

FDG-PET findings in three cases of Mills' syndrome

Primary lateral sclerosis (PLS) is a rare subtype of motor neuron disease that exclusively affects upper motor neurons, usually beginning in the lower limbs and, less frequently in the bulbar region or the upper limbs.¹ In contrast to amyotrophic lateral sclerosis (ALS), PLS typically has a symmetrical presentation and this characteristic was part of the initially proposed PLS criteria.² We report 18-fluorodeoxyglucose-positron-emission tomography (FDG-PET) findings in three cases with an asymmetrical subtype of PLS, more commonly known as Mills' syndrome.³ There is no universally accepted definition of Mills' syndrome, but it is mostly referred to as a slowly progressive motor syndrome with unilateral or asymmetrical pyramidal signs.⁴ In this syndrome, the disease process remains more or less restricted to the motor areas contralateral to the affected side, as suggested by a study visualising microglial activation using 11C-(R)-PK11195 PET.⁵

Three female patients presented with an asymmetrical form of pure upper motor neuron dysfunction, starting in the right arm (patient 1 and 2) and the right leg (patient 3). The asymmetrical presentation correlated with clear regions of hypometabolism on FDG-PET in the contralateral Rolandic and peri-Rolandic areas, as can be seen in ALS or PLS^{6–8} (figure 1). MRI of the brain was unrevealing in all three patients. Extensive

investigations did not reveal other underlying pathologies. Mutations in *C9orf72*, *SOD1*, *FUS* and *TARDBP* were excluded in all three patients. There was a concordance in limb dominance and site of onset, as all three patients were right handed.⁹

No clinical or electrodiagnostic signs of lower motor neuron involvement were noted up to 8 (patient 1), 4 (patient 2) and 2 years (patient 3) after disease onset. Over this period of time, the disease spread from the right arm to the right leg and, to a lesser degree, to the contralateral side (patient 1), remained restricted to the right arm (patient 2) and spread from the right leg to the right arm (patient 3). This suggests a disease propagation by contiguous spread, as opposed to a network-spreading pattern through the corpus callosum in typical PLS.

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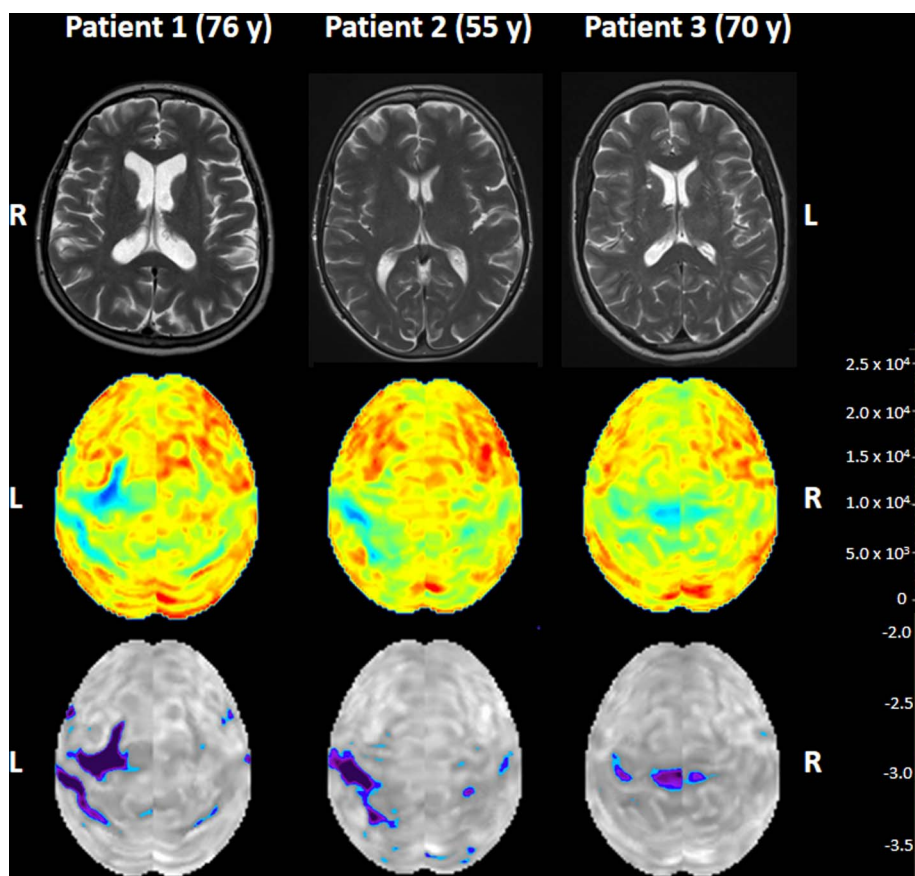


Figure 1 T2-weighted MRI (upper row) and stereotactic surface projections of the brain 18-fluorodeoxyglucose-positron-emission tomography (FDG-PET; middle row, cranial view) with corresponding Z-score images (comparing patient to healthy volunteers; lower row). No lesions on MRI that could explain the hypometabolism on FDG-PET were noted.

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Competing interests None.

Ethics approval Ethics approval was from our institutional IRB (UZ Leuven).

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