

Discomfort in children undergoing unседated MRI

Anna E. Westra · Maria P. A. Zegers · Rám N. Sukhai ·
Ad A. Kaptein · Herma C. Holscher ·
Bart E. P. B. Ballieux · Erik W. van Zwet · Jan M. Wit

Received: 20 September 2010 / Accepted: 4 November 2010 / Published online: 1 December 2010
© The Author(s) 2010 This article is published with open access at Springerlink.com

Abstract Magnetic resonance imaging (MRI) scans for research purposes usually do not directly benefit the children scanned, so that review boards need to assess whether the risk of harm or discomfort is minimal. This study aimed at providing empirical data on discomfort related to unседated MRI in children aged 5–12 years. Secondary objectives were to determine whether lower age is associated with higher levels of discomfort and to investigate which other characteristics of subjects and/or procedures may be associated with higher levels of discomfort. Self-report scores, observation scores, heart rate standard deviation scores, and incremental salivary cortisol levels were obtained from 54 children aged 5–12 years with non-acute conditions undergoing diagnostic MRI. Of the 54 children, 10 scored relatively high values

on the self-report score and on one or two of the other measures, and another 15 scored relatively high on the self-report score alone. Rather than an age effect, associations were found between parents' trait anxiety and observation score values and between use of contrast fluid (requiring the insertion of a venous cannula) and high incremental salivary cortisol levels. In conclusion, MRI-related discomfort may be regarded as minimal for more than half of children aged 5–12.

Keywords MRI · Research · Ethics · Risk assessment

Introduction

Magnetic resonance imaging (MRI) is a frequently used imaging technique not only for diagnostic purposes but also in research settings. For example, children have undergone MRI scans to study the brains of children at risk for attention-deficit/hyperactivity disorder, to compare MRI with conventional diagnostics techniques, to unravel the etiology of cerebral palsy, and to provide “healthy control” images [5, 8, 11, 13]. Such research MRI scans usually do not directly benefit the children scanned. This means that before the research can take place, review boards need to assess whether the risks of the procedure are minimal [3, 17, 21].

If the children do not need sedation, the risk of MRI-related physical harm is extremely low [4]. However, review boards need not only assess possible physical harm but also the expected discomfort caused by the study procedure at stake. Possible discomfort may seem rather trivial when compared with possible physical harm but should nevertheless also be limited, considering the fact that children have to endure the procedure solely for the

A. E. Westra (✉) · M. P. A. Zegers · R. N. Sukhai · J. M. Wit
Department of Pediatrics, Leiden University Medical Center,
P.O. Box 9600, 2300 RC, Leiden, The Netherlands
e-mail: a.e.westra@lumc.nl

A. A. Kaptein
Department of Medical Psychology,
Leiden University Medical Center,
Leiden, The Netherlands

H. C. Holscher
Department of Radiology, Haga Teaching Hospital/Juliana
Children's Hospital,
The Hague, The Netherlands

B. E. P. B. Ballieux
Department of Clinical Chemistry,
Leiden University Medical Center,
Leiden, The Netherlands

E. W. van Zwet
Department of Biostatistics, Leiden University Medical Center,
Leiden, The Netherlands

benefit of future others. This is clearly reflected in the US definition of “minimal risk” [18]. Other guidelines even explicitly distinguish expected discomforts from risks of harm and speak of “minimal risk” and “minimal burden” (the term “burden” referring to the expected discomforts) [3, 21].

A review of studies performed in adults has revealed that 4% to 30% of adults undergoing MRI experience some sort of anxiety, ranging from apprehension to severe reactions that interfere with the procedure [10]. Those few pediatric studies that have been published suggest that the confined space, loud noise, and the instruction not to move may also cause anxiety and distress in children. Marshall et al. found some form of anxiety in 25 of 85 children aged 10–18; Tyc et al. reported significant distress in about 16 of 55 children aged 8–22 [9, 16]. However, neither of these two studies included children younger than 8 years old. The other studies merely focused on the effect of interventions such as simulation scanners or play therapy [6, 12, 14, 15]. This implies that review boards often cannot base their judgments on the acceptability of expected discomfort on relevant group-level data. The Dutch Central Committee’s decision to reject all MRI studies that involve children below 8 years old, for instance, lacks a scientific basis [2].

In this research project, we aimed at providing empirical data on discomfort associated with unседated MRI in children aged 5–12 years. Secondary objectives were to determine whether lower age is associated with higher levels of discomfort and to investigate which other characteristics of subjects and/or procedures may be associated with higher levels of discomfort.

Methods

Subjects

All children aged 5–12 with non-acute conditions undergoing MRI between January and July 2009 in the Leiden University Medical Center (LUMC) and Juliana Children’s Hospital (JCH, The Hague) were asked to participate. Age 5 was set as the minimum age because children aged 4 or below are never scanned without sedation in these two hospitals. Children from non-Dutch-speaking parents and mentally retarded children were excluded. In total, 60 eligible children were scanned and were asked to participate. In six cases, the parent and/or child refused, mostly because the parent thought that the burden of the research project would be too high for their child. So, 54 children were included.

None of the two hospitals made use of special preparation procedures. Those children who had to receive contrast fluid during the MRI procedure got an appointment

with a phlebotomist before their appointment at the radiology department in order to get a venous cannula. The study was approved by the review boards of both hospitals.

Measures

Characteristics of the subjects and MRI procedures

Information about age, gender, prior experience with MRI, and use of potentially cortisol-level influencing medication was obtained from the parents. To measure the children’s level of understanding, children were asked whether they understood what was going to happen. The possible answers were “I don’t”, “A little bit”, and “I do”. Trait anxiety of the parent accompanying the child was assessed with the Spielberger State-Trait Anxiety Inventory [19]. The trait anxiety scale evaluates on a scale of 20 to 80 how anxious a person generally feels. Information regarding the body part scanned, the use of contrast fluid, and the duration of the scan were collected during the procedure.

Measures of discomfort

Procedural discomfort was for this particular procedure considered to be a combination of anxiety and/or unpleasantness prior to and during the procedure. Considering the lack of a suitable standardized questionnaire for children below 8 years old, we have not only measured self-report but have also collected observations of parents and MRI staff, heart rates, and salivary cortisol. Parents can assess their child’s responses in perspective of their regular behavior; MRI staff can compare the child’s responses with a broad range of other children’s responses. Increased heart rates and cortisol levels may indicate physiological arousal.

1. Self-report. Before the MRI procedure, the children were asked to indicate how they felt using the Facial Image Scale (FIS) [1]. The FIS comprises a set of five faces ranging from very happy to very unhappy, the middle face being neutral. Shortly after the MRI procedure, the children were asked to indicate on a FIS how they felt during the procedure. In addition, they were asked to indicate on a four-point scale whether they considered the procedure “very pleasant”, “fairly pleasant”, “unpleasant”, or “very unpleasant”. For this last question, we used words instead of a FIS.
2. Observations by parent and by MRI staff member. Prior to the procedure, the parent accompanying the child and the MRI staff member performing the procedure were asked to rate the child’s degree of anxiety on a five-point scale. Afterwards, they were asked to rate the child’s anxiety during the procedure. The questions

asked for this purpose were “What is your impression of the child at this moment?” and “What was your impression of the child during the procedure?”; the possible answers ranged from “very anxious” to “very relaxed”. In addition, after the MRI procedure, the staff member was asked to use a five-point scale to rate the child’s degree of observed cooperativeness. The question asked for this purpose again was “What was your impression of the child during the procedure?” the possible answers ranged from “very cooperative” to “counteracting a lot”.

3. Heart rate. Heart rates were obtained from all children scanned in the JCH at four time points (at start and after 1, 5, and 10 min). After calculating means and standard deviations for all seven age groups based on a previous study, individual heart rates were expressed as standard deviation scores (SDS) [20].
4. Salivary cortisol. Salivary cortisol has emerged in pediatric research as an easy-to-collect biologic marker of stress [7]. From each child, four samples were taken using Salivette® (Sarstedt, Etten-Leur, The Netherlands). We have used the cortisol assay of Roche Diagnostics, Modular E170 immunoanalyzer (Mannheim, Germany). The detection limit of this assay is 0.5 nmol/l. At a concentration of 3.1 nmol/l, the total variation is 12%, and the intra-assay variation 9%. Samples 1 and 2 were taken before and shortly after MRI; samples 3 and 4 were taken at the same time points the next day. All four values of one child were excluded because of daily steroid use. For the definition of outliers (for instance caused by tooth brushing), we used a robust method to fit a linear model for the logarithm of the measured salivary cortisol. As covariates, we included main effects for the patient, day, and time of day. We also included an interaction term between day and time of day to account for a possible effect of the MRI procedure. Seven out of 196 values were deemed outliers and were replaced by imputed values based on the fitted model. As parameter of MRI-related distress, we used the incremental salivary cortisol: $((\text{sample 1} + \text{sample 2}) - (\text{sample 3} + \text{sample 4})) / 2$, which was also expressed as a percentage of the average median value on the control day.
5. Comparison. Shortly after the MRI procedure, the children were asked if they remembered undergoing a blood draw or a vaccination, and if so, if they could compare that experience with the MRI procedure. The four possible answers were “I think the MRI scan was more unpleasant than the blood draw (or vaccination)”, “I think the blood draw was more unpleasant than the MRI scan”, “I think the blood draw was just as unpleasant as the MRI scan”, and “I think that neither the blood draw nor the MRI were unpleasant”.

Research procedure

Subjects were enrolled in the study upon arrival. While the children and parents were waiting in the waiting room, the researcher (AW or MZ) asked them if they wanted to participate, after a short explanation of the study. Those who were interested were taken to another room for a more comprehensive explanation of the rationale and study procedures. If willing to participate, the parent and child were asked to sign a consent form, to complete the first questions, and to provide the first saliva sample. During the MRI procedure, the heart rate of the child was measured by a heart rate appliance attached to one of the fingers of the child. Immediately after the MRI procedure, the child and parent were taken to a room to complete the remaining questions and take the second saliva sample. Finally, the parent and child were instructed how to take the third and fourth saliva samples at home the next day.

Data analysis

The characteristics of the subjects and procedures were analyzed descriptively using SPSS version 16 for Windows. Principal Component Analysis suggested using the following four (composed) measures of discomfort during the data analysis: self-report score (all three ratings), observation score (all five ratings), heart rate SDS, and incremental salivary cortisol. For each of these outcome measures, results were calculated for the total group as well as per age group (5–7 years, 8–9 years, and 10–11 years). With a one-way ANOVA, differences between the three age groups were assessed. The three self-report questions were also analyzed individually. Correlation between the four outcome measures was assessed using Pearson correlation coefficients. Finally, a backward regression analysis was performed on each of the four outcome measures using all eight characteristics of the subjects and procedures. Backward regression analysis is a stepwise approach which involves starting with all candidate variables and then testing them one by one for statistical significance, deleting any that are not significant. The procedure selects for small *p* values, so the *p* values of the remaining variables (if any) are biased and must be interpreted with caution.

Results

Characteristics of the subjects and of the MRI procedures

Table 1 lists several characteristics of the subjects and of the MRI procedures. Most subjects (33) were scanned in the JCH. The median age was 9.15 years (range 5–12), the median duration of the MRI procedure was 20 min (range

Table 1 Characteristics of the subjects and of the MRI procedures

Variable	Number
Age	
5–7	19
8–9	16
10–11	19
Gender	
Male	21
Female	33
Previous MRI experience	12
Level of understanding	
None	6
Little	22
Good	26
Location	
JKZ	33
LUMC	21
Body part scanned	
Head	19
Other	35
Use of contrast fluid	12

10–90), and the median value of parents' trait anxiety was 34 (range 20–55, $n=51$). In 35 of the cases, the body part to be scanned was not the head but, among others, the upper spine, the lower spine, the heart, or one of the extremities.

Discomfort

The median values and ranges of the four outcome measures are displayed in Table 2. The median self-report score value was 7 (range 3–12). This could be a combination of one happy FIS score shortly before the MRI (=2), one neutral FIS score regarding the MRI itself (=3), and “fairly pleasant” (=2). Table 3, showing the three individual self-report questions, reveals that the question how the child considered the procedure was answered negatively (“unpleasant” or

“very unpleasant”) in 24 of cases. All but three of these 24 children had a self-report score of ≥ 8 .

The median observation score value was 11 (range 6–19), which could be a combination of four times “relaxed” (=4 \times 2) and “not cooperative, not uncooperative” (=1 \times 3), or something alike. The median heart rate was -0.17 SDS (range -1.29 to 1.53), indicating that the heart rate was more often decreased than increased. The median incremental salivary cortisol value was 0.71 nmol/l (range -8.96 to 36.16). Median salivary cortisol values collected on the control day (samples 3 and 4) were 3.42 nmol/l (range 0.67 – 15.36) and 2.83 nmol/l (range 0.50 – 15.35); the median increment hence was approximately 23%.

None of these three measures was significantly correlated with the self-report score or with any one of the other measures: the correlation coefficients ranged from 0.245 ($p=0.09$) to -0.026 ($p=0.89$). However, the wide ranges around the median values indicate that also on these three measures, some children scored relatively high values. When defining relatively high values as a self-report score of ≥ 8 (25 cases), an observation score of ≥ 15 (eight cases), a heart rate SDS of ≥ 1 (four cases), and an incremental salivary cortisol level of ≥ 4 nmol/l (10 cases), 10 of the 54 children scored relatively high values on the self report score *and* on one or two of the other measures. Another 15 children scored relatively high on the self-report score alone. Nine children scored relatively high on one (8) or two (1) of the other measures, but not on the self-report score.

Of all 40 children who remembered undergoing a venipuncture (31) or vaccination (9), four indicated that the MRI procedure was more unpleasant than the other procedure, 24 indicated that they considered the other procedure as more unpleasant, six evaluated the procedures as equally unpleasant, and six did not consider any of the two procedures as unpleasant.

Associations

Table 4 summarizes the results of the backward analysis by showing the first and last steps for all four outcome

Table 2 Self-report score, observation score, heart rate, and incremental salivary cortisol per age group

Age (years)	Self-report score (scale 3–14)	Observation score (scale 5–25)	Heart rate ^a (SDS)	Incremental salivary cortisol (nmol/l)
	Median (range)	Median (range)	Median (range)	Median (range)
5–7	6 (3–11)	11 (8–19)	0.04 (-0.82 – 1.40)	0.81 (-8.96 – 6.87)
8–9	8 (5–10)	11 (8–19)	-0.44 (-1.29 – 0.73)	0.46 (-6.85 – 36.16)
10–11	7 (5–12)	11 (6–14)	-0.17 (-1.26 – 1.53)	1.00 (-5.49 – 16.51)
All ages	7 (3–12)	11 (6–19)	-0.17 (-1.29 – 1.53)	0.71 (-8.96 – 36.16)
ANOVA	$F=1.644$ ($p=0.203$)	$F=2.294$ ($p=0.111$)	$F=1.046$ ($p=0.364$)	$F=0.692$ ($p=0.506$)

^a $n=32$

Table 3 Self-report, per age group

	How do you feel? (before MRI) (Facial Image Scale)			How did you feel while in MRI? (Facial Image Scale)			The procedure was	
	1: very happy or 2: happy	3: neutral	4: unhappy or 5: very unhappy	1: very happy or 2: happy	3: neutral	4: unhappy or 5: very unhappy	1: very pleasant or 2: fairly pleasant	3: unpleasant or 4: very unpleasant
Age (years)								
5–7 (n=19)	15	2	2	9	6	4	14	5
8–9 (n=16)	10	5	1	5	9	2	7	9
10–11 (n=19)	14	4	1	8	7	4	9	10
All ages (n=54)	39	11	4	22	22	10	30	24

measures. This reveals, for instance, that after testing the eight characteristics of the subjects and procedures one by one for being significantly associated with the self-report score, deleting all that were not significant, none was left. Use of contrast fluid (with the preceding insertion of a venous cannula), however, was clearly associated with higher incremental salivary cortisol levels ($\beta -0.650, p<0.001$). Furthermore, a parent scoring high on the trait anxiety questionnaire was associated with a higher observation score ($\beta 0.373, p=0.005$) but a lower heart rate SDS ($\beta -0.395, p=0.038$).

Backward regression analysis also indicated a possible association between a lower age and a higher observation score value ($\beta -0.253, p=0.046$). The one-way ANOVA

analysis, however, did not show significant differences between the age groups (Table 2).

Discussion

We have provided empirical data on discomfort associated with unседated MRI in 54 children aged 5–12 years. The data reveal that 20 of the 54 children did not experience any demonstrable discomfort, and only four out of 40 children experienced the MRI procedure as being more unpleasant than a venipuncture or vaccination. However, 10 of the 54 children scored relatively high values on the self-report score *and* on one or two of the other measures, 15 children

Table 4 Backward regression analysis of subject characteristics and procedural characteristics on self-report score, observation score, heart rate, and incremental salivary cortisol

	Age	Gender M=1 F=2	MRI experience Yes=1 No=2	Level of understanding	Trait anxiety parent	Location JKZ=1 LUMC=2	Body part Head=1 Other=2	Use of contrast fluid Yes=1 No=2	Duration
Self-report									
First step	$\beta 0.193$ (p 0.206)	$\beta 0.104$ (p 0.517)	$\beta -0.047$ (p 0.783)	$\beta 0.134$ (p 0.391)	$\beta 0.037$ (p 0.818)	$\beta 0.211$ (p 0.264)	$\beta 0.124$ (p 0.474)	$\beta -0.163$ (p 0.402)	$\beta -0.113$ (p 0.606)
Last step									
Observation									
First step	$\beta -0.286$ (p 0.036)	$\beta 0.103$ (p 0.464)	$\beta -0.060$ (p 0.689)	$\beta 0.002$ (p 0.988)	$\beta 0.353$ (p 0.017)	$\beta -0.129$ (p 0.433)	$\beta -0.253$ (p 0.102)	$\beta -0.104$ (p 0.543)	$\beta 0.113$ (p 0.559)
Last step	$\beta -0.253$ (p 0.046)				$\beta 0.373$ (p 0.005)		$\beta -0.225$ (p 0.081)		
Heart rate									
First step	$\beta -0.266$ (p 0.176)	$\beta -0.236$ (p 0.318)	$\beta -0.169$ (p 0.390)	$\beta -0.475$ (p 0.041)	$\beta -0.461$ (p 0.033)	NA	$\beta -0.262$ (p 0.219)	$\beta -0.375$ (p 0.140)	$\beta 0.009$ (p 0.969)
Last step					$\beta -0.395$ (p 0.038)		$\beta -0.372$ (p 0.050)		
Cortisol									
First step	$\beta -0.030$ (p 0.820)	$\beta 0.198$ (p 0.164)	$\beta 0.085$ (p 0.578)	$\beta -0.056$ (p 0.685)	$\beta -0.103$ (p 0.463)	$\beta -0.217$ (p 0.223)	$\beta -0.038$ (p 0.809)	$\beta -0.687$ (p<0.001)	$\beta -0.113$ (p 0.577)
Last step						$\beta -0.233$ (p 0.071)		$\beta -0.650$ (p<0.001)	

scored relatively high on the self-report score alone, and another nine children scored relatively high on one or two of the other measures.

In order to be able to tell whether these 10, 25, or perhaps even all 34 children experienced considerable discomfort, one could opt for regarding one or a combination of several of the four measures as providing the “truth”. Yet, the very reason for choosing a wide range of assessment instruments was the lack of a “golden standard” for assessing potential discomfort. We believe that self-report is most valuable but not necessarily sufficient on its own in this age group. It is remarkable that only 10 out of 25 children with relatively high self-report values also scored relatively high on one or more of the other measures. Considering the subjective character of the concept of “discomfort”, we do nevertheless suggest to also take the other 15 high self-report scores seriously. On the other hand, nine children scored relatively high on one or two of the other measures without a corresponding high value on the self-report score. We believe that the value of such incidental high scores is limited: observers may project their own feelings to the child, and heart rates and cortisol levels may also rise as a consequence of “positive” stress (e.g., in the waiting line for the roller coaster). We hence suggest considering the discomfort level of the eight children in this category as “minimal”.

Rather than the expected age effect, we found associations between parents’ trait anxiety and high observation score values, and between use of contrast fluid and high incremental salivary cortisol levels. Regarding the trait anxiety, we speculate that anxious parents more often *thought* that their children were anxious because these children did not score high on other measures (they even had relatively low heart rates). The association between use of contrast fluid and high incremental salivary cortisol levels suggests that the insertion of the venous cannula prior to the MRI procedure was for many of the 12 children needing contrast a far more distressing event than the MRI procedure itself. This is in line with Tyc et al. whose sample of 54 children included 44 children requiring intravenous contrast, and who considered the insertion of the needle as part of the MRI procedure: a large proportion of children and parents reported this part of the procedure as being the most aversive part [16].

Our study has some limitations. The observation score did not include observation of the child by a psychologist. This could have made the observation score more accurate. Furthermore, because we performed our study with subjects undergoing diagnostic MRIs, it is uncertain to which extent the conclusions also apply to MRIs for research purposes. Children undergoing diagnostic MRIs may be concerned about the results of the scan, thus children undergoing research MRIs may experience less discomfort. Lastly, due

to our sample size and the large number of potential subject characteristics and/or procedural characteristics associated with higher levels of discomfort, these potential associations could not be optimally tested.

The results of this study indicate that MRI-related discomfort can be regarded as minimal for more than half of children aged 5–12. Review boards and researchers must be aware that there will also be children in whom the procedure may cause considerable discomfort. We could not find any experimental evidence for the Dutch Central Committee’s assumption that those children at risk for higher levels of discomfort can be identified by their age. The anxiety of the parent deserves consideration though, just as the fact that the insertion of a needle prior to the MRI procedure (in case contrast fluid need be given) can be a stressful event. Future research could explore alternative ways of measuring discomfort caused by medical procedures in relatively young children, such as adding narratives or drawings to the self-report score. Narratives of the children about their perceptions are a more direct way of assessing their emotions; drawings made by the children before and after the procedure would also shed light on their perceptions.

Acknowledgments We gratefully acknowledge the participating children and their parents for their time and effort. We also thank the MRI staff members of the LUMC and of the JCH for their contribution to this project.

Conflicts of interest None.

Funding The Netherlands Organization for Health Research and Development (grant number 92003475).

Open Access This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

References

1. Buchanan H, Niven N (2002) Validation of a Facial Image Scale to assess child dental anxiety. *Int J Paediatr Dent* 12:47–52
2. Central Committee on Research Involving Human Subjects (CCMO) (2004) CCMO Memorandum MRI research in minors. Available at http://www.ccmoonline.nl/hipe/uploads/downloads_catp/CCMOnotitie%20MRI%20bij%20kids%2014-102004_ENG.pdf. Assessed 13 October 2010
3. Council of Europe (1997) Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: convention on human rights and biomedicine. Council of Europe, Oviedo
4. Dempsey MF, Condon B, Hadley DM (2002) MRI safety review. *Semin Ultrasound CT MR* 23:392–401

5. Durston S, Hulshoff Pol HE, Schnack HG et al (2004) Magnetic resonance imaging of boys with attention-deficit/hyperactivity disorder and their unaffected siblings. *J Am Acad Child Adolesc Psychiatry* 43:332–340
6. Hallowell LM, Stewart SE, de Amorim E, Silva CT, Ditchfield MR (2008) Reviewing the process of preparing children for MRI. *Pediatr Radiol* 38:271–279
7. Hanrahan K, McCarthy AM, Kleiber C et al (2006) Strategies for salivary cortisol collection and analysis in research with children. *Appl Nurs Res* 19:95–101
8. Hermann BP, Dabbs K, Becker T et al (2010) Brain development in children with new onset epilepsy: a prospective controlled cohort investigation. *Epilepsia*. doi:10.1111/j.1528-1167.2010.02563
9. Marshall SP, Smith MS, Weinberger E (1995) Perceived anxiety of pediatric patients to magnetic resonance. *Clin Pediatr* 34:59–60
10. Melendez JC, McCrank E (1993) Anxiety-related reactions associated with magnetic resonance imaging examinations. *JAMA* 270:745–747
11. Mentzel HJ, Kentouche K, Sauner D et al (2004) Comparison of whole-body STIR-MRI and ^{99m}Tc-methylene-diphosphonate scintigraphy in children with suspected multifocal bone lesions. *Eur Radiol* 14:2297–2302
12. Pressdee D, May L, Eastman E, Grier D (1997) The use of play therapy in the preparation of children undergoing MR imaging. *Clin Radiol* 52:945–947
13. Robinson MN, Peake LJ, Ditchfield MR et al (2009) Magnetic resonance imaging findings in a population-based cohort of children with cerebral palsy. *Dev Med Child Neurol* 51:39–45
14. Rosenberg DR, Sweeney JA, Gillen JS et al (1997) Magnetic resonance imaging of children without sedation: preparation with simulation. *J Am Acad Child Adolesc Psychiatry* 36:853–859
15. Smart G (1997) Helping children relax during magnetic resonance imaging. *Am J Matern Child Nurs* 22:236–241
16. Tyc VL, Fairclough D, Fletcher B et al (1995) Children's distress during magnetic resonance imaging procedures. *Child Health Care* 24:5–19
17. U.S. Department of Health and Human Services (1983) Protections for Children Involved as Subjects in Research (45 CFR Part 46, Subpart D). *Fed Regist* 48:9814–9820
18. U.S. Department of Health and Human Services (1991) Basic HHS Policy for Protection of Human Research Subjects (45 CFR part 46, Subpart A). *Fed Regist* 56:28012–28022
19. Van der Ploeg HM, Defares PB, Spielberger CD (1980) Handleiding bij de Zelf-Beoordelings Vragenlijst (ZBV). Een Nederlandstalige bewerking van de Spielberger State-Trait Anxiety Inventory. [Manual of the Self-Assessment Questionnaire. A Dutch adaptation of the Spielberger State-Trait Anxiety Inventory]. Swets and Zeitlinger, Lisse
20. Wallis LA, Healy M, Undy MB, Maconochie I (2005) Age related reference ranges for respiration rate and heart rate from 4 to 16 years. *Arch Dis Child* 90:1117–1121
21. World Medical Association (2008) Declaration of Helsinki. Ethical principles for medical research involving human subjects (6th revision). World Medical Organization, Seoul