and simultaneously from the deltoid, biceps brachii and FDI muscles. To investigate the presence of contralateral and ipsilateral responses, we stimulated the optimal scalp position for each of the three muscles studied in the affected and unaffected hemisphere using a stimulus intensity of 100% of maximum stimulator output during tonic activation at about 20% of maximum voluntary contraction. To increase the possibility of detecting MEPs in paretic muscles, cortical stimulation was also performed with a non-focal circular coil centred over the vertex; moreover, the scalp was mapped systematically using a figure-of-eight coil and a standard TMS protocol evaluating the cortical representation of each tested muscle together with the deltoid muscle.[4] Cortical stimulation with a non-focal circular coil centred over the vertex was performed at an intensity corresponding to the maximum stimulator output, with a clockwise inducing current flow as viewed from above for the right motor cortex and vice versa for the left motor cortex, both at rest and during voluntary contraction of the tested muscles at approximately 20% of the maximum.

Two months after stroke, maximal TMS of the contralateral and ipsilateral motor cortex during voluntary contraction did not evoke a MEP in the right deltoid either with a focal or a non-focal coil. TMS mapping showed no representation of the right deltoid in the left motor cortex and adjacent areas (fig 1B). A large-amplitude MEP was recorded at rest in the left deltoid after stimulation of the opposite motor cortex (fig 1B); this might be due to an increase in the excitability of the right, intact motor cortex consequent to an imbalance in interhemispheric inhibition.[5] Seven months after stroke, when the patient had almost completely recovered, maximal TMS of the contralateral and ipsilateral motor cortex still did to not evoke an MEP in the right deltoid either with a focal or a non-focal coil.

Recently, fMRI studies allowed us to correlate the somatotopy of the primary motor cortex to anatomical landmarks. A study indicated that the segment of the precentral gyrus containing the hand function is a knob-like structure corresponding to the middle knee of the central sulcus shaped like an inverted omega.[6] It has been difficult to obtain a ''pure'' fMRI cortical activation of the shoulder muscles because the movement also propagates to the distal muscles during a shoulder motor task. Crafton *et al*[7] demonstrated that 63% of areas activated during shoulder movement were also activated during hand motor tasks, but they were able to individuate a centre of activation for the shoulder with Talairach's coordinates 23, −29 and 55. These coordinates corresponded with the area where the ischaemic lesion was localised in the patient we report. This area was medial to the hand cortical activation area obtained by a finger-tapping task as expected from the classical human primary motor cortex map.

The patient we report recovered almost completely, but we could not record MEPs in the right deltoid muscle after maximal stimulation of the contralateral motor cortex, and there was no representation of the right deltoid in the left motor cortex and adjacent areas. MEPs were not evoked also by maximal stimulation of the ipsilateral motor cortex. Few other patients who recovered voluntary activity in proximal muscles but had no motor responses to contralateral and ipsilateral TMS have been reported.[2] Recovery of proximal muscles in these cases may be mediated by elements other than the fast corticospinal neurones responsible for MEP generation. Slowly conducting contralateral or ipsilateral corticospinal projections or polysynaptic pathways, such as corticobulbospinal, corticoreticulospinal or corticopropriospinal projections, which cannot be probed by TMS, may compensate the reduction or even the complete loss of the fast corticospinal inputs to the motoneurones of proximal muscles after stroke.

A Uncini, C M Caporale
Department of Oncology and Neurosciences, ''G. d'Annunzio'' University and the Aging Research Center, Ce.SI, ''G. d'Annunzio'' University Foundation, Chieti-Pescara, Italy

M Caulo, A Ferretti, A Tartaro
Department of Clinical Sciences and Bio-imaging ''G. d'Annunzio'' University and ITAB–Institute for Advanced Biomedical Technologies, ''G. d'Annunzio'' University Foundation, Chieti-Pescara, Italy

F Ranieri, V Di Lazzaro
The Neurological Institute, Catholic University, Rome, Italy

Correspondence to: A Uncini, Clinica Neurologica, Ospedale ''SS. Annunziata'', via dei Vestini, 66013 Chieti, Italy; uncini@unich.it

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References

1 **Komatsu K**, Fukutake T, Hattori T. Isolated shoulder paresis caused by a small cortical infarction. *Neurology* 2003;**61**:1457.
2 **Turton A**, Wroe S, Trepte N, *et al*. Contralateral and ipsilateral EMG responses to cranial magnetic stimulation during recovery of arm and hand function after stroke. *Electroencephalogr Clin Neurophysiol* 1996;**101**:316–28.
3 **Alagona G**, Delvaux V, Gérard P, *et al*. Ipsilateral motor responses to focal transcranial magnetic stimulation in healthy subjects and acute-stroke patients. *Stroke* 2001;**32**:1304–9.
4 **Uy J**, Ridding MC, Miles TS. Stability of maps of human motor cortex made with transcranial magnetic stimulation. *Brain Topogr* 2002;**14**:293–97.
5 **Liepert J**, Hamzei F, Weiller C. Motor cortex disinhibition of the unaffected hemisphere after acute stroke. *Muscle Nerve* 2000;**23**:1761–3.
6 **Yousry TA**, Schmid UD, Alkhadhi H, *et al*. Localization of the motor hand area to a knob on the precentral gyrus. A new landmark. *Brain* 1997;**120**:141–57.
7 **Crafton KR**, Mark AN, Cramer SC. Improved understanding of cortical injury by incorporating measures of functional anatomy. *Brain* 2003;**126**:1650–9.

Rapid improvement of diffusion-weighted imaging abnormalities after glucose infusion in hypoglycaemic coma

Diffusion-weighted imaging (DWI) may detect hyperintense lesions in patients with transient hypoglycaemia-induced hemiparesis or coma, which are completely reversible after glucose infusion.[1–3] In vivo animal studies have documented the visualisation of such hypoglycaemia-induced changes of signal intensity and the reversal by glucose intake in detail.[4] However, the time necessary for hyperintense lesions on DWI to disappear after glucose infusion in humans is still unclear. We treated a patient in a hypoglycaemic coma with DWI abnormalities in the splenium of the corpus callosum and the bilateral posterior limbs of the internal capsules, which were drastically improved 2 h after glucose infusion.

A 54-year-old woman was taken to an emergency department after being found in an unresponsive state. The patient had had type 2 diabetes mellitus, hypertension and hyperlipidaemia for 7 years, controlled by oral drugs. On arrival, she was comatose (Glasgow Coma Scale 4; E1, V1, M2). Her pupils exhibited isocoria (2 mm/2 mm) and were reactive to light. Tetraparesis and decerebrate rigidity to pain was evident. Her blood pressure was 91/40 mm Hg and her heart rate was 88 beats/min. She had spontaneous respiration and a normal temperature. Magnetic resonance imaging (MRI) and magnetic resonance angiography were carried out immediately, as we considered the possibility of brain stem infarction. DWI showed hyperintense lesions in the splenium of the corpus callosum and the bilateral posterior limbs of the internal capsules (fig 1A). T2-weighted and fluid-attenuated inversion recovery sequences showed no abnormal lesions, and magnetic resonance angiography showed no major abnormalities, including basilar artery occlusion. Laboratory examinations showed no metabolic abnormalities except for severe hypoglycaemia with a blood glucose concentration of 1.8 mmol/l. The patient was immediately given 40 ml of 50% glucose infusion; she recovered consciousness shortly afterwards. The abnormal hyperintense lesions had almost disappeared on DWI obtained 2 h after glucose infusion (fig 1B), and had completely disappeared 2 days later (fig 1C). Blood glucose concentrations after glucose infusion and 2 days later were 13.9 and 6.5 mmol/l, respectively. The final cognitive function was completely normal in her daily life. The patient's hypoglycaemia was due to low dietary intake and irregular medication in the 4 days prior to admission. The duration of hypoglycaemia was not apparent.

Follow-up MRI has been carried out between 8 h and 10 days in previous cases,[1–3] hence the duration of DWI abnormalities cannot be exactly known. But in reality, the hyperintense lesions on DWI had almost disappeared in only 2 h in our patient. The in vivo animal study of hypoglycaemia found complete apparent diffusion coefficient (ADC) normalisation except in the periventricular regions by 10 min after glucose infusion.[4] Glucose deprivation is widely assumed to lead to severe brain energy failure, reduction of cell membrane ionic pump activity and consequent shift of cerebral water from the extracellular space to the intracellular space. The fast recovery of the clinical symptoms and normalisation of imaging abnormalities presumably resulted from the immediate intravenous glucose supplementation. Although, in our patient, follow-up MRI was carried out in 2 h after glucose infusion and rapid improvement in DWI abnormalities was detected by chance, there is a possibility that the actual duration of DWI abnormalities in previous case reports also might be short, as in our patient.

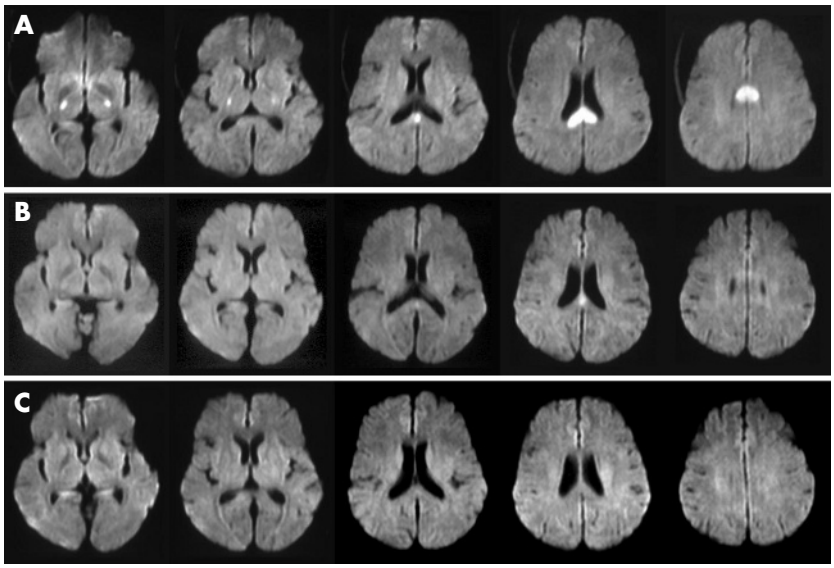

Figure 1 (A) Diffusion-weighted imaging (DWI) on admission showing hyperintense lesions in the splenium of the corpus callosum and the bilateral posterior limbs of the internal capsules. (B) DWI obtained 2 h after glucose infusion showing almost full recovery except for a small part of the splenium of the corpus callosum. (C) DWI obtained 2 days after glucose infusion showing complete regression of the hyperintense lesions.

In previously reported cases, several marked MRI findings were shown. DWI and ADC were more sensitive than fluid-attenuated inversion recovery imaging to detect the abnormal lesions.[2 3] The initial ADC values were moderately decreased, but were fully reversible.[2 3] Perfusion-weighted MRI showed no perfusion deficit[2] or a slight increase in relative cerebral blood volume restricted to the lesion seen on DWI.[3] Magnetic resonance angiography detected no haemodynamically relevant stenosis or vasospasm.[1–3] DWI showed changes localised in the splenium,[2] the internal capsule[1 3] and the corona radiata.[1 2] In our patient, the lesions were located in the splenium and the internal capsule.

Typical lesions in more severely affected patients had different localisations including the basal ganglia, the pons, the temporal and occipital cortices, and the hippocampus. Magnetic resonance signal changes in the splenium have been found in various pathological conditions such as alcohol use, infections, hypoglycaemia, trauma, salt abnormalities and seizure.[5] DWI often showed other areas of involvement, particularly the posterior limb of the internal capsule.[5] T2-relaxation MRI studies of healthy patients showed heterogeneous water content in the splenium and the posterior limbs of the internal capsule, but tissue myelin water content was relatively higher.[6] Effects associated with the splenium and the posterior limb of the internal capsule injury as described above can compromise cellular fluid regulation.[5] Our findings may support the hypothesis that the splenium and the posterior limb of the internal capsule can more easily affect cellular fluid mechanics compared with the surrounding tissue in some pathological conditions.[5]

In conclusion, abnormal hyperintense lesions on DWI in hypoglycaemic coma may disappear rapidly after glucose infusion.

J Maruya, H Endoh, H Watanabe, H Motoyama, H Abe

Department of Neurosurgery, Cardio-Neuro Vascular Center, Tachikawa General Hospital, Nagaoka, Niigata, Japan

Correspondence to: J Maruya, Department of Neurosurgery, Akita Red Cross Hospital, 222-1 Nawashirosawa, Kamikitate, Akita 010-1495, Japan; jmaruya@archosp-1998.com

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References

1 **Aoki T**, Sato T, Hasegawa K, *et al*. Reversible hyperintensity lesion on diffusion-weighted MRI in hypoglycemic coma. *Neurology* 2004;**63**:392–3.
2 **Bottcher J**, Kunze A, Kurrat C, *et al*. Localized reversible reduction of apparent diffusion coefficient in transient hypoglycemia-induced hemiparesis. *Stroke* 2005;**36**:e20–2.
3 **Cordonnier C**, Oppenheim C, Lamy C, *et al*. Serial diffusion and perfusion-weighted MR in transient hypoglycemia. *Neurology* 2005;**65**:175.
4 **Hasegawa Y**, Formato JE, Latour LL, *et al*. Severe transient hypoglycemia causes reversible change in the apparent diffusion coefficient of water. *Stroke* 1996;**27**:1648–56.
5 **Doherty MJ**, Jayadev S, Watson NF, *et al*. Clinical implications of splenium magnetic resonance imaging signal changes. *Arch Neurol* 2005;**62**:433–7.
6 **Whittall KP**, MacKay AL, Graeb DA, *et al*. In vivo measurement of T2 distributions and water contents in normal human brain. *Magn Reson Med* 1997;**37**:34–43.

Familial Creutzfeldt–Jakob disease with E200K mutation presenting with neurosensorial hypoacusis

Creutzfeldt–Jakob disease (CJD) is characterised by rapidly progressive dementia, myoclonus, ataxia, visual disturbances and motor dysfunction. Neuropathological examination shows diffuse spongiosis, neuronal loss, gliosis and a variable degree of amyloid plaque deposition composed of protease-resistant prionic protein (PrP^{RES}) in several locations, including the brain stem. The most frequent clinical presentations are dementia, ataxia or visual symptoms. Most of the cases are sporadic. Only 10–15% are familial, and the most frequent point mutation is E200K. The course of disease, investigation results and neuropathology are similar to those of the sporadic form of CJD. The typical clinical presentation of E200K is a rapidly progressive dementia with myoclonus and pyramidal, cerebellar or extrapyramidal signs.[1] We report a familial case with an unusual onset, with deafness and polyneuropathy.

A 53-year-old man presented with subacute progressive bilateral hypoacusis, with tinnitus in the left ear. He was a frequent diver and the symptoms were attributed to barotrauma. During the following months, his hypoacusis worsened and he progressively developed bilateral stocking-type paresthaesia and gait instability. On examination, he was alert and cooperative, although communication was mildly affected because of the hypoacusis. He showed emotional lability; his speech was slow but fluent, and he was partially disoriented in time. Extrinsic ocular motility, cranial nerves and muscular strength were normal. Lower limbs showed mild hypertonia, right extensor plantar response, stocking-type hypoaesthaesia and hypopallaesthaesia, and moderate gait ataxia. An audiometric examination showed bilateral neurosensorial hypoacusis, and nerve conduction studies showed a mixed axonal polyneuropathy. Computed tomography and magnetic resonance imaging of the brain were normal and the electroencephalography (EEG) showed non-specific changes.

These symptoms led to an initial suspicion of a paraneoplastic disorder, and an examination for malignant disease was started. At this moment, we learnt that the patient's mother had died of neuropathologically confirmed CJD; hence we conducted a CSF 14-3-3-protein detection test, which was positive. Serial EEGs showed repeated non-specific changes. Brain stem auditory evoked potentials (BAEPs) could not be performed, owing to lack of patient collaboration.

During the following 2 weeks, myoclonus appeared and rapidly generalised, mental status deteriorated and progressive ataxia confined the patient to bed. He died of respiratory infection 10 months after onset of symptoms.

Neuropathological examination showed neuronal loss, microspongiosis and astroglial and microglial proliferation predominantly in the isocortex, entorhinal cortex, and hippocampal CA1 region, striatum, amygdala and cerebellar cortex. Punctate, synaptic-like deposits of PrP^{RES} in the cerebral and cerebellar cortices were found, as well as scattered large PrP^{RES} deposits in the granular layer of the cerebellum. The mesencephalon did not show spongiosis, but gliosis in colliculum and periaqueductal grey matter were detected.

Marked neuronal loss and gliosis in the vestibular and cochlear nuclei were observed, associated with PrP^{RES} deposition (fig 1). Western blot of PrP^{RES} showed a three-band pattern, with an unglycated fragment migrating at 21 kDa, corresponding to PrP^{RES} type 1. Genetic sequencing of PrP showed the presence of the E200K mutation in heterozygosis. No insertions or deletions were found in the 51–91 region. The patient was heterozygotic for the M/V polymorphism at codon 129.