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Inducing Stable Brain MRI to Infants Treated in the NICU

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Newborns and premature infants generally undergo brain MRI tests under sedation and anesthesia. Sedation or anesthesia has a risk of side effects and may be contraindicated in newborns or premature infants with congenital diseases. Therefore, this study tested subjects by applying a self-sleep induction method. This study compared and analyzed a group (Group A), which tested 42 subjects using a sedation method (used chloral hydrate or Midazolam) for the brain MRI examination, and a group (Group B), which tested 84 subjects under self-sleep induction by applying a wrapping after feeding technique using a vacuum splint (MedVac). For image analysis, this study conducted SNR analysis between the two groups, calculated Cohen's Kappa coefficient to test the agreement between observers, and analyzed the examination time to evaluate the efficiency of the examination. The results of image analysis (SPSS independent sample t-test) were evaluated as T1 (p=0.101) and T2 (p=0.319), and the inter-observer agreement test (p=0.075) and statistical analysis of test time (p=0.160) were also statistically significant. There was no difference. Brain MRI through sleep induction is considered a safe and efficient test method.

Keywords : self sleep induction, brain MRI, neonates

1. Introduction

Among tests that can check the brain development of newborns, brain magnetic resonance imaging (MRI) is better than brain ultrasound for checking the structures and abnormalities of the brain because it is highly sensitive and has high contrast between tissues.[1,2] Therefore, it is useful for examining the development of the brain and identifying the abnormalities of the brain.[1,2] The importance of evaluating neurodevelopmental prognosis has been emphasized more[4,5] as the number of premature infants less than 37 gestational weeks is increasing[3] and the survival rate of high-risk premature infants with neuro-developmental abnormalities is improving. As a result, brain MRI imaging has been increasing as a complementary test to brain ultrasound because diagnosing neurological complications in newborns, especially very low birth weight or premature infants, is very important.[6,7] Since brain MRI scans take a relatively long time and are sensitive to motion artifacts caused by movement, appropriate sedation therapy is required for newborns.[8] chloral hydrate (CH; Pocral syrup, Hanlim, Seoul, Korea) and midazolam are generally used for the sedation treatment for newborns.[9] All sedation and anesthesia have inherent risks and, although it has been reported that these risks are low, only a few studies have actually examined the adverse reaction of newborns to them.[8,10,11] In addition, sedation and anesthesia may be contraindicated in newborns or premature infants with congenital diseases. One of the methods to perform a brain MRI scan for the newborn without sedation or anesthesia is the wrapping after feeding technique. The temperature and humidity of the MRI laboratory must always be kept constant because the laboratory has precision electronic devices composed of state-of-the-art semiconductors and parts. Therefore, the temperature and humidity of the laboratory should be maintained at 22 ± 2 °C and 50-60 %, respectively. A strong magnetic field is required to operate an MRI device. Electricity shall run through a huge gradient coil to induce electromagnetic waves and generate this magnetic field. Vibration and movement are generated when applying a magnetic field to the coil, and a high-pitched noise is created at this time. Some 3T (Tesla) class MRI devices create noise over 100db, while 90db is equivalent to the sound that one hears when standing

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under Niagara Falls. Examining newborns under these noise and temperature conditions of the laboratory different from those of the incubator has caused a lot of trial and error. It is possible to induce sleeping naturally by having an international breastfeeding specialist nurse maintain a stable biorhythm through regular feeding, moving the newborn to the MRI laboratory in an incubator, applying earplugs to reduce noise and eyeshade to block the light, and wrapping the newborn in a warm blanket and decrease motion artifact using a vacuum splint.[12] This study was conducted to identify the quality of images and evaluate the effectiveness of the test when experienced radiologists and nurses carried out the brain MRI scans for newborns and premature infants by performing the self-sleep induction process according to the process currently used at the hospital.

2. Materials and Methods

2.1. Research subject

This study retrospectively analyzed newborns and premature infants who were tested with the same test protocol among those who were admitted to the neonatal intensive care unit (NICU) between January 1, 2019, and August 30, 2021, and underwent brain MRI. This study has 126 subjects (56 boys (44 %) and 70 girls (56 %)). Their mean age was 40.1 days and the mean gestational age was 31.7 weeks. Their mean weight was 1.63 kg.

2.2. Research method

This study compared and analyzed the Group A (42 subjects), which received the test under a sedation therapy by using chloral hydrate or Midazolam, and the Group B (84 subjects), which received the test under self-sleep induction using feeding and a wrapping technique. The MRI device of this study was Discovery MR750W 3.0T (GE Health Care, U.S.A), and this study used a 32-Channel HEAD coil. This study used MedVac Bag (CFI Medical Solutions/Contour Fabricators, Fenton, MI, USA), which passed the “MRI Safe” standard defined in the FDA Consensus Standard ASTM F-2503-13, as the vacuum splint to fix the subject. The scan parameters were identically for both groups (Table 1), and the total scan time was 544 seconds.

2.2.1. Test Procedure of Group A

Chloral hydrate was orally administered to the subject in the NICU. After sedation, the subject was transported to the MRI laboratory in a mobile incubator with a pediatric resident and an MRI examination was performed without a separate device for sedation. When the subject became conscious or the image was judged to have no diagnostic value due to movement during the MRI examination, the appropriate dose of midazolam was administered intravenously up to 2 times after contacting the medical attendant upon the request of the radiologist to proceed with the examination. Oxygen saturation (SpO2) and pulse rate of the subject were monitored in all procedures of the examination.

2.2.2. Test Procedure of Group B

The MRI examination time was planned based on the subject's regular feeding time in coordination with the MRI laboratory and the NICU. After taking the subject to the MRI laboratory in a mobile incubator, a NICU nurse certified by the International Board of Lactation Con-

Fig. 1. (Color online) Prepare a vacuum bag before wrapping the patient.

Table 1. Scan parameters for brain images.

	TR (ms)	TE (ms)	FOV (mm)	Matrix	FA (°)	Scan time (s)
3D T1 FSPGR	8.8	3.4	220	220×220	8	191
T2	4500	160	200	228×228	160	60
T2 FLAIR	9000	145	200	260×260	160	108
SWAN	45	23	200	384×224	15	144
DWI	5000	75	220	160×160	90	41

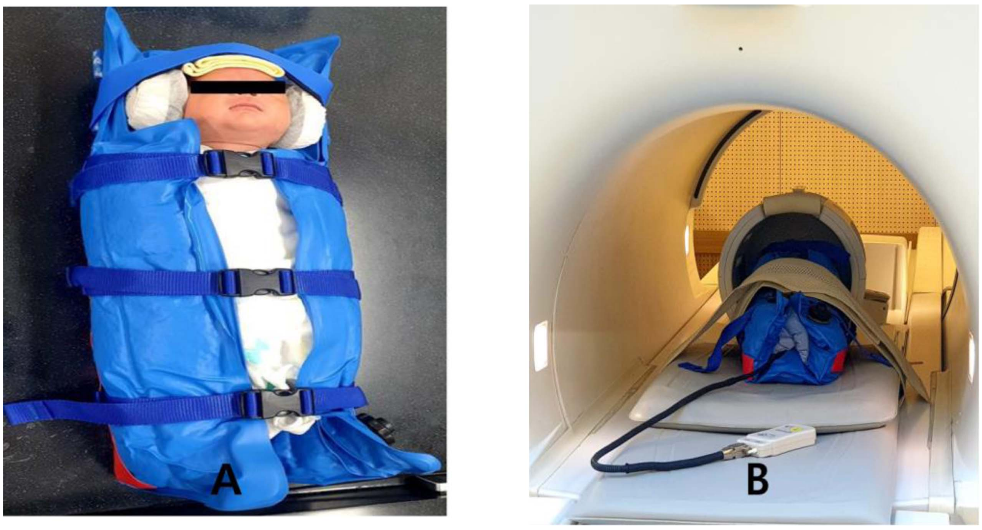

Fig. 2. (Color online) Photo of an infant swaddled in a MedVac bag prior to being placed in the scanner.

sultant Examiners (IBLCE) gave formula or pre-contracted breast milk to the subject before the MRI examination. When the subject fell asleep after feeding, the subject was wrapped using a MedVac Bag (Fig. 1, 2) and a sponge was placed behind the subject's neck to secure the airway to prevent airway obstruction. The MedVac Bag was fixed after deflating it using a pump. Earplugs and headphones were used together to protect the hearing of the subject (Fig. 1, 2). The subject became awake, and the feeding was repeated to perform the test. A pacifier was used in some cases to induce a smooth sleep. Oxygen saturation (SpO2) and pulse rate of the subject were monitored in all procedures of the examination.

2.3. Evaluation of Images

Evaluation of Images: The 3D T1 and T2 images of the two groups were analyzed using quantitative and qualitative methods. For quantitative analysis, this study established the region of interest (ROI) in the pons in the axial projection image to examine the difference in signal intensity (SI) between the Group A and the Group B and measured the pixel value of it five times (Fig. 3). The mean value was used for the analysis. Measured data were applied to Eq. (1) to calculate the signal to noise ratio (SNR) of the image. The SNR was used to compare the groups.

For qualitative analysis, image quality was evaluated on a 5-point scale. Images obtained by enhancing 3D T1 and T2 were independently evaluated by two radiologists. The score ranged from 1 to 5: Very Poor=1, Poor=2, Fair=3, Good=4, Excellent=5. Qualitative evaluation of white matter and gray matter classification, distortion and artifact

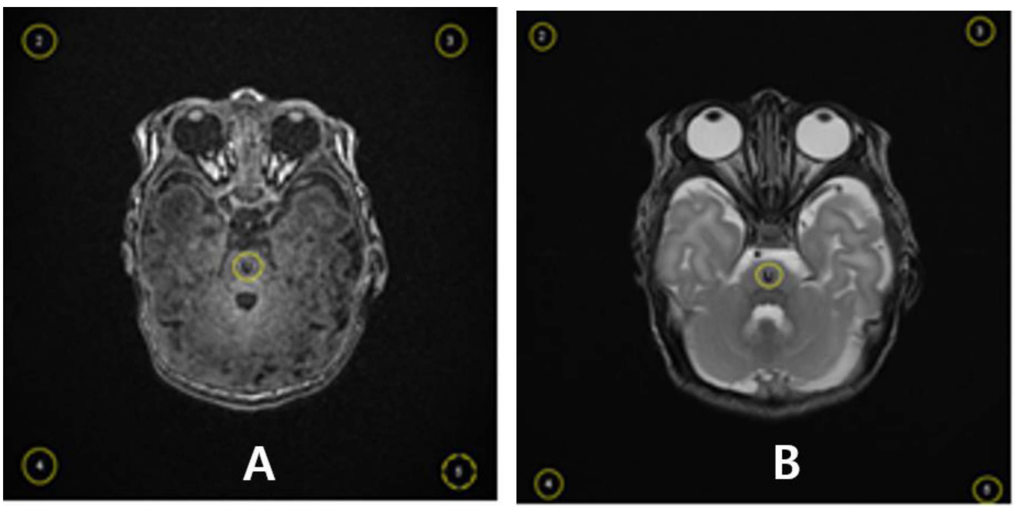

Fig. 3. (Color online) ROI of brain and background (a) 3D T1WI FSPGR, (b) T2WI.

due to movement, and overall image quality were evaluated. Cohen's Kappa coefficient was used to statistically analyze the score acquired for each image.

Image classification of white matter and gray matter was scored from 1 to 5: Very Poor=1, Fair=3, and Excellent=5. Distortion and artifact due to movement was also scored from 1 to 5: Very Severe=1, Little=3, and No=5. Overall image quality was measured in terms of radiology and reading: Worst=1, Moderate=3, and Best=5.

2.4. Comparison of Exam Time Measurement

To test the test efficiency of the two groups, this study summed the scan time from the start time of the brain protocol of the laboratory console computer until the end time, excluding the test preparation time for each group. Afterward, this study conducted an independent two-sample t-test using SPSS ver 26.0 (SPSS Inc. Chicago, USA).

2.5. Statistical Analysis

Independent two t-test was used to quantitatively analyze the difference in image quality between the two groups (SPSS ver 26.0). Moreover, Cohen's kappa coefficient was used to check the degree of agreement between observers before carrying out qualitative analysis (SPSS ver 26.0). An independent two-sample t-test was also used to test the difference in test time between the two groups.

3. Result

3.1. Quantitative Evaluation

The 3D T1 SNR of the Group A (sedation therapy) was 232.73±11.75 (mean±standard deviation), which was higher than that of the Group B (self-sleep induction) (Table 2).

An independent two-sample t-test was performed to analyze the difference in SNR values between the two groups. The study found out that the two groups did not have significantly ($p<0.05$) different SNR values (t=1.667, p=0.101). Therefore, the SNR of the Group A and that of the Group B were not different (Table 2).

The T2 image SNR of the Group A (sedation therapy) was 176.35±8.22 (mean±standard deviation), which was larger than that (174.51±5.79) of the Group B (self-sleep induction) (Table 3). An independent two-sample t-test was performed to evaluate the difference in SNR values between the two groups. The result showed that they were not significantly ($p<0.05$) different (t=1.005, p=0.319). Therefore, the SNR of the Group A was not different from that of the Group B (Table 3).

Table 2. Quantitative analysis value of measured SNR in 3D T1.

		SNR			t (p)
		N	Mean (M)	Standard Deviation (SD)	
3D T1	Group A (sedation)	42	232.73	11.75	1.667 (0.101)
	Group B (self sleep)	84	228.57	6.91	

Table 3. Quantitative analysis value of measured SNR in T2.

		SNR			t (p)
		N	Mean (M)	Standard Deviation (SD)	
T2	Group A (sedation)	42	176.35	8.22	1.005 (0.319)
	Group B (self sleep)	84	174.51	5.79	

3.2. Qualitative Evaluation

Cohen's kappa coefficient was used to examine the degree of agreement between two radiologists. This study measured 126 cases without a missing value (Table 4).

Regarding the white matter and gray matter classification, the kappa value, represented by the Landis and Koch classification value, was 0.656 for T1, showing substantial agreement, and 0.533 for T2, indicating moderate agreement.

Regarding the classification of artifact due to movement, the kappa value of T1 was 0.852, showing almost perfect

Table 4. Effective measured values between observers using statistical programs.

	Case					
	Valid measurement		Missing value		Total value	
Doctor1, Doctor2	N	Percent	N	Percent	N	Percent
	126	100.0 %	0	0.0	126	100.0 %

Table 5. Measurememt of effective agreement using Kappa coefficient of cohen between observers.

Symmetric measure				
		Value	Approximate T Valueb	Approximate Significance
White Matter T1	Coincidence Measure Kappa	.656	7.594	.000
White Matter T2	Coincidence Measure Kappa	.533	6.060	.000
Motion Artifact T1	Coincidence Measure Kappa	.852	12.449	.000
Motion Artifact T2	Coincidence Measure Kappa	.717	11.632	.000
Comprehensive Evaluation T1	Coincidence Measure Kappa	.788	9.047	.000
Comprehensive Evaluation T2	Coincidence Measure Kappa	.419	4.798	.000

Table 6. Exam time measurement comparison.

	Exam Time (s)			t (p)
	N	Mean (M)	Standard Deviation (SD)	
Group A (sedation)	42	1157.71	365.62	-.450 (0.653)
Group B (natural sleep)	84	1189.85	350.98	

agreement, and that of T2 was 0.717, demonstrating substantial agreement.

Regarding the comprehensive image quality evaluation, the kappa value, the measure of agreement, of T1 was 0.788, indicating substantial agreement, while that of T2 was 0.419 showing moderate agreement.

3.3. Comparison of Exam Time Measurement

An independent two-sample t-test was conducted to evaluate the difference in the exam time between the two groups. The results showed that they were not significantly ($p<0.05$) different ($t=-.450$ $p=0.653$). Therefore, there was no difference in test time between the Group A and the Group B (Table 6).

4. Discussion

During brain MRI examination, sedation therapy can inhibit the deterioration of image quality due to movement and can help the examination by reducing the discomfort and anxiety of ill children. Previous studies have reported different occurrence probabilities of adverse events after sedation or anesthesia and age has been reported as a risk factor that can cause side effects in sedation and anesthesia therapy.[13-15] CH is one of the most commonly used drugs for sedation in newborns and premature infants. It is known that after it is orally administered, it takes 15-30 minutes to be effective and it is effective for 1-2 hours.[16] Although CH has been widely used for sedation therapy in children, it is difficult to predict when CH becomes effective and it is often administered multiple times because it may fail to sedate a patient.[17,18] The incidence of cardiac arrest induced by sedation or anesthesia is three times higher in children than in adults.[19] The occurrence probability of cardiac arrest due to anesthesia is 1.4 cases per 10,000 anesthetic cases, and more than half of these incidents occur in children under 1 year old.[20] Although sedation and anesthesia therapies have these risks, they have been frequently performed by unskilled medical staff due to practical reasons in the South Korean medical community, such as a shortage of anesthesiologists. The A-jou university Hospital recognized this risk and has been conducting brain MRI scans for newborns and premature infants by wrapping them with a MedVac after feeding since July 2017.

Hunger causes infants to move and cry, while satiety is known to calm infants and induce sleep because it makes them feel comfortable.[21] Newborns exhibit several types of reflex movements that cannot be controlled due to the immaturity of the central nervous system. The moro reflex, one of them, is an involuntary protective motor response to sudden stimuli.[22] Wrapping an infant can inhibit the moro reflect, a startle reflex.[23,24] It was determined that the method of wrapping an infant using a vacuum splint could protect the infant from noise and peripheral nerve stimulation (PNS) felt during an MRI examination. This study tried to reduce the risk of sedation and anesthesia, explain the technique that could help newborns and premature infants tolerate brain MRI scans better, and identify the usefulness by using the advantages of feeding and wrapping. This study collected data using a retrospective survey method and analyzed differences in image quality and exam time.

The results showed that image quality was not significantly different between the group treated with sedation therapy (Group A) and the group treated with self-sleep induction (Group B) (Table 2-5). The image quality of the

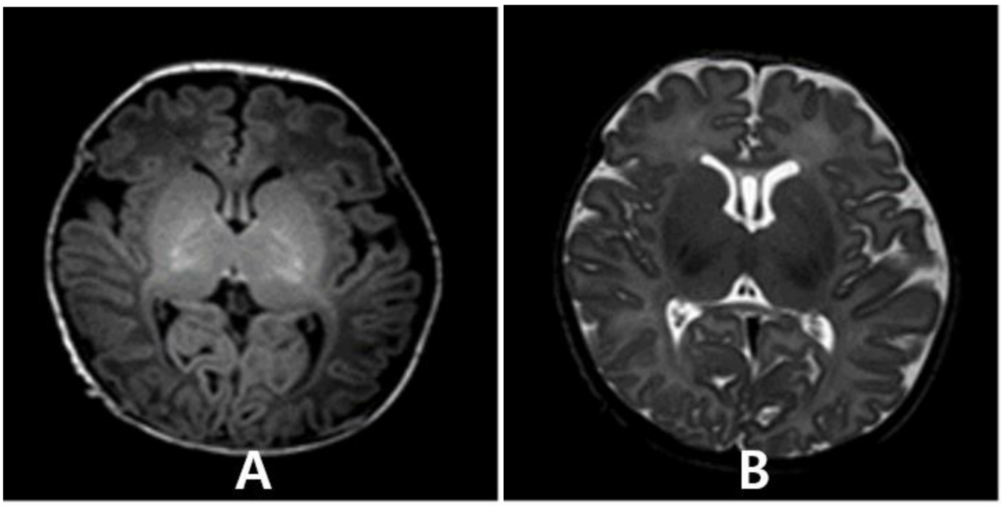

Fig. 4. Images acquired using self sleep induction (a) Ax 3D T1WI FSPGR, (b) Ax T2WI.

Group B was not lower than that of the Group A (Fig. 4). and It could provide sufficient imaging information for diagnosis and treatment planning (Fig. 4). Therefore, it was determined that the examination method using self-sleep induction provided sufficient information for diagnosis and was a safe test method without the side effects that a patient might experience during the examination and the adverse effects of sedation and anesthesia that could occur later.

This study analyzed the difference in exam time between the two groups using an independent two-sample t-test to identify the efficiency in the exam time. It was found that exam time was not significantly different between the Group A and the Group B (Table 6). self-sleep induction did not increase exam time. When considering fasting, pre-treatment, and vial sign observation after the exam, self-sleep induction may reduce the time and cost actually required for the exam even further.

Lastly, two radiologists may not be sufficient for the qualitative evaluation, and it is necessary to supplement the observer's evaluation part in future studies. Since it is not easy to distinguish the white matter and gray matter of infants in T1 images, it is believed that T2 images should be used for qualitative evaluation. It can be said that the T2 image is more representative of the qualitative evaluation than the T1 image.

The limitations of this study were that it was a retrospective study, this study did not include all the children who had undergone the same procedure in the hospital, and this study could not include MRI scans of other areas such as the abdomen or spine. In addition, since the experiment was carried out only at 3.0T, a comparative experiment of 1.5T and 7T is required for additional experiments. However, this study proposed a safe MRI exam method for newborns and premature infants. It would be good to conduct additional studies in the future to understand the economic impact of it on medical cost reduction or evaluate the satisfaction of pediatricians and caregivers.

5. Conclusion

This study was carried out to reduce the risk of sedation and anesthesia therapies, to explain a technique that could help newborns and premature infants tolerate brain MRI scans better, and to understand the effectiveness of the examination compared to the quality of the image. self-sleep induction technology through feeding and wrapping is a safe and effective examination method, and it provided good image quality sufficient to obtain information necessary for diagnosis and treatment planning. The quality of the images acquired by the self-sleep induction was not lower than that of the conventional brain MRI images obtained by sedation and anesthesia. Moreover, the exam time did not increase, either. Therefore, the self-sleep induction method through feeding and wrapping is not only safer than the conventional sedation method but also a more efficient and economical method for human resources utilization.

Nomenclature

ms : mili second
mm : milimeter
s : Second
FA(°) : Flip angle : °

Formulae

(1) SNR = SI(Signal intensity) / Background Noise SD (Stansard Deviation)

$$SNR = \frac{SI}{Background\ Noise\ SD}$$

Unit of measurement: point

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