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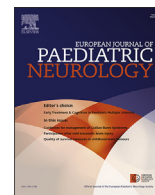
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Official Journal of the European Paediatric Neurology Society



## Original article

# Melatonin in neuropaediatric MRI: a retrospective study of efficacy in a general hospital setting

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## ABSTRACT

**Background:** Melatonin may offer a safe and cheap alternative to general anaesthesia and sedatives in neuropaediatric MRI. The purpose of our study was to evaluate its efficacy during a daily scanning programme and to assess its financial benefit.

**Methods:** Neuro-MRI scans, performed in a general hospital setting after administration of melatonin in 64 children aged 10 months–5 years, were retrospectively reassessed by an experienced paediatric neuroradiologist, rating them as diagnostically contributing or as failed. The financial benefit was calculated.

**Results:** 49/64 scans (77%) were diagnostically contributing, in 11 (22%) no movement artefact was seen in any sequence; 15/64 scans failed (23%), in 3/15 because of serious movement artefacts, in 12/15 the scan was not started. Repeat scans under general anaesthesia were performed in 17 cases (27%): in the 15 failed cases and in 2 cases initially assessed as failed, but were considered diagnostically contributing in the present study. The financial benefit at the time the scans were made was approximately 13,360 Euro.

**Conclusions:** In this retrospective study, the use of melatonin in neuropaediatric MRI, made during a daily scanning programme with a remote waiting room, was associated with a high success rate in infants and young children. A minority of scans had no movement artefacts, indicating most children were not asleep. The sleep-inducing effect of melatonin could therefore not be proven, but the high success rate may be attributed to the sedative and/or anxiolytic effect of melatonin. Only a minority of scans had to be repeated under general anaesthesia, leading to a reduction of scan related costs.

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**Abbreviations:** MRI, Magnetic Resonance Imaging; GA, general anaesthetic; ABR, auditory brain stem response; EEG, electroencephalogram; SlDep, sleep deprivation; ASA, American Society of Anesthesiologists; DC, diagnostically contributing; F, failed.

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## 1. Introduction

Magnetic resonance imaging (MRI) is widely used to demonstrate or rule out central nervous system pathology in children. For scans to be successful, the children are required to lie still during scan acquisition. This may be challenging for both children and their parents prior to and during the procedure, related to distress caused by unfamiliar circumstances and noise associated with MR acquisition. In order to limit the number of failed MRI scans, general anaesthesia (GA) or sedatives are commonly used in infants as well as in older children who are not capable of comprehending the MRI procedure and its requirements, with GA generally resulting in the highest success rate.<sup>1–3</sup> Sedatives and GA, however, require the presence of anaesthesiologists or trained nurses and expensive MRI compatible respiration and resuscitation equipment, because of the risk of cardiorespiratory adverse reactions.<sup>2–4</sup> Limited anaesthesiology resources may result in longer MRI waiting lists.

Many alternative techniques for anxiety reduction have been reported with comparable success rates. The ‘swaddle and bottle’ technique may be successful in neonates and infants up to the age of approximately 8 months.<sup>5</sup> In toddlers from the age of approximately 4 years different strategies to achieve a high success rate have been reported including pre-procedural visits to the MRI; mock MRI scanners with play therapists and the use of storybooks, MR compatible audio/visual systems with goggles,<sup>6</sup> CDs with MR associated noise, and DVDs.<sup>3</sup> Nowadays, the availability of YouTube information videos may also contribute. However, some of these techniques require dedicated personnel, expensive investment in materials, are time consuming and may only be feasible in hospitals dedicated to children.

Melatonin may offer a safe, feasible and cheap alternative to GA and sedatives. It has been proven to have a mild sedating, hypnotic and anxiolytic effect,<sup>7–11</sup> without the risk of upper airway obstruction or loss of gag and cough reflexes. Consequently, it does not require the presence of an anaesthesiologist.<sup>8,12</sup> Other advantages are a quick recovery time, without the short-term side effects of vomiting, unsteadiness, agitation, hyperactivity and next-day drowsiness, often associated with sedation.<sup>3</sup> The use of melatonin has been studied in children undergoing MRI, electroencephalography (EEG) and auditory brainstem response (ABR) studies,<sup>12–21</sup> with variable efficacy. These studies have been performed during a programme dedicated to the examined children, in specialised children hospitals, with a waiting space adjacent to the scanner, or after sleep deprivation (SlDep).

The purpose of the present study was to examine the efficacy of melatonin in neuropaediatric MRI, within the setting of a daily scanning programme at a university hospital.

## 2. Materials and methods

### 2.1. Patients

All children aged 10 months to 5 years, who underwent a neuro-MRI with melatonin from January 2013 to October 2014,

were retrospectively identified. Children scanned under GA, under sedation or without were not included. The scans for this study were selected from our hospital database. The clinical diagnosis and queries were similar for children scanned with melatonin and GA. Children who were swaddled or were given additional oxazepam were excluded. Only MRI scans of children with American Society of Anaesthesiologists (ASA) physical status grade 1 (normal healthy patient without systemic disease) were assessed.<sup>22</sup>

### 2.2. Procedure

After the appointment for an MRI scan was ordered, the parents received a letter explaining the MRI procedure and a form concerning contra-indications. If they had any query concerning a contra-indication applicable to their child or to themselves, they were urged to notify a secretary at the MRI planning desk, who would relay the call to an MRI radiology technician for adequate advice.

The child and its parents/carers arrived at the paediatric department 60–90 min prior to the scheduled time of the MRI scan. If intravenous contrast was needed, the child received an EMLA superficial anaesthetic cream patch on the arm, followed by the introduction of an intravenous cannula, shortly before the melatonin was given. Approximately 45–60 min prior to the intended scan time, the children were given a melatonin tablet in yoghurt, apple sauce, water or lemonade.

To facilitate the procedure, the treating paediatric neurologist decided to use melatonin instead of GA, according to the local guidelines: 3 mg for children 10 months–1 year; 5 mg for children 1–4 years; and 10 mg for children 4–5 years. However, the paediatric neurologist could decide to alter the dose if considered necessary.

The child waited on a general hospital bed in a darkened room with its parents/carers at the paediatric department on the third floor. When the radiology technicians decided the child could be scanned, they would notify the paediatric department. The child was then transported on the bed accompanied by its parents/carers and a nurse, or in the arms of the parents/carers from the paediatric department through a brightly lit corridor to an elevator. The MRI room was situated on the ground floor. From the elevator the bed was rolled past the MRI waiting room to the entrance of the MRI scanning room. The total journey would take approximately 10 min. No special adjustments were made to the beds to make them less noisy. Prior to entering the scanning room, the children and parents/carers were checked for metal to ensure safe entrance. The child was then lifted from the bed onto the MRI scanning table. In infants, muffling stickers were placed over the ears for hearing protection. Older children were scanned with headphones, with or without music. If children did not fall asleep or if they woke up, but were otherwise calm enough, the MRI scan was started. One of the parents/carers sat at the head end of the scanner machine during the procedure and could be seen by the child via an angled mirror attached to the head coil. After the scanning procedure, the child and its parents/carers were allowed to go home, if the child was well.

### 2.3. Scan protocols and assessments

All scans were done on a 1.5 Tesla MR system, using a regular head coil and if applicable a spine surface coil. The MRI studies were performed during daytime, mostly between the end of the morning to halfway the afternoon, whenever a scanning slot had been available during planning of the procedure. Regular neuropaediatric-, tumour-, hydrocephalus-, epilepsy-, inner ear-, spine-, and spina bifida protocols were applied. The protocol duration ranged from approximately 10 to 50 min, including positioning of the patient on the scan table. In case children moved, radiology technicians could apply periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLOR) k-space trajectory or BLADE (the commercial name introduced by Siemens), which compensates for movements, while maintaining the contrast features of conventional scans.

The contribution of the BLADE sequences to the DC scans was assessed, leaving out the patients scanned with hydrocephalus protocol, as in this protocol BLADE is standardly used. An example of a T2 weighted scan in a child with bilateral polymicrogyria scanned without and with BLADE is provide in Fig. 1.

All scans, which had originally been assessed by various neuroradiologists, were retrospectively reassessed by an experienced paediatric neuroradiologist (\*), without previewing the original report.

Every sequence of a scanning protocol was assessed separately. If a sequence showed movement artefacts but was still considered assessable, it was recorded as 'moved, but assessable'. If structures were not properly distinguishable due to movement artefacts, the sequence was considered 'failed'. The number of non-moved, moved, contributing and failed sequences were recorded.

The entire scanning protocol was subsequently rated as diagnostically contributing (DC) or failed (F), taking the clinical information and query into account. An MRI scan was considered to be DC, if (1) a diagnosis could be made based on the MRI scan or (2) the MRI scan contributed to the diagnostic process (e.g. a normal scan in query abnormalities in children with mental retardation, or an unexpected finding was noted, not directly relevant to the query). An example of a diagnostically contributing scan with 4 sequences more or less hampered by movement artefacts, but considered diagnostically contributing is provided in Fig. 2. An MRI scan was considered to have failed when (1) no sequences were could be obtained, (2) the entire MRI scan was not assessable because of movement, or (3) in the presence of moved scans, assessment of the remaining non-moved sequences provided insufficient information for the diagnostic process.

### 2.4. Economic benefit

The economic benefit of using melatonin was evaluated by deducting the costs which have been made by scanning children with melatonin and adding the extra costs for those which required a repeat scan under GA, from the cost which would have been made when all children would have been scanned under GA. Included in the price of an MRI scan with melatonin were the pre-scan nurse handling at the paediatric

department and the transportation to the MRI scanner with an accompanying nurse. The price of a tablet of melatonin was negligible. Included in the price of a scan under GA were the pre-scan preparation by the anaesthesiologist, the presence of the anaesthesiologist during the scan and a 2–4 h after stay and assessment at the anaesthesiology department. GA consisted of a larynx mask and administration of propofol.

## 3. Results

Sixty-four children (males  $n = 33$ ), aged 10 from months to 5 years with a median age of 2.6 years were planned for a scan with melatonin.

In children that started the scan ( $n = 52$ ), the used scan protocols with intended scan time slots were: neuropaediatric in  $n = 31$  (30 min), tumours  $n = 4$  (45–60 min), epilepsy  $n = 2$  (30 min), hydrocephalus  $n = 10$  (10 min), spine  $n = 2$  (30 min), spina bifida  $n = 2$  (30 min) and various  $n = 1$ . None of the children with an actual scan time longer than 15 min needed a repeat scan.

The melatonin dosage used was 3 mg in 2 children, 5 mg in 34 children, and 10 mg in 26 children; in 2 children a scan was made with a dose varying between 3 and 10 mg. The actual scan duration noted was 10–29 min (Q1-Q3 range; median 23 min). No side effects of melatonin were noted during scanning by the parents and the radiology technicians, and no post-scan calls were made by parents after returning home.

In 49/64 children (77%) the scans were considered DC. Of the 64 children, 38 children were 0–3 years with 29 DC scans (76%) and 26 children were 3–5 years with 20 DC scans (77%). Thirty-three children were male with 27 DC scans (82%) and 31 were female with 22 DC scans (71%). In 11/49 (22%) no movement artefact was noted in any sequence of the scanning protocol. Of these 11 children 4 (36%) were 0–3 years and 7 (64%) were 3–5 years. 15/49 (31%) had one or more moved, but no failed sequences; and 26/52 (23 DC and 3 F) had one or more moved or failed sequences.

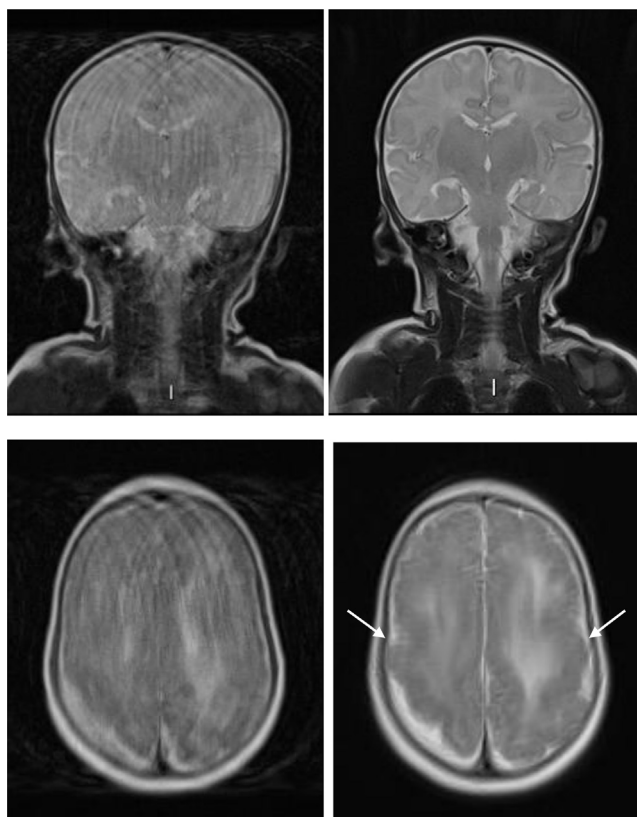
In 15/64 (23%) children the scans were considered to have failed: in 12 patients the scan had not been started, and 3 showed extreme movements. In 17/64 (27%) children a repeat MRI scan had been performed with GA: in 15 who had a failed scan; and in 2 for whom the treating paediatric neurologist had requested a repeat scan under GA after the initial assessment, but whose scans were considered DC during the re-analysis for this study.

One or more BLADE sequences were applied in 27 of the 52 children (52%) with started MRI scans. The use of the BLADE technique definitely contributed in 15/27 cases (56%). In 2 children (7%) its contribution was doubtful. In 10/27 (37%) they did not contribute, partly because conventional sequences showed no movement artefacts and were useful for a final assessment, or the BLADE sequences themselves were extremely moved.

### 3.1. Economic benefit

At the time, the price for a neuropaediatric MRI scan with melatonin was approximately 320 Euro. Depending on the scan time and post-scan assessment time by the





**Fig. 1 – a: Coronal T2 TSE with movement artefacts. b: Same patient as in a., coronal T2 BLADE shows a normal image of the frontotemporal brain. c: Axial T2 TSE with movement artefacts. d: Same patient as in c., axial T2 BLADE shows bilateral polymicrogyria (white arrows).**

anaesthesiologist, the price under GA was on average approximately 720 Euro. The total costs for 64 children with melatonin was calculated at  $64 \times 320 = 20,480$  Euro. The extra costs for 17 children with repeat MRI under GA would be  $17 \times 720 = 12,240$  Euro. The price for scanning all children under GA would have been  $64 \times 720 = 46,080$  Euro. The economic benefit was  $46,080 - 32,720 = 13,360$  for the entire group and 209 Euro per patient.

#### 4. Discussion

In this retrospective study we have presented our experience with the use of melatonin in a younger paediatric population, scanned in a normal hospital environment and during a daily programme. In the total group of 64 children, 77% of the MRI scans contributed to the diagnostic trajectory. The percentage of DC scans was comparable in the male and female group. In 22% of the children no movement artefacts were seen, suggesting that the vast majority of the children did not sleep during the total scanning time. The scans in the group of children between 3 and 5 years showed ‘no movement artefact’ more often than the scans in children between 10 months and 3 years. However, although movement artefacts were present, most children were lying sufficiently still to

obtain a diagnosis. A new MRI under GA was considered necessary in 17 children (27%), including two with scans that had originally been reported as failed, but were considered diagnostically contributing in the re-analysis for this study.

Melatonin is known for its sleep-inducing and anxiolytic effect,<sup>7–21,23</sup> and is successfully administered to children with ADHD, autism spectrum disorder and developmental delay to improve sleep.<sup>9,10</sup> Moreover, melatonin premedication has shown positive effects when given before the induction of GA.<sup>23</sup> Its contribution to sedation in MRI is disputed.<sup>20</sup> Challenges in the use of melatonin in MRI procedures are transfer of the child from the bed to the scanning table, and the loud rattling noise during the scan acquisition, produced by switching of the magnetic gradients which reverberate against the surrounding mounting. Particularly, the DWI, an important sequence to include in a neuropaediatric protocol, is one of the loudest sequences with a noise level up to 115 dB.<sup>24</sup> This makes hearing protection absolutely necessary. The loud noise contributes to anxiety in children and potentially interferes with the effect of melatonin for the induction and maintenance of sleep.

A total of 7 EEG studies have reported the sleep-inducing effect of melatonin, its efficacy, comparison with SlDep and sedation and the capability of enhancing the effect on sedation. The reported success rates varied between 73.3% and 93%<sup>12–18</sup> In one study, its use in auditory brainstem responses (ABR) was published with a success rate of 86.4%.<sup>21</sup> The efficacy of melatonin in MRI has been described in one letter to the editor with a success rate of 44%,<sup>13</sup> and in one study with an unselected group of children scanned with melatonin with a 55% success rate.<sup>19</sup> Furthermore, a non-contributing effect on sedation in MRI has been described.<sup>20</sup>

It is difficult to compare the overall success rate of our study with results from previous studies because of different pre-procedural methods, differences in dose, timing of administration, the duration of medical procedures, time during the day and different definitions of success rate, which will be discussed in the separate paragraphs.

##### 4.1. Preparatory measures to diminish anxiety

In previous studies, preparatory measures to diminish anxiety have not been discussed. In our study, we provided the parents with general information on the MRI procedure in a booklet. We made no special adjustments in the MRI scanner environment for children. Prior to scanning, only two children of our study group visited the MRI scanner with a play therapist several days prior to the actual scanning date. Because of the small number we were not able to analyse its possible beneficial effect on the efficacy of melatonin in these patients. Several studies emphasize the importance of a child and family friendly MRI environment and involvement of parents for their high success rate.<sup>25–26</sup>

##### 4.2. Optimal melatonin dose

The optimal melatonin dose for sleep-induction is unknown. In different studies performed in children, the melatonin dose varied between 2.5 and 20 mg. One study reported that a dose of 0.25 and 0.5 mg/kg melatonin was equally effective in

reducing anxiety.<sup>23</sup> A later study, describing sleep-inducing effects in children with chronic sleep onset problems, found no dose–response relationship, even with a dose range of 0.05–0.15 mg/kg.<sup>27</sup> In 2003, Zhdanova and Tucci stated that a dose as low as 0.1–0.3 mg is efficient in promoting sleep.<sup>28</sup> In previously mentioned EEG, ABR and MRI publications, the doses varied between 2.5 and 20 mg, depending on the age or weight of a patient.<sup>12–19</sup> In our study the doses varied from 3 to 10 mg dependent on age. We cannot report on dose related success rate as this was not part of this study.

#### 4.3. Timing of melatonin administration

It is important to consider the timing of melatonin administration with respect to the duration of the medical procedures. Time to maximum serum/plasma concentration after oral melatonin intake has been shown to be approximately 50–60 min.<sup>18</sup> The reported sleep latency in EEG and MRI studies varies between average 21–31 min.<sup>13,16</sup> The reported time between intake and start of EEG procedures varied from directly prior to the EEG up to 35 min.<sup>16,19</sup> In our study, melatonin was administered approximately one hour prior to the MRI scan. However, because scans were made during a normal day programme, the actual time between intake and scan could become longer.

#### 4.4. Sleep latency onset and duration

In one sleep EEG study, sleep latency onset and duration were assessed after melatonin and chloral hydrate, both combined with SDep. The sleep latency onset was similar in both groups, but sleep duration was significantly shorter with melatonin compared to chloral hydrate (median 30 min vs 60 min, respectively).<sup>15</sup> MRI procedures usually last between 10 min with fast imaging for hydrocephalus and approximately 55 min, for instance for a combined brain and spine scan. The short scans would fall within the sleep duration effect, however the longer scans could potentially be more vulnerable to movement. The median scan duration in this study was 23 min, with 22% of children having non-moved scans, suggesting they were asleep.

#### 4.5. Scan time during the day

The time during the day at which the medical procedures takes place may also affect the success rate. As in previous studies, the MRI procedure in our study was performed late in the morning to halfway afternoon, but scanning at night could be more appropriate and lead to a higher success rate in older children.<sup>14,16,21</sup> Eisermann et al. studied the effect of melatonin in EEG monitoring, using partial SDep the night before, and recording during the day time nap in younger children and at the beginning of the afternoon in adolescents.<sup>16</sup> Sleep was obtained in 80% of children. Nordahl et al. achieved a 93% success rate in MRI in very young children with autism, developmental delay and normal development, scanned during natural nocturnal sleep, without melatonin.<sup>25</sup> Dean III et al., also obtained an MRI success rate of 93% in children under the age of 4 years, using natural sleep combined with noise reduction and immobilizers.<sup>26</sup> Important for this

success were a dedicated pre-scan preparation, a child- and family-friendly MRI environment, involvement of parents and the availability of scanning facilities in the evening. We obtained a high success rate without particular environmental adjustments in the scanning room and without taking into account the time at which natural sleep takes place.

#### 4.6. Effect of sleep deprivation on success rate of melatonin

In an attempt to improve the success rate of melatonin, several medical procedures have used SDep combined with melatonin. Methods used to obtain SDep consist of keeping a child awake longer at night, waking them earlier in the morning and preventing falling asleep while travelling to the hospital.<sup>17,19</sup> The results vary from no increase of success rate<sup>17,21</sup> to an increase from 55% to 76%.<sup>19</sup> One study using only SDep in non-invasive medical procedures (amongst which MRI), however, showed that nursing care hours, from intake to discharge, were significantly longer in sleep deprived patients compared with non-sleep deprived patients.<sup>29</sup> In order to assess the actual effect of melatonin, SDep was not used in our study.

#### 4.7. Additional diagnostic value of the BLADE technique

Several studies (not using melatonin) have shown the additional diagnostic value of applying the BLADE technique in children and adults.<sup>30,31</sup> In our study the contribution in protocols where BLADE was added when a child moved, the contribution to DC was definite in approximately half of the patients and not contributing in 1/3. However, the low number of patients makes a definite comment on its contribution limited.

#### 4.8. Effect of definition of success rate

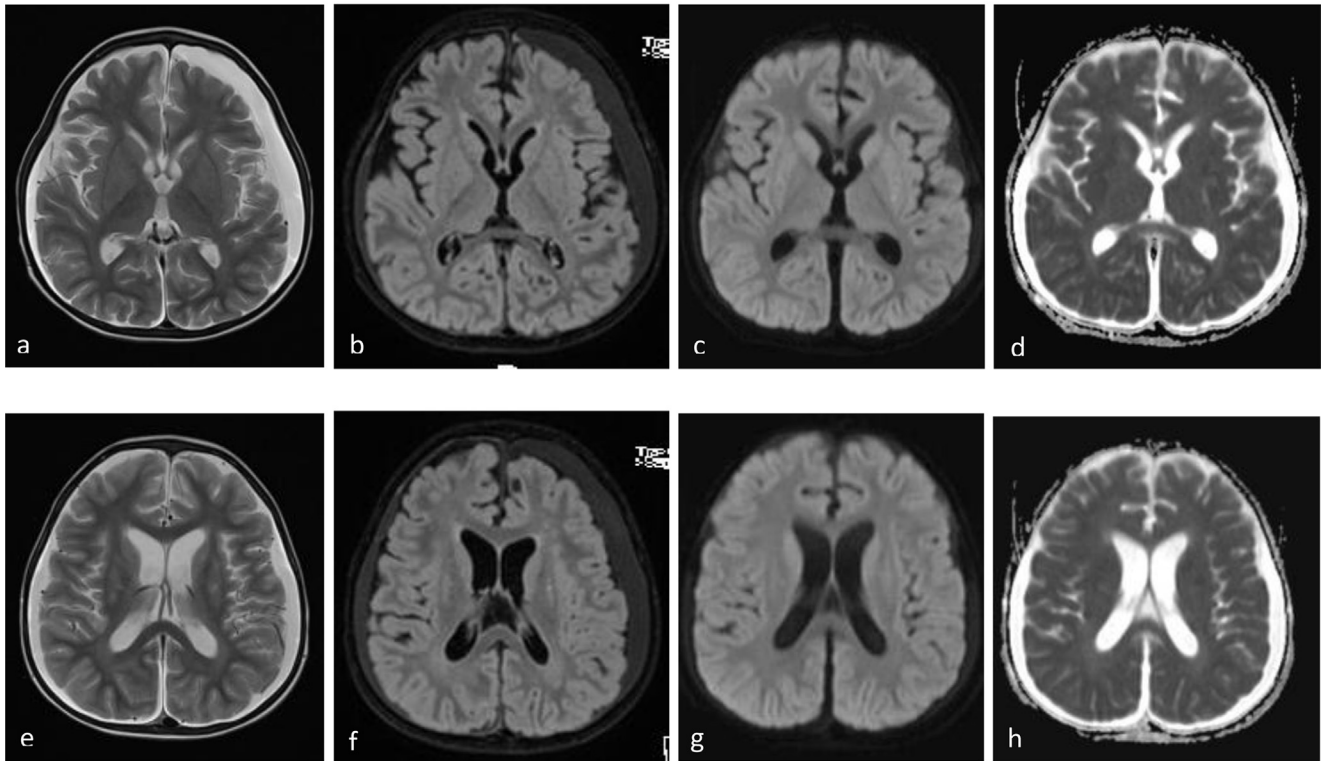
The definition of ‘contributing to the diagnostic trajectory’ was used in our study as a measure of success rate, as this has the greatest relevance to and resemblance with daily practice. In most previous studies, falling asleep was the most commonly used requirement for defining a procedure to be successful. Our success rate was clearly higher than in the previous MRI studies<sup>13,19</sup> and comparable with previous EEG<sup>16</sup> and ABR studies.<sup>21</sup>

In this study we looked at the actual scan time, independent of the planned scan protocol. It is difficult to assess a relation between scan length and success. A short scan time may be related to a specific protocol (hydrocephalus) or may be related to a failed scan. Furthermore, a planned scan protocol could last longer than the actual scan time if a child moved too much during the last part of the scan and the scan needed to be stopped prematurely. None of the children with an actual scan time longer than 15 min needed a repeat scan.

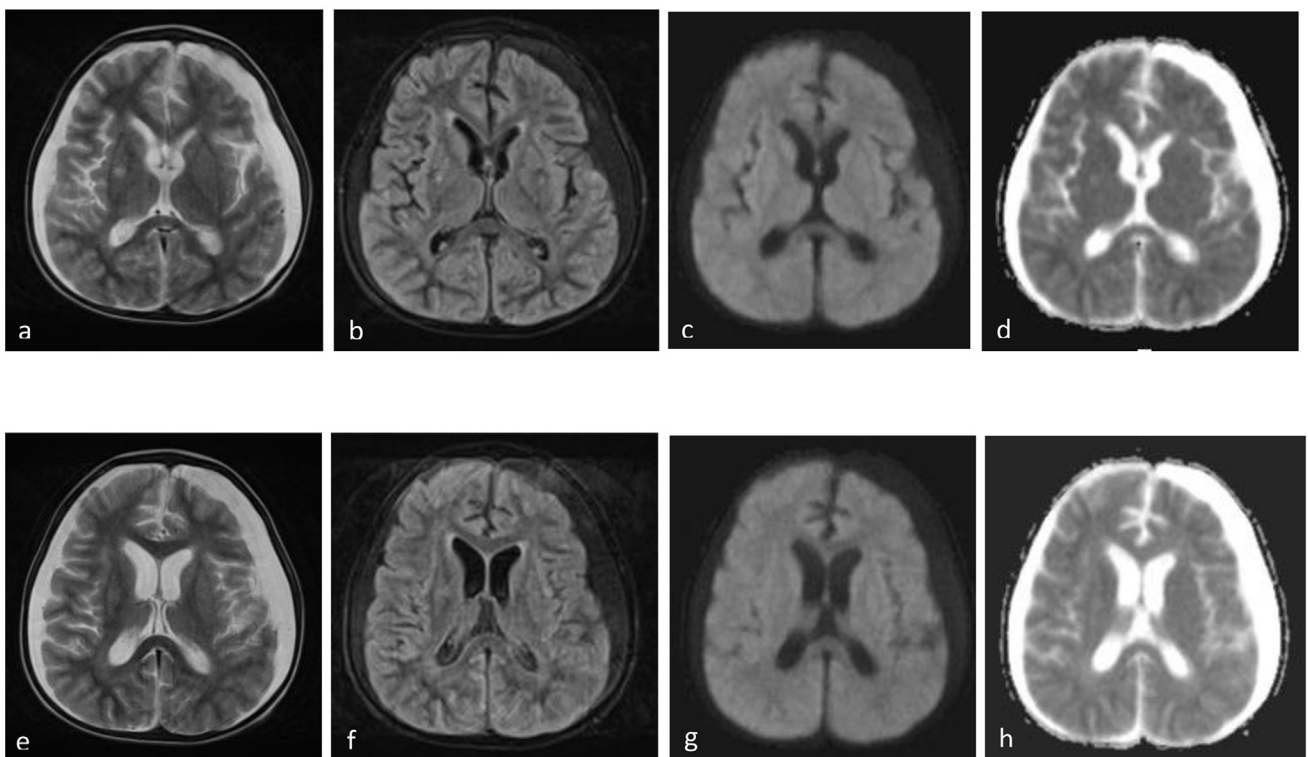
#### 4.9. Economic benefit

In our retrospective study with children from 10 months to 5 years, the high number of scans not requiring a repeat scan with GA (73%), led to a considerable reduction in costs. This has not been reported previously for MRI. In a study by Schmidt et al., melatonin reduced the need and frequency of

A



B



GA for ABR investigations by >80%, making its use cost-effective.<sup>21</sup>

GA, sedation and other methods of reducing anxiety like play therapy and the use of mock scanners are costly, also because of their time consuming preparation and post-procedural care.<sup>32</sup> In a study by Vanderby et al., in 2011, the average MRI visit duration of an awake child was 2 h and 21 min, while sedated children had a 3 h and 38 min visit and anaesthesia visits lasted on average 4 h and 7 min.<sup>33</sup> Visit costs for children scanned with sedation and anaesthesia were approximately 3 and 9 times higher, respectively, compared with those scanned without.

Melatonin is cheap, because of its label 'food supplement' and wide availability. Its toxicological profile is remarkably safe even with high doses and also when used in children.<sup>9</sup> It does not require expensive MR compatible resuscitation equipment and the presence of an anaesthetist or a play therapist, and a post MRI hospital stay is not needed.

In this study a repeat scan under GA was made in 17 children with a waiting time between 12 and 81 days (for unknown reasons). In The Netherlands, all scans are paid for by the Medical Insurance companies, therefore if a scan needs to be repeated under GA, this does not have any financial consequences for the parents/carers.

#### 4.10. Strengths and weaknesses

The main strength of our study is that we have scanned one cohort with melatonin and the scans were systematically reassessed by one expert paediatric neuroradiologist. Testing the efficacy in a general university hospital may be beneficial to other general hospitals which are not particularly dedicated to children.

Its main weakness is that it is a retrospective study and not a prospective case-control study, performed under controlled circumstances. Because of the retrospective

**Fig. 2 – It shows a first scan made with sedation (A) and a second scan made with melatonin (B).**

**Fig. 2A. a–h MRI scan made prior to scan with melatonin:**

#### Clinical information:

- Patient with high risk acute lymphoblastic leukemia for which prophylactic chemotherapy. Infection with streptococcus mitis with suspected meningitis. Increasingly drowsy with seizures. Presently lowered consciousness, spontaneous overextension, bilateral Babinski and divergent gaze.
- Query: Intracerebral pathology?

Protocolled as standard with Gadolinium, made under sedation with anaesthetist (and not GA, because of compromised medical situation). Contrast enhanced sequences are not shown. Two brain levels are shown. a and e: Axial T2. b and f: Axial MPR 3D FLAIR SPACE. c and g: Axial DWI. d and h: Axial ADC.

#### Findings:

##### T2 and FLAIR:

- Bilateral subdural effusion with slightly higher signal on FLAIR (Figure a and f) suspect for high protein level. Bilateral areas of slightly elevated signal on T2 in the cranial putamen. Prominent lateral and third ventricles without periventricular oedema. No abscess.

##### DWI/ADC:

- No diffusion restriction in parenchyma and effusions.

#### Conclusion:

- Bilateral areas of subacute ischemia in putamen? No acute ischemia. No empyema.

**Fig. 2B. a–h MRI scan made 9 days later with melatonin assessed for the present study.**

#### Clinical information:

- Same patient with newly developed leftsided paresis. Suspicion of vasculopathy.
- Query: Ischemia right hemisphere? Increase in hydrocephalus? Decrease in enhancement of intracranial structures? Abscess formation?

Protocolled as standard with Gadolinium. Incomplete because of movement. Sequence with Gadolinium was not made. a and e: Axial T2 BLADE. b and f: Axial FLAIR BLADE. c and g: Axial DWI. d and h: Axial ADC.

#### Findings:

##### T2 and FLAIR:

- FLAIR more than T2 shows movement artefacts. Small area of increased signal in the right putamen, new compared with previous scan, suspicious for subacute ischemia. Lateral ventricles and third ventricle remained unchanged and prominent. Effusion unchanged on the left, slight rightsided increase.

##### DWI and ADC:

- Suboptimal quality due to movement artifact.
- No acute ischemia. No abscess. No diffusion restriction in effusions suspect for empyema.

#### Conclusion:

- Although all sequences were hampered more or less due to movement artefacts (and no sequences were made with intravenous Gadolinium), all sequences could be assessed sufficiently and all queries could be answered adequately. Considered for study as diagnostically contributing.



design, we have not been able to prove the efficacy of melatonin in inducing sleep in infants and young children undergoing MRI. With this design, no pre-defined criteria were available to decide whether to scan with melatonin instead of GA. The decision was based on the expectation of the paediatric neurologist that melatonin would be effective and on the fact that scanning with melatonin offered a reduced waiting time compared with GA. No selection was made by the paediatric neurologist in terms of clinical diagnosis or medical urgency and the decision to use melatonin was independent of the scan protocol/length. This may have led to a bias. The retrospective design also did not allow obtaining parental feedback on the use of melatonin and no comment can be made on parental experience.

Another weakness of this study is that even though a scan could be diagnostically contributing, subtle abnormalities which could be relevant for making a definite diagnosis, could potentially be missed. For example assessment of an MRI in a child with epilepsy, insular polymicrogyria may be seen on a thick sliced T2 BLADE (Fig. 1), however the presence of a small cortical dysplasia could be missed.

The journey from the paediatric department to the MRI unit may have had a negative effect on the success rate. This rate could potentially have been higher, if a quiet and dark waiting room for the children would have been available next to the MRI unit.

As all scans were made in a time window of 45–60 min (never shorter) between the administration of melatonin and the start of the MRI scan, we cannot comment on the effect of a shorter or longer time window on the success rate.

The effect of melatonin is still questionable, as several factors may have led to a positive bias towards scans considered as DC. Different protocols were used with different slice thicknesses, scan time duration, and variable use of BLADE sequences in some patients. Children with a hydrocephalus protocol and those with BLADE would potentially have a bigger chance of succeeding, even without melatonin. Furthermore, if scans were stopped prematurely because of movement, these could still be assessed as DC.

In conclusion, in this retrospective study, the efficacy of melatonin was tested in its application in children undergoing MRI of the central nervous system, ranging from 10 months to 5 years. We have shown that, despite the fact that the majority did not fall asleep, a high success rate of 77% of scans contributing to the diagnostic trajectory may be achieved with melatonin, even when using a remote waiting room and performed during a normal day MRI programme. The high success rate can be partially explained by the used definition of diagnostically contributing scans. The restricted number of patients with no movement artefacts in their scans, suggests that the sleep-inducing power of melatonin under these circumstances is limited, but the children may have benefitted from the anxiolytic and/or sedative effect. As the majority of children did not require a repeat scan with GA, a reduction in scan related costs was achieved.

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## Declaration of Competing Interest

None of the authors have a conflict of interest to disclose.

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