Research Square

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Myelination of Cingulate Fasciculus on T2-Weighted MR Images

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Abstract

Objective: To observe the myelination process of cingulate fasciculus (CF) by using T2 W images and use this data for myelination assessment of newborns.

Materials and Methods: This research retrospectively analyzed 842 patients under 16 months which underwent MRI examination for any reason and focused on the 102 babies which diagnosed as normal after two years follow-up. Myelination of CF was categorized to seven stages (stage 0 to stage 6) in all cases; than this data was analyzed to evaluate the efficacy of determining physiological myelination age.

Results: We find some cut-off months correlates with the patient myelination process. Myelination of CF mainly started at 4^{th} month and must be observed before 5^{th} month. In the 6^{th} month CFs must be thickened; and at the 8^{th} month, some subcortical branches should be seen adjacent to CF. Anterior or posterior portions of CF should be seen before 10^{th} month. Although stage 5 and 6 may differ between patients, any of this stage should be seen before 12^{th} month.

Conclusion: Our study suggests that T2 myelination of CF is efficient method in evaluating myelination process between 4^{th} and 12^{th} months-age.

Introduction:

Myelination assessment has evolved to become a routine aspect of pediatric neuroimaging. By reviewing a combination of T1- and T2-weighted (T2W) MRI, as Barkovich reported before, the radiologists and clinicians can quickly and reliably determine whether the development of myeline of a child is normal, delayed, or abnormal [1]. There are many studies about when myelination has begun after MRI-based myelination map has been extracted by Barkovich [2, 3]. The map, the worldwide known myelination map, is not mainly based on the tract, unlikely he used classical anatomical landmarks that could be more feasible to use. We know that myelination occurs along the fiber paths. However, we only use this knowledge in a limited range of clinical trials [4]. Using some other landmarks will also help us to specify the time of myelination more precisely without possibly requiring additional radiological imaging.

Herein, we tried to demonstrate longitudinal myelination map of cingulate fasciculus (CF) which is one of the most distinctive fiber tracts in the brain, forming a near-complete ring from the orbital frontal cortices, along the dorsal surface of the corpus callosum, then down the temporal lobe towards the pole. Recently, attention is focused on those relatively common states for which there is repeated evidence of changes at CF. These conditions are schizophrenia, attention deficit hyperactivity disorder, depression, post-traumatic stress disorder, obsessive compulsive disorder, and autism spectrum disorder [5]. Thus, we wanted to evaluate the myelination of the cingulum, which is not much known in the literature.

To the best of our knowledge, except for some classical pathways such as optical and motor trajectories, tract-based T2 evaluation of CF myelination has not been done yet. In this study, T2-based myelination map of CF was tried to be created. Our aim in this study was to reveal the myelin development atlas of

the track. We think that this data can shed light on future studies for brain development, and also this map can be used in routine practice for evaluation of brain maturation.

Material-methods:

Population

All MR images of pediatric patients under 16-months-old age were evaluated for the study. In all, 842 patients that underwent cranial MRI between March 2015 and August 2017 and had at least 2 years follow-up were included to our study. Any pathology that can affect myelination was excluded from the study. Premature and hypotonic babies were also excluded. In all, 102 babies diagnosed as normal after two years follow-up were included the study.

MR Protocol

All the patients underwent the 3T MRI system (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany by using 64 channel head coil). MR compatible anesthesia devices and special incubators were used for sedation. Clinical sequences in our routine clinic were composed of three plane T2 W (Table 1), axial plane T1 W and FLAIR imaging, isovolumetric T1 W, diffusion weighted imaging, and if needed susceptibility weighted imaging and post-contrast imaging. For patient selection, all sequences were evaluated for excluding the pathologic cases.

Table 1
Scanning parameters of T2 weighted sequences

	TR/TE	SLİCE thickness	fa	fov	resolutıon (phase)
AXIAL T2	3660/106	2 mm	144	190	512 (75%)
CORONAL T2	6200/100	4 mm	150	190	512 (92%)
SAGITTAL T2	6000/100	3.5 mm	150	190	512 (75%)

[Table 1 near here]

Image analysis

A neuroradiologist with 12 years' experience in pediatric neuroimaging evaluated the MR images without the knowledge of the patient age and noted the findings about myelination of CF. The entire three plane T2 W images were evaluated for myelination analyses. The myelination was classified as follows: group 0, No myelination; group 1, tiny-linear myelination of body; group 2, thickened myelination of body; group 3, development of branch myelination; group 4, pre- or post-callosal myelination; group 5, myelination of adjacent white matter; and group 6, myelination of temporal and parahippocampal segments. Samples of sagittal-coronal and axial plane T2 W images are given in Fig. 1–3.

[Figures near hear]

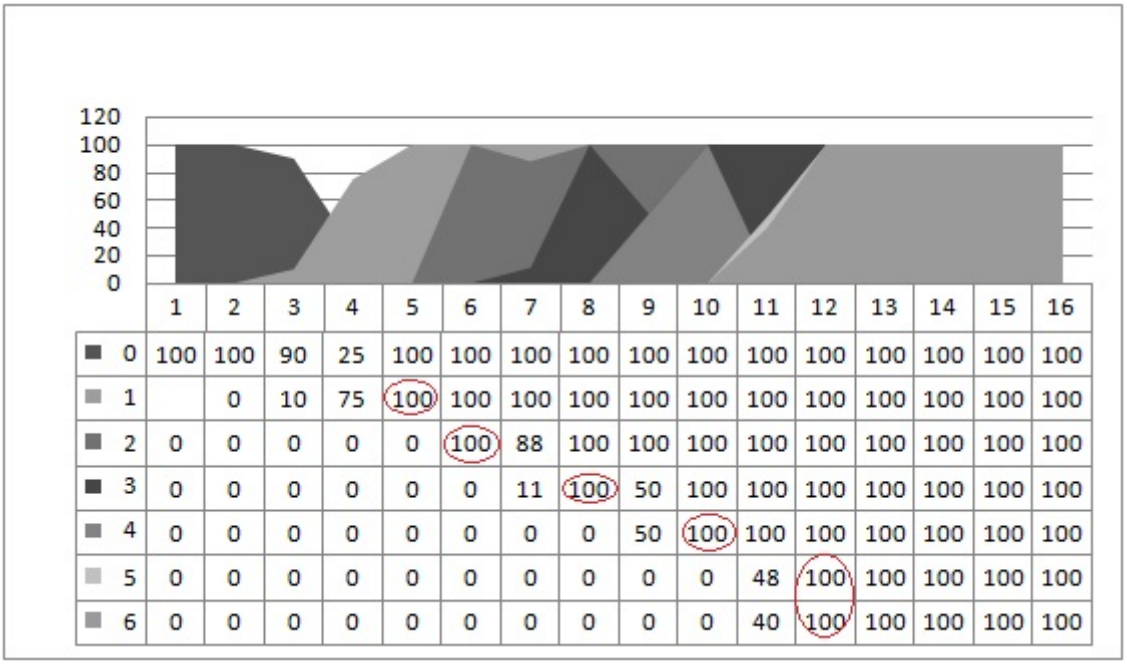
Statistical analysis

The child's age was correlated with myelination groups by using students's t test. Statistical significance was considered at the level of 0.05.

Results:

The chronology of myelination is presented in Table 2.

Table 2: Percentages of myelination steps of cingulate fascicule.



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
0	100	100	90	25	100	100	100	100	100	100	100	100	100	100	100	100
1		0	10	75	100	100	100	100	100	100	100	100	100	100	100	100
2	0	0	0	0	0	100	88	100	100	100	100	100	100	100	100	100
3	0	0	0	0	0	0	11	100	50	100	100	100	100	100	100	100
4	0	0	0	0	0	0	0	0	50	100	100	100	100	100	100	100
5	0	0	0	0	0	0	0	0	0	0	48	100	100	100	100	100
6	0	0	0	0	0	0	0	0	0	0	40	100	100	100	100	100

[Table 2 near here]

The hypointensity of CF was not demonstrated before 4th month in all subjects. A tiny hypointense line was initially revealed it the 4th month and should be seen at least in the 5th months at the body of CF. In the 6th month CFs started to be thickened; and at the 8th month, some subcortical branches started to be elongated. Anterior or posterior portions of CF started to be appeared as hypointense in the 9th month. All patients had hypointense anterior or posterior parts from the 10th month onwards. Due to myelination of surrounding fibers, it was hardly to differentiate CFs solely with T2 W images after 11-12th month.

Discussion:

Neuroscience is challenging because of the intrinsic complexity of the human central nervous system (CNS) showing regional variation and specialized organization [6]. Although the function and histology of many organs have been clearly demonstrated, there are still questions to answer about the development

of the CNS. Thus, researches on cognition and diseases has been recently increased. As the structure of brain has been more clarified compared to the function, its function with some internal pathways has not completely expressed. One of the less known function in this subject is the role of myelination in cognition and memory [7]. This has made myeline and myelination an important issue in the researches [8]. MRI has been widely used in determination of myelination in several brain areas [9]. We focused to the myelination of CF, since we believe that addition of this assessment method could ensure more accurate results in chronology of myelination. Our results show that signal changes of CF on T2-weighted MRI correlated with patients' age.

Virschow had previously described myeline in 1858, but the myeline-producing cell was identified in the mid-1900s [10]. When Virchow analyzed the fine structure of the brain in the 1850s, he realized that there were different types of cells within the neuroglial constitution called 'Nervenkitt'. However, he could not identify these structures precisely because of insufficient cell staining [10]. According to Ramon y Cajal (1909 and 1911), it was Deiters (1865) who first identified cells except neurons in CNS [11]. del Río-Hortega applied a staining method involving silver carbonate and was able to distinguish four types of oligodendrocytes [12]. The importance of myeline has been further demonstrated in subsequent years. Myeline wraps around the axons and increases the speed of the axon potential by 10–100 times due to its special formation [13]. For this reason, myelination is an important milestone in brain maturation especially in functional development.

In pediatric neuroimaging, evaluation of the degree of myelination in brain maturation is an important step [14]. The myelination maps based on T1 and T2 W MRI defined by Barkovich have been the well-known and most used technique for identifying brain maturation (9). With the myelination of white matter, it appears as hyperintense on T1W images and hypointense on T2 W images. Some studies reported that T1W images revealed myeline content more accurately and earlier compared to T2 W images. Unfortunately, T1W images have lower resolution than T2 W images and are less successful to detect the tracts. Also, T1W images became to be ineffective in investigating the myelination 6 months after birth and completely ineffective after the end of the first year [15]. Due to these factors, we focused to the T2 W images.

There are many other imaging modalities in evaluation of myeline quantification like diffusion tensor imaging [16], magnetization transfer imaging [17], quantitative T2 measurement [18], functional connectivity mapping [19], and multiparametric mapping of myeline water fraction [20]. However, in all myeline is assessed qualitatively, and there is no in vivo imaging method to show myeline amount and structure directly [7]. Again, the maturation of tracts can be evaluated by using fractional anisotropy values, but the relationship between these values and total amount of myelination was not clearly defined [13]. Myelination is a continuous process, and recent studies showed that myelination of some tracts may continue even after third decade. Thus, standardization of MRI findings are more important than the assessment of myeline amount [21]. Furthermore, the more complicated the imaging modalities, the more they are away from clinical use.

The classification by Barkovich is made according to some commonly known landmarks of the brain, and the strength of this classification was mainly its simplicity. However, it is insufficient for actual functional determinations of the tracts, and also there are some gaps between patients' ages. Functional determination of tracts is a trendy research area in physchomotor development. Therefore, we wanted to classify myelination by evaluating the tract on T2-weighted images. We chose CF analysis because of the easy evaluation of its location without performing tractography. Our findings showed that tract-based analysis on T2-weighted imaging is an efficient way to evaluate the myelination. In evaluation of myelination, not only CF could be used, but also the other areas, such as uncinate, superior-inferior frontooccipitale fascicules could be evaluated by the same way.

Our study has several limitations except for the retrospective design. The primary limitation is that tractography with which we could evaluate the localization of CF more accurately was not performed. Second, classification of myelination of CF used in our study was relatively subjective. Lastly, although image analyses were very effective between 4–10 months, it was ineffective except for this period.

In conclusion, between 4th and 10th months, overall maturation of brain can be analyzed with the evaluation of CF using only T2-weighted images. In addition, with the monthly assessment of CF myelination, we achieved more accurate and clear findings.

Declarations

Ethics approval and consent to participate: Koc University ethics committee that approved the study

Consent for publication: Not applicable

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: MSA analyzed and interpreted the patient data; SG was a contributor in writing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials: The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

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Figures

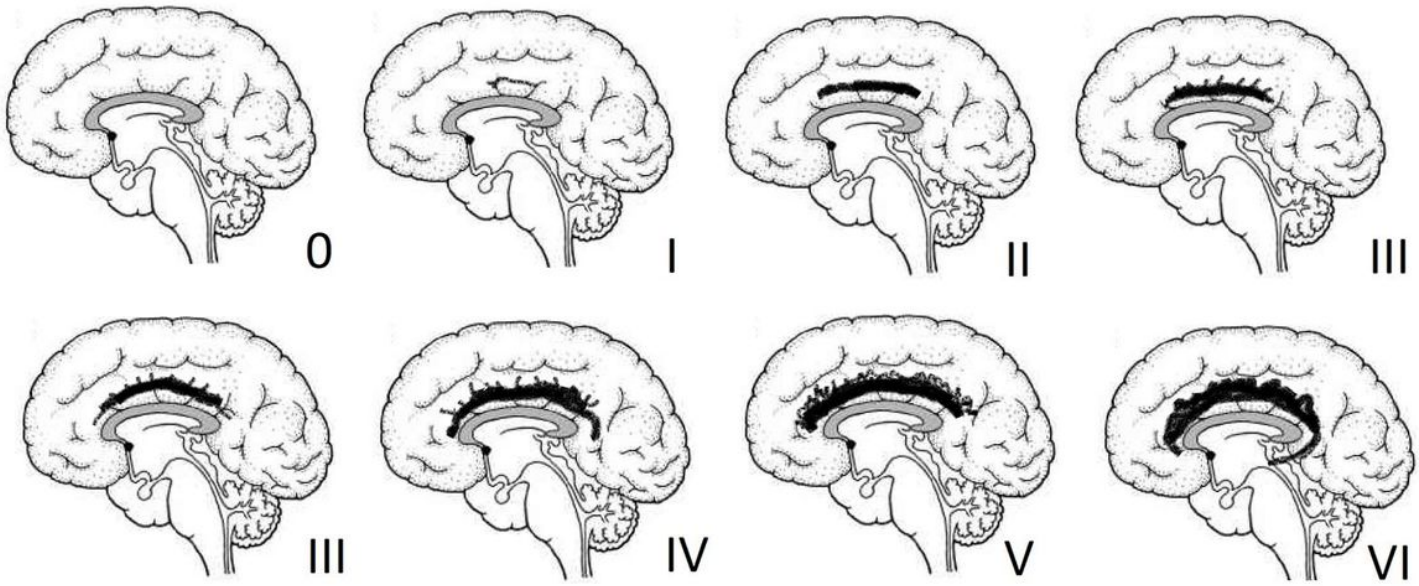

Figure 1

Figure 1

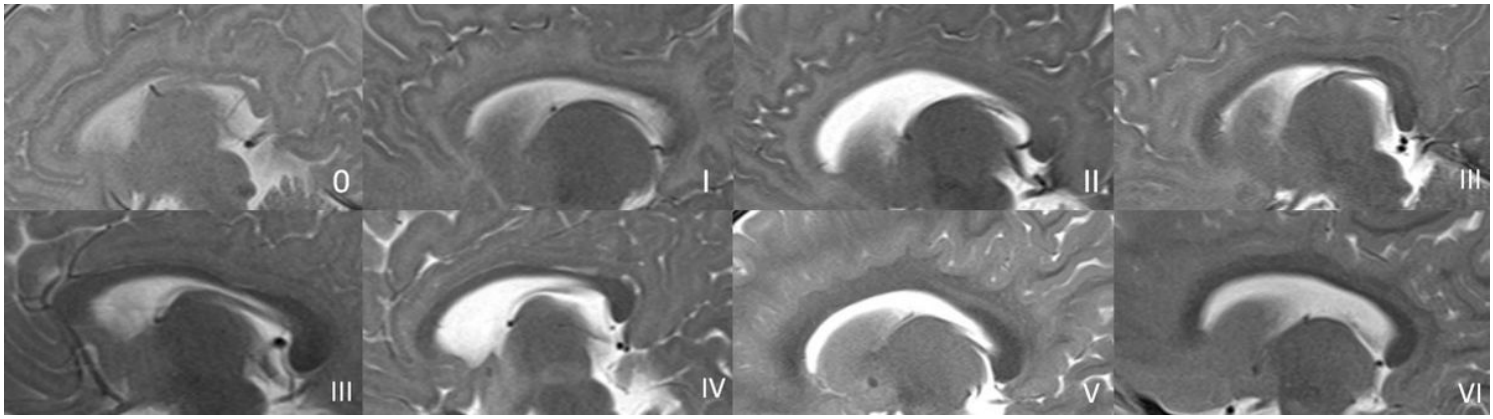

Figure 2

Figure 2

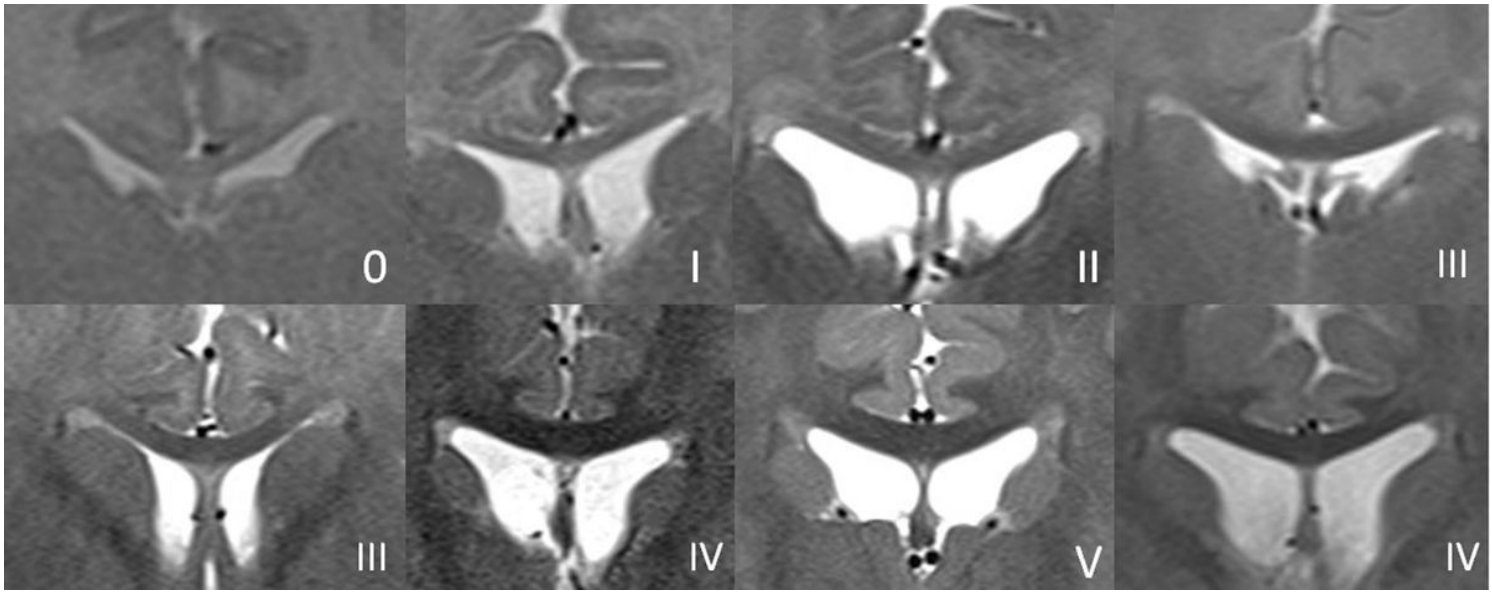

Figure 3

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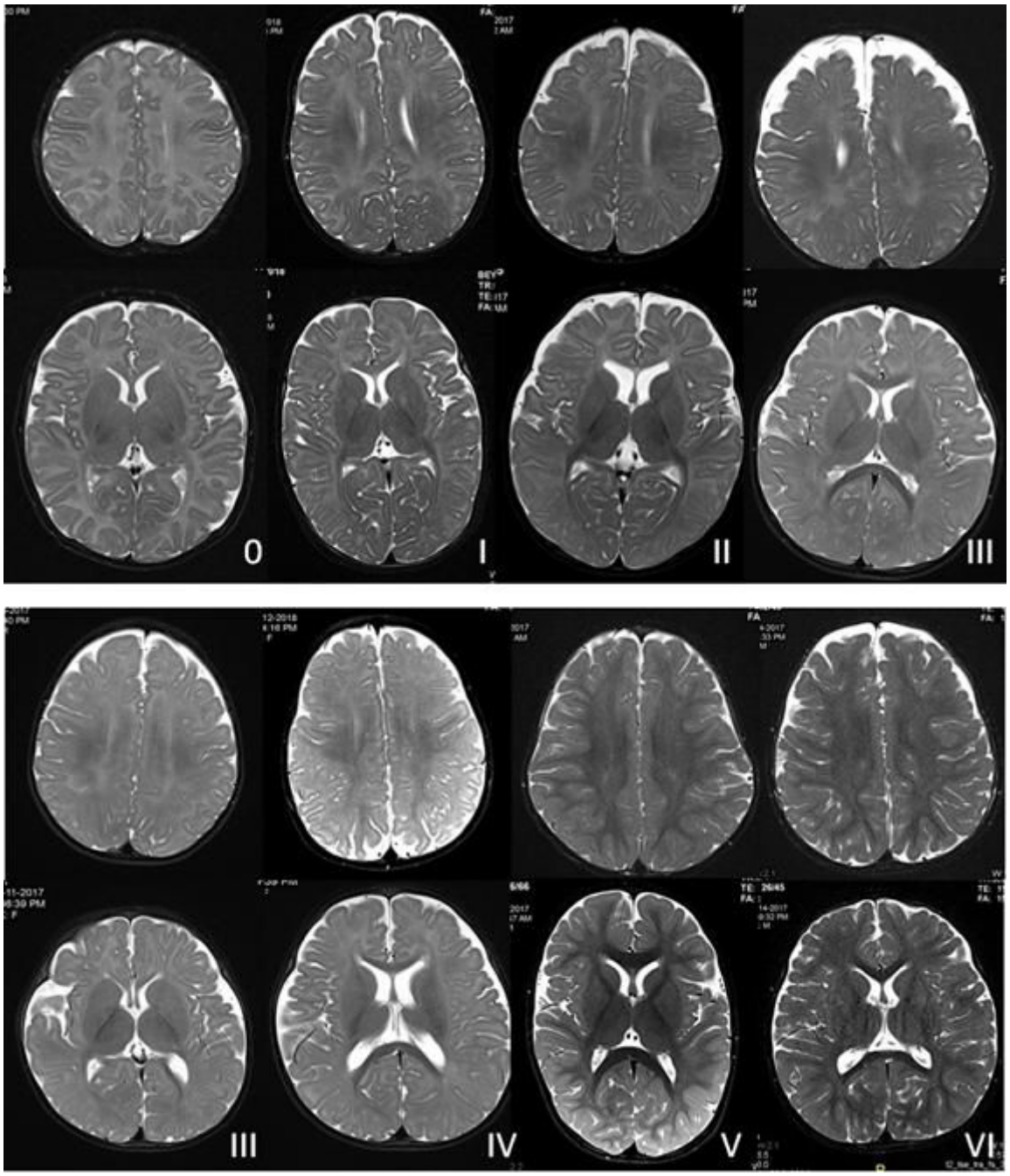

Figure 4

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