An analysis of brain iron dynamics using quantitative susceptibility mapping in children with febrile seizures.

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INTRODUCTION

Febrile seizures (FS) are one of the most common neurologic disorders of infants and young children.

The pathophysiology of FS has been suggested a link with iron deficiency, which is proven clinically as lower hemoglobin and/or serum ferrous/ferritin levels, but the causal relationship is still unclear.

Brain myelination undergoes rapid progression during early childhood. This process is essential for establishing connectivity within the developing brain, facilitating rapid and synchronized information transfer across neural systems.

Given that FSs are age-dependent, there is a suggested link between their pathogenesis and myelination.

OBJECTIVES

The present study aims to examine brain iron dynamics in children with FS using quantitative susceptibility mapping (QSM) and clinical parameters

QSM is a magnetic resonance imaging (MRI) technique that enables the quantification of susceptibility-changing materials, including iron, by direct estimation from phase imaging, which shows a high correlation with myelin histology. (Representative images are shown in Figure 1)

Since the magnetic susceptibility of the human brain is mainly influenced by iron (higher QSM value) and myelin (lower QSM value), the progress of myelination can be understood as changes in QSM values.

The relationship between QSM values and iron dynamics markers in serum and cerebrospinal fluid (CSF) was also evaluated.

This study was approved by the institutional review board.

METHODS

We conducted a single-center observational cohort study, enrolling children with FS and age-matched patients without known seizures.

Using voxel-based QSM analysis, we compared the whole-brain pattern of susceptibility patterns and then examined associations with clinical data.

Cases with known underlying diseases, elevated cerebrospinal fluid cell counts, or brain MRI abnormalities were excluded.

RESULTS

Twenty-three children with FS and 23 age-matched patients are enrolled (details are provided in Table1).

Voxel-based QSM analysis shows the FS had significantly higher QSM values in precuneus, superior parietal lobe, and anterior cingulate gyrus than non-FS. (depicted as yellow points in Figure 2)

In additional analysis (not shown here), among **Recurrent FS**, right SPL (superior parietal lobe), left precuneus, and left ACG (anterior cingulate gyrus) are associated with higher QSM values.

And among **Febrile status epilepticus**, right ACG is associated with higher QSM values.

On the contrary, there were no areas where QSM values were significantly high in the non-FS group.

Laboratory data (iron dynamics markers) were shown in Table 2. Serum iron, CSF iron, and CSF ferritin were significantly lower in the FS group.

CONCLUSION

Voxel-based QSM analysis suggested brain regions were statistically significantly associated with recurrent febrile seizures and febrile status epilepticus.

Lower levels of cerebrospinal fluid iron and/or ferritin may be linked to myelination, brain QSM values, and the type of febrile seizures.

This study highlights the potential of QSM as an imaging biomarker.

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Figure 1

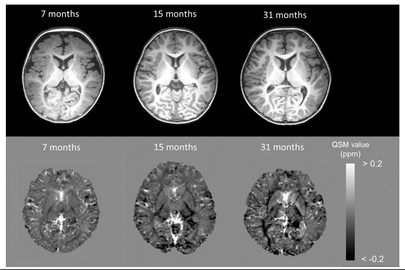
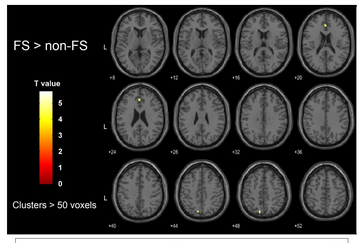


Figure 2



yellow areas are higher QSM compared with non-FS

Table 1

[1] FS group 23 subjects (18 boys) 27 ± 22 months
[2] non-FS group 23 subjects (14 boys) 26 ± 17 months

Indication for MRI			
FS group		non-FS group	
Simple FS	7	Developmental delay	11
Complex FS	16	Headache	3
Recurrent FS	12	Short stature	2
Febrile status epilepticus	3	Emesis	2
Hemiconvulsion	1	Others	5
Total	23	Total	23

Table 2	FS group	non-FS group	*p*-value
Hemoglobin (g/dL)	11.4 (n=22)	12.3 (n=16)	n.s.
MCV (fl)	74.7 (n=22)	78.9 (n=16)	n.s.
Serum Iron (μg/dL)	**27.5 (n=14)**	**68.7 (n=9)**	**<0.01**
Serum Ferritin (ng/mL)	46.4 (n=14)	39.9 (n=9)	n.s.
CSF Iron (μg/dL)	**1.0 (n=11)**	**26 (n=2)**	**<0.01**
CSF Ferritin (ng/mL)	**0.4 (n=11)**	**5.5 (n=2)**	**<0.01**

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