

Emotional impairment in a patient with amyotrophic lateral sclerosis: a ^{99m}Tc-HMPAO SPET brain study

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Abstract

Behavioral abnormalities have been reported in patients with amyotrophic lateral sclerosis (ALS) but their aetiology is not yet clearly defined. *We report* the case of a 48 years old woman with long standing bulbar onset ALS referred to our department for brain perfusion scan for the evaluation of behavioral and emotional disorders. *The patient's* scores on the neuropsychological tests were satisfactory while magnetic resonance imaging showed no structural brain abnormalities. However, cerebral blood flow imaging with single photon emission tomography with technetium-99m-hexamethyl propylamine oxime demonstrated bilateral frontal cortex hypoperfusion, as well as perfusion defects in the left parietal, temporal and occipital lobes. *In conclusion*, the reduced regional cerebral blood flow in the frontal lobes might be suggestive of underlying cortical disturbance and potentially explain the patient's symptoms.

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Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal, neurodegenerative disease characterized by muscular paralysis due to progressive degeneration of motor neurons in the motor cortex, brain stem and spinal cord. Although ALS is considered a pure motor neuron disease, cognitive, behavioral and/or emotional disorders may also occur. With technetium-99m-hexamethyl propylamine oxime (^{99m}Tc-HMPAO) single photon emission tomography (SPET) qualitative and semi-quantitative information (regional cerebral blood flow-rCBF) is provided [1, 2]. This information may be helpful in the evaluation of the patient's cognitive/emotional/behavioral status. We present the case of a 48 year old female suffering from ALS with emotional impairment.

Case presentation

A 48 years old woman with ALS was admitted to the neurology department of our hospital for evaluation of newly onset of behavioral and emotional changes. The first symptoms of ALS appeared 5 years ago with dysarthria and dysphagia being the main features suggestive of bulbar involvement and the patient was classified in the type of bulbar onset of ALS or progressive bulbar palsy. Subsequently over the years, classical 'Charcot's disease' became evident with progressive impairment of walking and peripheral muscle atrophies. Noticeably, during the last months the patient developed outbursts of frustration and inappropriate laughter.

Physical examination revealed severe dysarthria and dysphonia as well as mastication and deglutition impairment. Interestingly, due to her severe impairment of speech, the patient communicated with the environment via handwriting. The patient had peripheral muscle atrophies, with hyperreflexia of the arms and legs. Hoffmann's sign was positive bilaterally. Jaw jerk and palpebral reflexes were released. Sparse fasciculations were noticed in some peripheral muscles, a sign confirmed by electromyography. Electromyogram also demonstrated prolonged F-waves and spontaneous activity mainly in peripheral muscles of more than three regions. Hematological and biochemical blood tests were normal. No medication was used as part of the patient's treatment.

Due to her behavioral symptoms, the patient underwent non-verbal neuropsychological testing because of her speech impairment; her scores on the Test of Non-Verbal Intelligence (TONI-2) and Wisconsin Card Sorting Test (WCST) were satisfactory related to her educational level.

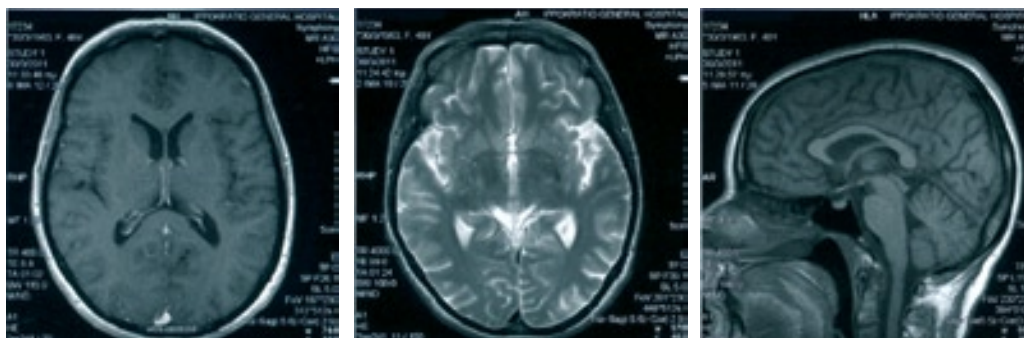


Figure 1A. Brain MRI scan of our patient: (a) Transaxial T1 with i.v. contrast, (b) transaxial T2 and (c) sagittal T1 weighted images. Absence of pathological MRI sign or pathological enrichment.

We performed brain magnetic resonance imaging (MRI). Transaxial T1- and T2-weighted images and FLAIR images were acquired before and after intravenous (i.v.) administration of contrast medium. The scan displayed no pathological sign or enrichment concerning the structures of the cerebral parenchyma (Fig. 1A).

In an effort to explain patient's emotional disorders, the patient was referred to the department of Nuclear Medicine for brain perfusion scan. Strict patient preparation is of utmost importance. Prior to the examination, the patient was ordered to avoid stimulants (caffeine, cola, etc), as well as alcohol and smoking. An i.v. cannula was placed and the subject remained for 30min in a comfortable supine position in a quiet, dimly-lit room with minimalization of external stimulations; injection of ^{99m}Tc-HMPAO followed. She was instructed to keep her eyes open and not to speak, read or move from 15min before until 15min after the injection of the radiopharmaceutical. The brain scan was performed 30min after i.v. bolus administration of 740MBq of ^{99m}Tc-HMPAO. We used pertechnetate from a twice eluted generator and the radiopharmaceutical was injected 15min after radioligand reconstruction. A SPET scanner incorporating a dual head rotating gamma-camera equipped with a low energy high resolution parallel-hole collimator was used (Axis VT, Philips, USA). Images were acquired at 180 angles, with an interval of

3° in a step and shoot mode without scatter correction. A 128x128 matrix was applied for the acquisition detecting more than 5x10⁶ events. Scanning was completed in 20min (20s per step in 60 steps). Unprocessed projection data had been reviewed in cinematic display prior to filtering. No artifacts were assessed. Image reconstruction was performed by ordered-subset expectation maximization (OSEM) reconstruction method concerning the entire brain volume. Postreconstruction filtering data was filtered only in y axis and low-pass (Butterworth) filter was used (cut-off 0,20~order 7,00). After completion of image processing, qualitative and semi-quantitative (rCBF) evaluation was performed. Quantification of the relative rCBF was carried out by normalizing the regional mean count densities to the cerebellum, which served as region of reference; we compared regional blood flow abnormalities of 12 regions of interest (ROI) including bilaterally the cortical lobes, thalamus and basal ganglia with the rCBF of the cerebellum. The scan demonstrated bilateral frontal cortex hypoperfusion, especially in the left lobe, as well as hypoperfusion in the left parietal, temporal and occipital lobes (Fig. 1B, 2). These findings, mainly bifrontal rCBF reduction, were consistent with behavioral/emotional impairment and may explain the patient's recently developing symptoms. On the other hand, brain MRI showed no morphological brain abnormalities and it was read as normal.

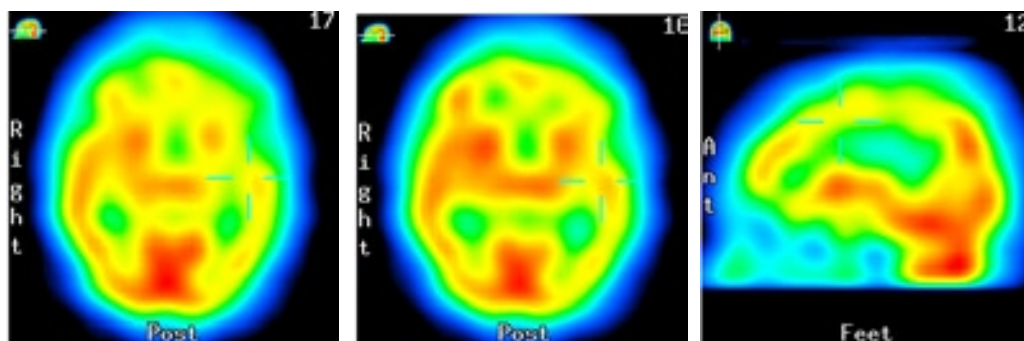


Figure 1B. Corresponding ^{99m}Tc-HMPAO brain SPET images, demonstrating bilateral frontal rCBF reduction as well as hypoperfusion in the left parietal and left occipital lobes (arrows).

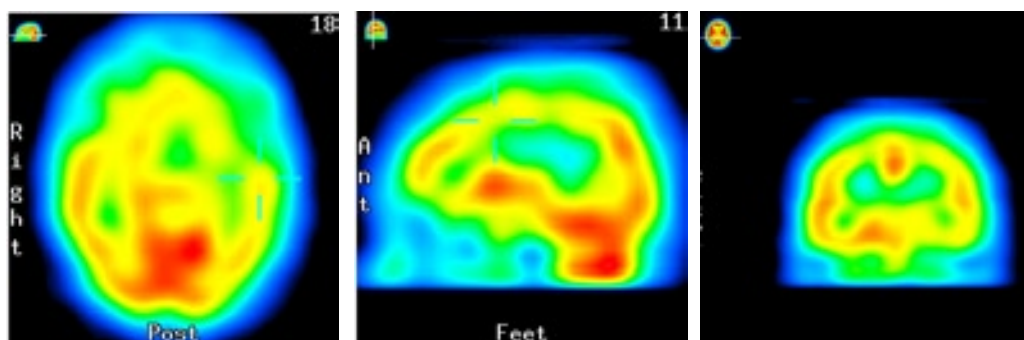


Figure 2. Selected transaxial, sagittal and coronal ^{99m}Tc-HMPAO SPET images of the patient, showing hypoperfusion in both frontal lobes as well as flow deficits in the left parietal and temporal cortex (arrows).

Discussion

Amyotrophic lateral sclerosis (ALS) is a degenerative disorder of neurones in the brainstem, spinal cord and motor cortex which presents with progressive muscular weakness and atrophy. Its aetiology remains unknown. The annual incidence rate of the disease is 1.89 per 100,000 people with average prevalence 5.2 per 100,000 in western countries [3]. The mean age of onset of ALS is about 60 years with approximate life expectancy of 2-5 years, depending on the form of the disorder [3-6].

Amyotrophic lateral sclerosis is subdivided in two main types; spinal onset ALS ('Charcot's ALS') and bulbar onset ALS (progressive bulbar palsy). Almost two thirds of the patients with ALS suffer from the spinal form of the disorder characterized by amyotrophy and hyperreflexia of the limbs. Patients with bulbar onset ALS present with dysarthria and dysphagia, symptoms reflecting the affection of the lower brainstem. Interestingly, spinal symptoms practically always become evident in the course of bulbar onset ALS. Bulbar onset ALS has worse prognosis than the spinal form. However, regardless of the type of the disease, its course is progressively fatal and the patient dies of respiratory failure since there is no effective treatment other than supportive management. Until now, riluzole (2-amino-6-(trifluoromethoxy) benzothiazole) is the only drug proven to slow the progression of the disease and increase life expectancy [7-11].

Our patient after a 5 years clinical course of ALS displayed inappropriate laughter and outbursts of frustration. These emotional changes raised the suspicion of underlying cortical degeneration despite the fact that her cognitive status appeared normal, as it was assessed by neuropsychological testing. Brain MRI did not reveal any structural abnormalities. However, due to the high clinical suspicion and the known limitations of routine anatomical imaging in evaluation of the patient's cortical function, she was referred to our department for cerebral SPET scan with ^{99m}Tc -HMPAO.

Brain ^{99m}Tc -HMPAO SPET is a useful diagnostic tool for the assessment of rCBF in dementia, epilepsy, cerebrovascular disease and other brain diseases [1, 12-20]. The basic principle of brain perfusion SPET study is that the regional deposition of ^{99m}Tc -HMPAO in the brain is proportional to the rCBF [2, 21]. Due to its lipophilic nature, this compound crosses the normal blood-brain barrier, enters the brain cells and remains there due to its conversion to a hydrophilic compound. Since practically no redistribution of the radiopharmaceutical occurs, it is retained in brain neurons for many hours, providing 'frozen' brain flow images at the time of injection. After proper patient preparation and following the strict procedure protocol, measurement of rCBF using ^{99m}Tc -HMPAO is easy to perform and is reliable for clinical evaluation [1, 22, 23]. This study is unable to offer absolute quantitative information of CBF; however information concerning rCBF parameters can be easily obtained after comparison to the flow of a reference region which is usually the cerebellum [1, 2]. This information is complementary to information acquired by conventional structural neuroimaging modalities, such as computerized tomography (CT) and MRI.

In the present study, perfusion brain SPET demonstrated marked reduction of the bilateral frontal flow, as well as rCBF defects in the left parietal, temporal and occipital

lobes. Although it is not clear whether these perfusion abnormalities are the cause or the result of neuronal degeneration, they might be associated with the patient's behavioral/emotional symptoms [20-27]. Such functional changes precede MRI findings and underscore the usefulness of neuronuclear imaging modalities (such as SPET and positron emission tomography (PET)) in the investigation of cerebral disease [20].

In conclusion, in a patient with amyotrophic lateral sclerosis, perfusion defects were detected by ^{99m}Tc -HMPAO SPET mainly in the frontal lobe and might explain her emotional impairment.

The authors declare that they have no conflicts of interest.

Bibliography

1. Kapucu OL, Nobili F, Varrone A et al. EANM procedure guideline for brain perfusion SPECT using ^{99m}Tc -labelled radiopharmaceuticals, version 2. *Eur J Nucl Med Mol Imaging* 2009; 36(12): 2093-102.
2. Syed GMS, Eagger S, Toone BK et al. Quantification of regional cerebral blood flow (rCBF) using ^{99m}Tc -HMPAO and SPECT: choice of the reference region. *Nucl Med Commun* 1992; 13: 811-16.
3. Wijsekera LC, Leigh PN. Amyotrophic lateral sclerosis. *Orphanet J Rare Dis* 2009; 4: 3.
4. Norris F, Shepherd R, Denys E et al. Onset, natural history and outcome in idiopathic adult motor neuron disease. *J Neurol Sci* 1993; 118: 48-55.
5. Worms PM. The epidemiology of motor neuron disease: a review of recent studies. *J Neurol Sci* 2001; 191: 3-9.
6. Logroscino G, Traynor BJ, Hardiman O et al. Descriptive epidemiology of amyotrophic lateral sclerosis: new evidence and unsolved issues. *J Neurol Neurosurg Psychiatry* 2008; 79: 6-11.
7. Bensimon G, Lacomblez L, Meininger V. The ALS/Riluzole Study Group. A Controlled Trial of Riluzole in Amyotrophic Lateral Sclerosis. *N Engl J Med* 1994; 330: 585-91.
8. Lacomblez L, Bensimon G, Leigh PN et al. A confirmatory dose-ranging study of riluzole in ALS. ALS/Riluzole Study Group-II. *Neurology* 1996; 47: S242-50.
9. Mitchell JD, O'Brien MR, Joshi M. Audit of outcomes in motor neuron disease (MND) patients treated with riluzole. *Amyotroph Lateral Scler* 2006; 7: 67-71.
10. Andersen PM, Borasio GD, Dengler R et al. Good practice in the management of amyotrophic lateral sclerosis: clinical guidelines. An evidence-based review with good practice points. EALSC Working Group. *Amyotroph Lateral Scler* 2007; 8: 195-213.
11. Andersen PM, Borasio GD, Dengler R et al. EFNS task force on management of amyotrophic lateral sclerosis: guidelines for diagnosing and clinical care of patients and relatives. *Eur J Neurol* 2005; 12: 921-38.
12. Devous MD Sr. Functional brain imaging in the dementias: role in early detection, differential diagnosis, and longitudinal studies. *Eur J Nucl Med Mol Imaging* 2002; 29: 1685-96.
13. Matsuda H. Role of neuroimaging in Alzheimer's disease, with emphasis on brain perfusion SPECT. *J Nucl Med* 2007; 48: 1289-300.
14. Karatzas N. Applications in neurology and psychiatry. In: Karakatsanis K, Karatzas N, Gotzamani-Psarakou A, Arsos G (eds) *Nuclear Medicine* 2003, Ziti, Thessaloniki.
15. Goffin K, Dedeurwaerdere S, Van Laere K, Van Paesschen W.

- Neuronuclear assessment of patients with epilepsy. *Semin Nucl Med* 2008; 38: 227-39.
16. Masdeu JC, Irimia P, Asenbaum et al. EFNS guideline on neuroimaging in acute stroke. Report of an EFNS task force. *Eur J Neurol* 2006; 13: 1271-83.
 17. Camargo E. Brain SPECT in neurology and psychiatry. *J Nucl Med* 2001; 42: 611-23.
 18. Goshen E, Zwas ST, Shahar E, Tadmor R. The role of ^{99m}Tc -HMPAO brain SPET in paediatric traumatic brain injury. *Nucl Med Commun* 1996; 17: 418-22.
 19. Newberg AB, Alavi A. Neuroimaging in patients with head injury. *Semin Nucl Med* 2003; 33: 136-47.
 20. Silverman DHS, Sr Devous MD. PET and SPECT imaging in evaluating Alzheimer's disease and related dementias. In: Eil PJ, Gambhir SS (eds) *Nuclear Medicine in Clinical Diagnosis and Treatment* 2004, Churchill Livingstone, Edinburgh, London, New York, Oxford, Philadelphia, San Francisco, Sydney.
 21. Payne JK, Trivedi MH, Devous MD. Comparison of ^{99m}Tc -HMPAO and xenon-133 measurements of regional cerebral blood flow by SPECT. *J Nucl Med* 1996; 37: 1735-40.
 22. Verbruggen AM. Lipophilic tracers for the study of regional cerebral blood flow. In: Eil PJ, Gambhir SS (eds) *Nuclear Medicine in Clinical Diagnosis and Treatment* 2004, Churchill Livingstone, Edinburgh London New York, Oxford Philadelphia San Francisco Sydney.
 23. Thomsen G, de Nijs R, Høgh-Rasmussen E et al. Required time delay from ^{99m}Tc -HMPAO injection to SPECT data acquisition: healthy subjects and patients with rCBF pattern. *Eur J Nucl Med Mol Imaging* 2008; 35: 2212-19.
 24. Waldemar G, Vorstrup S, Jensen TS et al. Focal reductions of cerebral blood flow in amyotrophic lateral sclerosis: a ^{99m}Tc -d,l-HMPAO SPECT study. *J Neurol Sci* 1992; 107: 19-28.
 25. Phukan J, Pender NP, Hardiman O. Cognitive impairment in amyotrophic lateral sclerosis. *Lancet Neurol* 2007; 6: 994-1003.
 26. Gibbons ZC, Richardson A, Neary D, Snowden JS. Behaviour in amyotrophic lateral sclerosis. *Amyotroph Lateral Scler* 2008; 9: 67-74.
 27. Zago S, Poletti B, Morelli C et al. Amyotrophic lateral sclerosis and frontotemporal dementia (ALS-FTD). *Archives Italiennes de Biologie* 2011; 149: 39-56.



Pablo Picasso. *Science and Philanthropy* (1897). Oil in canvas.