

# Single photon emission computed tomography in the identification of new variant Creutzfeldt-Jakob disease: case reports

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New variant Creutzfeldt-Jakob disease may be associated with exposure to the causative agent of bovine spongiform encephalopathy.<sup>1</sup> Currently, a reliable diagnosis is possible only after neuropathological examination of the brain, which is risky for patients and diagnosticians.<sup>2</sup> The sensitivity and specificity of recently developed techniques are not known for new variant Creutzfeldt-Jakob disease, and they are available only in highly specialised centres.<sup>3 4</sup>

Single photon emission computed tomography is a readily available neuroimaging technique that uses intravenously administered radioactive ligands to map different aspects of brain function.

We report the findings on this technique using the cerebral perfusion tracer hexamethylpropyleneamine-oxime (HMPAO) in two patients with neuropathologically confirmed new variant Creutzfeldt-Jakob disease.

## Patients, methods, and results

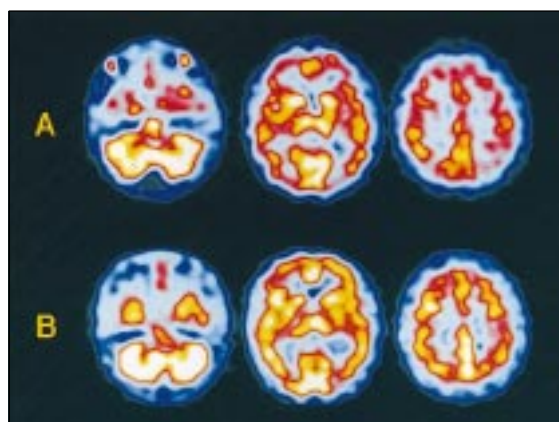
**Case 1**—A 28 year old woman developed paraesthesia of her right arm, then right leg, and later both left arm and leg. Six months later she complained of weight loss and fatigue, and had mild ataxia. After 1 year, speech, memory, and behavioural abnormalities were identified, her ataxia had worsened, and choreiform movements were noted. Six months later she developed myoclonus, primitive responses, pyramidal signs, and severe limb and truncal ataxia. Finally, she became rigid and mute; she died 23 months after the onset of her symptoms. An electroencephalogram taken 11 months after initial presentation showed no abnormalities. A repeat tracing 3 months later showed no abnormalities either, and at that time, results from magnetic resonance imaging of the brain were reported as normal apart from showing mild atrophy. Simultaneous single photon emission computed tomography showed hypoperfusion, most marked in the left temporoparietal region. The diagnosis of new variant Creutzfeldt-Jakob disease was established histopathologically.

**Case 2**—A woman aged 34 was admitted to a psychiatric unit with a 9 month history of presumed agitated depression. Neurological examination gave normal results, and antidepressant treatment was started. Over the next 2 months she developed delusional thoughts and became unsteady. An electroencephalogram showed diffuse slowing, and magnetic resonance imaging of the brain was reported to be normal. She continued to deteriorate with worsening psychiatric symptoms, progressive ataxia, bulbar palsy, and incontinence. Single photon emission computed tomography (two weeks after the magnetic resonance study) showed widespread reduction in cortical perfusion (figure). Over the ensuing months she became more withdrawn, ataxic, and rigid. Finally, she had rest and stimulus sensitive myoclonus, and was

mute. She died 14 months after the onset of her illness. The histopathological findings were characteristic of new variant Creutzfeldt-Jakob disease. Serial electroencephalographic recordings (the last was performed 10 days before her death) showed progressive slowing of background rhythms but no typical periodic complexes.

## Comment

The two patients presented consecutively at this institute, and necropsy confirmed that they had died of new variant Creutzfeldt-Jakob disease. As with other cases of the disease identified to date, early diagnosis was hampered by the absence or subtlety of neurological features, and by comparatively normal results in investigations. The clinically important abnormalities of cerebral perfusion on single photon emission computed tomography, when findings on electroencephalography or cerebral magnetic resonance imaging were normal, raised or supported the diagnosis of an organic encephalopathy in both cases. Similar abnormalities shown in single photon emission computed tomography have been reported in sporadic Creutzfeldt-Jakob disease, and a patient who died 7 weeks after onset had a unilateral perfusion deficit corresponding to the clinical, electroencephalographic, and pathological abnormality.<sup>5</sup> Although the perfusion abnormalities seen here are non-specific and cannot be claimed to be diagnostic of new variant Creutzfeldt-Jakob disease, they are more marked and widespread than those associated with depression. Consequently, the technique may prove useful in raising the possibility of the disease in young patients presenting with unusual psychiatric or neurological syndromes, with normal or unhelpful results in routine investigations.



Axial sections on single photon emission computed tomography through cerebellum, basal ganglia, and parietal region in case 2 (A) showing widespread reduction in cortical perfusion, and in age matched, healthy subject (B) for comparison

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## Social alcohol consumption and low Lp(a) lipoprotein concentrations in middle aged Finnish men: population based study

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Light or moderate alcohol consumption decreases the risk of coronary heart disease.<sup>1</sup> Beneficial changes in high density lipoprotein cholesterol concentrations are, however, observed at quite high levels of alcohol consumption—that is,  $\geq 20$  units per week, 1 unit being 10-12 g.<sup>2</sup> Therefore, other factors may be responsible for decreasing the risk of coronary heart disease when alcohol is consumed in social amounts. We studied the relation between light and moderate alcohol intake and Lp(a) lipoprotein concentrations. Lp(a) lipoprotein is an independent risk factor for coronary heart disease<sup>3</sup> and is affected by alcohol misuse.<sup>4</sup>

### Subjects, methods, and results

We performed a population based cross sectional study of 300 men aged 40-60 years selected randomly by age stratification; 259 (86%) participated in the study. Subjects were divided into four groups by alcohol consumption: abstainers (mostly lifetime teetotalers; 37 men) and three groups of drinkers. Drinkers in the lowest third consumed  $< 39$  g alcohol/week (74 men), those in the middle third 39-132 g/week (75), and those in the highest third  $> 132$  g/week (73). Alcohol intake was ascertained from a questionnaire on the amount and quality of alcoholic beverages consumed during the previous two weeks. Plasma Lp(a) lipoprotein concentrations were determined by a two site immunoradiometric assay that showed a close correlation with two different enzyme linked immunoassays ( $r \geq 0.96$ ). Liver function was assessed by measuring lipid and enzyme concentrations in fasting blood samples using standard techniques. Statistical analysis was carried out with the SAS software package. The groups were similar for age and smoking habits. The body mass index, waist to hip ratio, systolic and diastolic blood pressure, and alanine aminotransferase values were highest in subjects in the third drinking

$> 132$  g/week compared with those in the two lower thirds and with non-drinkers ( $P < 0.001$  for each parameter, analysis of variance). The mean concentrations of serum  $\gamma$ -glutamyltransferase increased with increasing alcohol intake—that is, 34, 33, 49, and 64 U/l respectively for teetotalers, and the lowest, middle, and highest third of drinkers ( $P < 0.001$ ). Blood glucose and serum insulin values did not differ between the groups. Lp(a) lipoprotein concentrations were higher (median, 206 mg/l) in the teetotalers than in the drinkers. Lp(a) lipoprotein concentrations for the lowest, middle, and highest alcohol thirds were 137, 109, and 94 mg/l ( $P < 0.05$ , Kruskal-Wallis test) (figure). As noted in other white populations, we observed a highly skewed distribution of Lp(a) lipoprotein concentrations and a wide range within the population. The ranges were similar in the study groups (figure). Lp(a) lipoprotein concentrations showed a weak but significant correlation with body mass index, waist to hip ratio, and insulin concentrations (Pearson's correlation coefficients  $-0.15$ ,  $-0.14$ , and  $-0.15$  respectively,  $P < 0.025$  for each correlation). There were no significant differences in high density lipoprotein (means for the teetotalers, and the lowest, middle, and highest thirds of alcohol consumption 1.19, 1.19, 1.23, and 1.27 mmol/l respectively) or low density lipoprotein cholesterol concentrations between the groups.

### Comment

Our report shows that social drinking—that is,  $< 39$  g alcohol/week or 1-4 units/week—is associated with low Lp(a) lipoprotein concentrations in middle aged men. No changes were observed in high density lipoprotein cholesterol or low density lipoprotein cholesterol concentrations, blood pressure, or liver enzyme concentrations.