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Letter to the Editor

Striatal hyperperfusion on arterial spin labelling MRI may not necessarily reflect disease activity in leigh syndrome

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Letter to the Editor

With interest we read the article by Loiselet et al. about a study of the cerebral blood flow (CBF) by means of arterial spin labelling (ASL) magnetic resonance imaging (MRI) in 27 patients with a genetically confirmed Leigh syndrome undergoing MRI for an “acute episode of Leigh syndrome” (AELS) (n=15) or for routine MRI (rMRI) (n=15) [1]. It was found that the CBF is increased 2.8 fold in the striatum bilaterally in the AELS group [1]. It was concluded that increased CBF is a hallmark of AELS, which may facilitate early diagnosis of disease activity in Leigh syndrome [1]. The study is appealing but raises the followin1g comments

and concerns.

It is unclear what the authors mean with an “AELS”. When searching PubMed for this term, 37 hits could be achieved but, except for the index article, no other study uses this term. We should know the clinical manifestations the 15 MID patients presented with during an AELS and if the authors mean a stroke-like lesion (SLL), the morphological equivalent of a stroke-like episode (SLE), a seizure, acute deterioration of the phenotype, acute lactic acidosis, or acute ataxia, which are known as a phenotypic features of Leigh syndrome [2]. We should know how an AELS manifested on T1, T2, fluid attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI) modalities and on magnetic resonance spectroscopy (MRS). According to figure 3 an AELS is iso-intense on DWI and on T2 [1], which excludes a SLL/SLE [3]. Anyhow, SLLs are additionally characterised by increased perfusion on perfusion weighted imaging (PWI). We also should know the serum lactate values during an AELS and if the patient presented with seizures during such an episode. It should be mentioned how often such AELS recurred and if any treatment was applied. In case the authors mean acute ataxia we should know how it was possible to carry out the investigation without sedation or even anesthesia.

According to the method section, group-I patients presented with acute neurological signs such as ataxia, dystonia, hypotonia, or central apnoea [1]. These heterogeneous manifestations may have variable etiologies. If these events are interpreted as AELS it should be explained how acute central apnoea fits to a bilateral striatal lesion on ASL-MRI. Central apnea is more likely due to affection of the brainstem than due to a basal ganglia lesion, making interpretation of the increased CBF in the striatum challenging. Furthermore, hypotonia in Leigh syndrome is usually a permanent condition why atonic seizures should be excluded as the cause acute hypotonia. Permanent hypotonia in Leigh syndrome is usually due to affection of the brainstem and not related to affection of the basal ganglia [4].

A further limitation is that group-I and group-II were genetically heterogeneous. Group-I included 5 patients carrying a variant of nuclear genes and 10 patients carrying variants in mtDNA located genes. Group-II included 4 patients carrying a variant in an mtDNA located gene and 11 patients with a nuclear defect. We should know if CBF differed between these two subgroups in group-I and how it can be explained that such genetically heterogeneous patients can present with a common phenotypic feature.

Unclear is how many patients were truly investigated. According to the abstract, 27 patients

underwent ASL-MRI [1]. According to tables 1 and 2 30 patients were included [1].

Overall, this interesting study has a number of limitations which should be met before drawing conclusions as those presented. Particularly, a definition of the term AELS is required, discrepancy between variable clinical manifestations and uniformly increased striatal CBF should be explained, and why the heterogeneous genetic background manifests with acutely increased CBF.

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