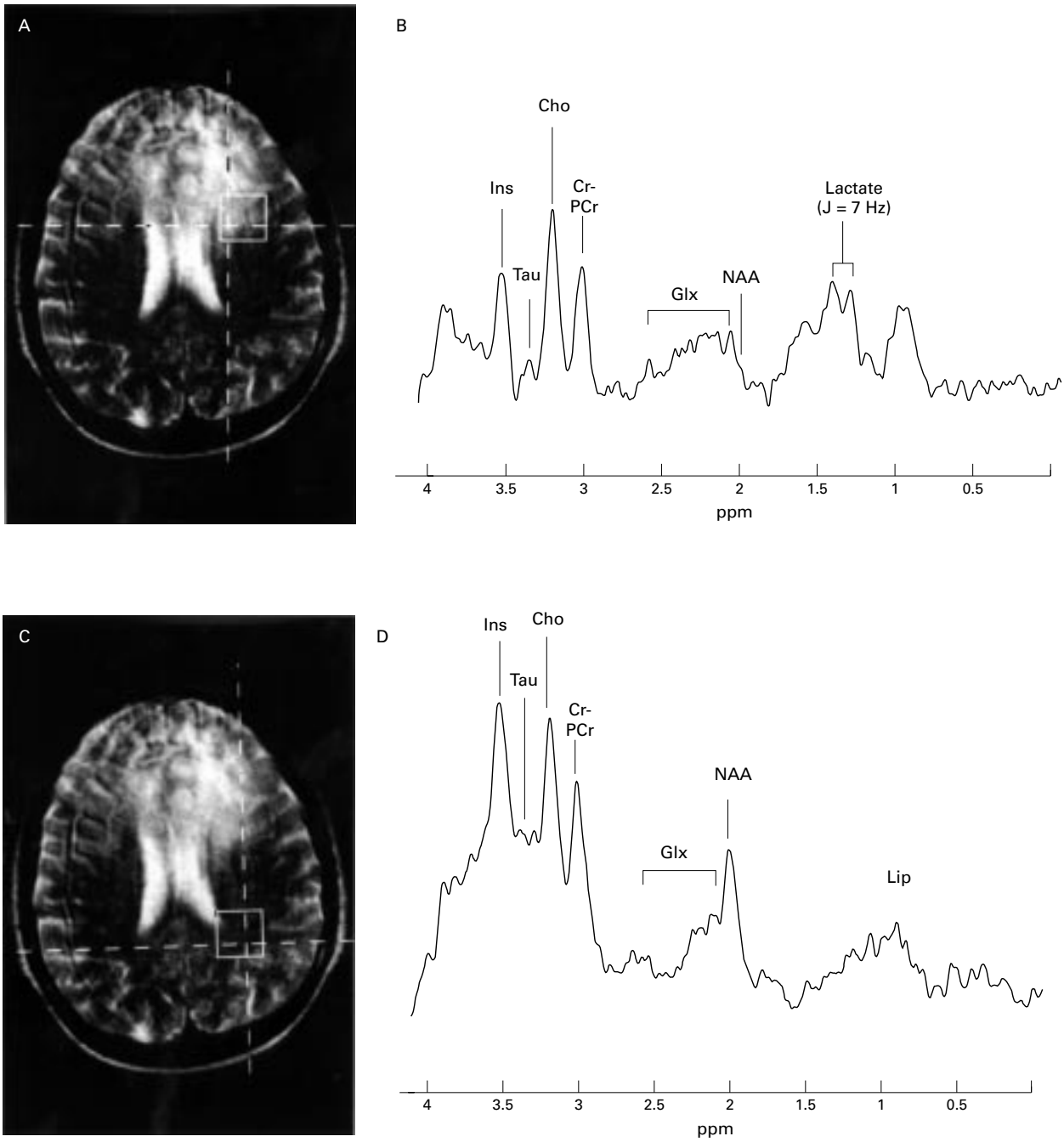
LETTERS TO THE EDITOR

In vivo cerebral proton MRS in a case of subacute sclerosing panencephalitis

Subacute sclerosing panencephalitis (SSPE) is a rare encephalopathy caused by persistent defective measles virus in the CNS. Brain lesions may involve all regions of the CNS. The pathophysiological events associated with the disease are characterised by a perivascular infiltration by monocytes and astrocytic proliferation, neuronal degeneration, and demyelination.[1] The exploration of SSPE by brain proton magnetic resonance spectroscopy (MRS) might be of interest to evaluate the extent of the metabolic lesions across the brain. We report here cerebral MRS findings in a 17 year old boy with SSPE.

The first symptoms—difficulties at school—appeared at the age of 16. Six months later, abnormal movements occurred. The symptoms progressed rapidly over the next 2 months with myoclonic jerks and behavioural changes. On admission to the neurological pædiatric unit, the patient presented an inappropriate gelastic affect with tangential speech but without any temporospatial desorientation. An EEG was characterised by high amplitude slow waves recurring periodically every 4–6 seconds. The patient had had a severe measles infection at the age of 6 months and had been vaccinated against measles at the age of 2. A slight increase in protein concentration (0.51 g/l) was found in his CSF. Immunoelectrophoresis of CSF showed an inflammatory process with oligoclonal bands. The diagnosis was confirmed by a considerable increase of specific antimeasles virus antibody in serum and CSF. A decline in clinical status was seen during the 3 weeks in hospital with a vegetative state, decerebrate



(A and C) Location of the 2 spectroscopic volumes of interest (VOI = 2×2×2 cm) displayed on T2 weighted MRI showing asymmetric frontal white matter hypersignals. (B) Short echo STEAM spectra obtained from the frontal brain lesion and (D) from the parieto-occipital brain lesion in the patient with SSPE. Ins=myoinositol (3.54 ppm), Tau=taurine/scylloinositol (3.33 ppm), Cho=choline containing compounds (3.20 ppm), Cr-PCr=creatine/phosphocreatine (3.04 ppm), Glx=glutamate-glutamine (2.10–2.45 ppm), NAA=N-acetylaspartate (2.02 ppm), Lip=lipids and/or proteins (between 1.5 and 0.2 ppm).

postures, and impaired respiratory function leading to death. Written informed consent was obtained from the patient's father to perform the MRS examination after standard MRI.

Magnetic resonance studies were performed on a Siemens Magnetom SP63 (Erlangen, Germany) equipped with a 1.5 T magnet at the Timone Hospital in Marseille. Standard MR images were acquired using a T1 weighted FLASH 2D gradient echo sequence (flip angle 90°, TE 10 ms, TR 350 ms, slice thickness 8 mm) in sagittal, coronal, and transverse planes and a T2 weighted turbo spin echo sequence (TPSE: TE=90 ms, TR=3500 ms, slice thickness 5 mm) in the transverse plane. Single voxel proton MR spectroscopy was performed at 63 MHz immediately after standard imaging using the STEAM (stimulated echo acquisition mode, TE/TM/TR = 20/30/1500 ms). Two spectra were acquired from two volumes of interest (VOI = 2 cm×2 cm×2 cm). The first VOI was located in the frontal white matter lesion and the second was located in the parieto-occipital white matter, where there were no apparent lesions (figure A). Spectra were processed using GIFA software (MADelsuc, CBS, Montpellier, France) on a Silicon Graphics Indigo station as previously described.[2]

Brain MRI shows asymmetric and bilateral white matter and cortical lesions in the frontal lobes (figure (A and C)). As presented in the figure (B), the spectrum obtained from the frontal brain lesion of this patient was very abnormal. It was characterised by a dramatic decrease in NAA resonance, an increase in inositol and choline resonances, and the presence of a lactate signal (doublet with 7 Hz J-coupling centred at 1.33±0.02 ppm). Inositol and choline signals were also increased in the parieto-occipital white matter as displayed in the figure (D). Nevertheless, the NAA signal was not reduced. The Glx/S ratio was also decreased in the parieto-occipital VOI. No lactate signal was detected on this spectrum.

The spectrum recorded on frontal white matter displayed severe metabolic anomalies in agreement with the presence of white matter changes found by MRI. Hypotheses can be proposed which relate these metabolic variations to the neuropathological characteristics of the SSPE. Because NAA is a neuronal marker,[3] the large decrease in NAA probably reflects the severe neuronal loss usually found in SSPE. As inositol is a glial cell marker,[3] the increase in the inositol signal can be related to active gliosis. The lack of a mass effect related to œdema suggests that the accumulation of lactate signal shows macrophagic infiltration[3] rather than hypoxic/ischaemic damage. The increase of choline signal might be related either to demyelination or to inflammation.[3] The creatine-phosphocreatine resonance is within normal values suggesting that appreciable necrosis did not occur in this patient.

In the posterior part of the brain, MRI did not display intense white matter lesions, contrasting with the significant metabolic impairment seen by MRS. Although no decrease in NAA was found, the increase in inositol might suggest that glial proliferation takes place before neuronal loss. Regarding the lack of widespread white matter hypersignals on MRI in this region, the rise in choline signal might reflect inflammation rather than demyelination.

These findings show that MRS is better than MRI in showing the diffuse nature of SSPE. In the posterior brain, where MRI lesions are small or absent, severe metabolic alterations take place, involving mainly glial cell activation and inflammatory processes, possibly because of virus reactivation or autoimmune reactions. The presence of MRI lesions in the frontal lobe seems to be associated with major neuronal impairment or loss, in the presence of an active metabolism of glial cells without necrosis.

In conclusion, it could be useful to carry out in vivo brain MRS at the time of MRI examination to evaluate the extent of brain damage in patients with subacute sclerosing panencephalitis.

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Alternating hemiplegia of childhood or Hashimoto's encephalopathy?

A healthy 14 year old boy had an episode of fever (38.5°C) for 1 day followed, 2 days later, by a progressively worsening confusional state, with slurring of speech, dizziness, and unsteady gait lasting 5 hours. Three months later he had a tonic attack followed by a prolonged postcritical coma which lasted 3 days. On both occasions haematological and biochemical blood tests, brain CT and MRI, CSF examination, and EEG were normal. A few days later, he had another tonic attack of 1 minute, with a confusional state, nominal dysphasia, and left hemiplegia for 8 hours followed by stupor for 3 days. The patient was therefore admitted to our hospital where nominal dysphasia, dystonia, dysmetria, tremulousness, increased deep tendon reflexes, ankle clonus, nystagmus and an enlarged thyroid gland were noted. During his stay in hospital, the patient had a paroxysmal horizontal nystagmus with bilateral mydriasis followed by a tonic attack, involving the right side of the body, with subsequent drowsiness and right hemiplegia for about 10 hours. The next morning he seemed recovered after the nocturnal rest. During that episode several examinations were carried out. EEG recording during wakefulness and spontaneous sleep showed irregular slow waves of 2 Hz–3 Hz on the left frontal region. Brain CT and MRI showed a mild reduction of volume of the left nucleus caudatus, MR angiography was normal. Ictal brain SPECT showed left hemispheric hypoperfusion. Biochemical evaluation encompassing lactate, pyruvate, ketone bodies, amino acids, ammonia, platelets, and protein C and S plasma concentrations performed ictally as well as interictally were normal. Postictal SPECT and EEG performed the next day were normal. A week later, the patient experienced a further tonic attack involving the left side of the body with subsequent drowsiness and left hemiplegia lasting 8 hours, which disappeared after nocturnal rest. EEG recording performed during that episode showed irregular slow waves of 2 Hz–3 Hz on the right hemisphere. Because of the alternating hemiplegic episodes associated with transient hemispheric hypoperfusion, flunarizine (10 mg/day) was administered.

Thyroid function investigation displayed a Hashimoto's thyroiditis, as serum TSH concentration ws 4.8 mUI/l (normal range 0.3–3.1 mUI/l), antithyroglobulin antibodies 1/100 (normal range <1/100), thyroid microsomal antibodies 1:25.600 (normal range <1/100), and TSH receptor antibodies were absent. Serum T3, free T3, T4, and freeT4 concentrations were normal. Flunarizine treatment was maintained for 28 months at the dose of 10 mg/day, and no further clinical relapses occurred during the follow up period. After 8 months, L-thyroxine (50 µg/day) was given in addition to flunarizine because of mild hypothyroidism. Neurological examination and quantitative neuropsychological tests were still normal. The thyroid microsomal antibody concentrations were unchanged at 1/25 600.

Alternating hemiplegia is a main feature of alternating hemiplegia of childhood (AHC), in which multiple paroxysmal manifestations, especially tonic-dystonic attacks, oculomotor disturbances, and the consistent restorative effect of sleep can occur. All these features were present in our patient and AHC was considered as a possible diagnosis. However, we cannot definitely state that the normalisation of the clinical findings after nocturnal rest, which occurred on two occasions in our patient, was related to the restorative effect of sleep or simply appeared during sleep by chance. The appearance of symptoms at the age of 14 years and the absence of mental deterioration were not consistent with AHC.

On the other hand, acute and relapsing neurological symptoms can also occur in patients with Hashimoto's encephalopathy. In our patient the presence of Hashimoto's thyroiditis and a history of a febrile illness just before the onset of the clinical picture manifested by confusional state and coma, are compatible with Hashimoto's encephalopathy. Transient hemiparesis has also been reported in patients with Hashimoto's encephalopathy,[1] however, to our knowledge clear cut transient, recurrent, and alternating hemiplegia episodes restored after sleep have never been reported. EEG findings such as left frontal and right hemispheric slow waves, appearing in our patient during the right and left hemiplegic episodes respectively, and the interictal normalisation are consistent with AHC. However Hashimoto's encephalopathy