Parieto-occipital hypoperfusion in late whiplash syndrome: first quantitative SPET study using technetium-99m bicisate (ECD)

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Abstract. Brain single-photon emission tomography (SPET) with \( N,N'\text{-1,2-ethylene-diylbis-L-cysteine diethyl ester dihydrochloride (ECD) was performed on ten patients with a clinically high grade late whiplash syndrome and on 11 controls. Two independent readers blinded to the clinical diagnosis were able to separate the ten patients from normal controls. All these patients had qualitative bilateral parieto-occipital hypoperfusion. To confirm this, the perfusion rate of parieto-occipital over global (perfusion index) was calculated after drawing elliptical regions of interest in transversal-oblique slices. The perfusion indices in patients were significantly lower than in controls as tested by the Mann-Whitney \( U \) test. This quantitative study proves our recent qualitatively analysed observation (Lancet 1995; 345: 1513–1514).

Key words: Technetium-99m bicisate – Single-photon emission tomography – Late whiplash syndrome – Parieto-occipital hypoperfusion – Perfusion index


Introduction

Chronic symptoms after whiplash injury of the neck are sometimes debilitating and may persist for years. This so-called late whiplash syndrome includes neck and head pain and other disturbances, e.g. nystagmus, oscillopsia, dizziness, vertigo, tinnitus, blurred vision and depression. Some of these patients have cognitive disturbances (especially concerning concentration and complex attentional processing), and it has been speculated that these could be caused by drugs [1] or by structural damage to the brainstem or the frontobasal regions [2]. Due to head restraints in modern cars, so-called whiplash injury today normally produces a head impact which can lead to direct brain damage. In addition, Omomaya et al. have shown in rhesus monkeys that pure whiplash can produce direct brain injury [3]. Controlled and blinded studies in mild head injury show that single-photon emission tomography (SPET) with hexamethylpropylene amine oxime (HMPAO) detects more cerebral lesions than X-ray computer tomography (CT) or magnetic resonance imaging (MRI) [4]. In patients with subjective post-concussive complaints after mild head injury, brain SPET also shows abnormalities [5]. We found parieto-occipital hypoperfusion in most patients with cognitive disturbances after whiplash injury detected by SPET and HMPAO [6]. These findings were based on qualitative observations of two independent readers blinded to the clinical diagnosis. Quantitation of brain perfusion using SPET has not yet been undertaken. In addition, since the new radiopharmaceutical \( N,N'\text{-1,2-ethylene-diylbis-L-cysteine diethyl ester dihydrochloride (ECD; bicisate; Neurolite) seems to be superior to HMPAO for evaluating discrete diminished brain perfusion [7], we used ECD instead of HMPAO in the following quantitative study.

Materials and methods

Patients

We investigated ten patients with a mean age of 41 years (SD: 12 years) who had persistent concentration and memory disturbances and, in addition, visual disturbances (blurred vision, scintillating scotoma and/or oscillopsia) 1–4 years after whiplash injury due to rear-end car collision. The correlates of neuropsychological tests, such as the cognitive section of the Cambridge Examination for Mental Disorders of the Elderly (CAMCOG), and clinical findings with hypoperfusion patterns – emphasizing disturbed visuospatial processing in these patients – have been analysed separately. Two independent readers blinded to the clinical diagnosis were able to separate the ten patients from normal controls. These patients all had bilateral parieto-occipital hypoperfusion and normal cranial CT or MRI scans. There were no anamnestic hints of other neurovascular or neurodegenerative diseases, or of basilar artery
migraine or other type of migraine. None of the patients received vasoactive or neuroactive drugs. Furthermore, there was no clinical evidence of brain injury (commotio or contusio).

**Controls**

Eleven normal control subjects with a mean age of 43 years (SD: 18 years) were investigated. In this group cranial CT or MRI scans were not performed.

**SPET**

We used a Picker 3-headed SPET camera [Prism 3000 XP, Picker International, Highland Heights, Ohio; 40 angular increments over 120° at 30 s per view, filters: Metz, Ramp, low-energy (140 keV), ultra-high-resolution (LEUHR) collimator, 64x64 matrix]. The head of the patient was aligned parallel to the orbitomeatal line with the aid of a laser beam.

**Tracer**

Administration of radiotracers was precisely defined by a standard protocol (patients had to rest for 20 min in a dark, quiet room; slow intravenous injection; closed eyes). 650 MBq ⁹⁹ᵐTc-ECD (Neurolute, DuPont Merck Pharmaceutical Co., Billerica, Mass.) was administered exactly 10 min after preparation using manufacturing instructions. The labelling efficiency was >95% as tested by thin-layer chromatography on silica gel plates using ethyl acetate as the solvent. Brain imaging was started 30 min after the intravenous injection.

**Image analysis**

Reconstruction of transversal-oblique, coronal and sagittal slices was done by using Picker Odyssey hard- and software. Eighteen transversal-oblique, 18 coronal and 18 sagittal slices were obtained. Each slice was on average 6.33 mm thick. We calculated the perfusion ratio of parieto-occipital over global in height of basal ganglia (perfusion index) by drawing elliptical regions of interest (ROIs) in three adjacent transversal-oblique slices. The shape and size of parieto-occipital ROIs were the same in all patients and controls. The shape and size of global ROIs were fitted to the actual head form by manipulation. The position of all ROIs was adjusted to the corresponding anatomical localisation. We used the region utility software of Picker Odyssey.

**Results**

The perfusion index of left parieto-occipital over global (par.occ.L/glob) was 1.224±0.091 (mean±SD) in controls and 1.099±0.055 in patients. The perfusion index of right parieto-occipital over global (par.occ.R/glob) was 1.257±0.065 in controls and 1.120±0.043 in patients. The perfusion index of mean parieto-occipital of both sides over global (par.occ.LR/glob) was 1.241±0.063 in controls and 1.109±0.041 in patients (Table 1, Fig. 1). The difference in perfusion indices between patients (pat) and controls (con) was highly significant as tested by the Mann-Whitney U test:

- par.occ.L/glob con-pat: P=0.0031;
- par.occ.R/glob con-pat: P=0.0002;
- par.occ.LR/glob con-pat: P=0.0003 (Table 1).

So, in the investigated whiplash patients as compared with normal controls, there was bilateral parieto-occipital hypoperfusion.

**Discussion**

In this quantitative study we were able to confirm and prove our recently published findings [6] based on qualitative observation by two independent readers that most patients with late whiplash syndrome have mainly parieto-occipital hypoperfusion. In this study and this group of patients, this difference was statistically significant as compared with normal controls.

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