JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 23, Number 5, 2013

Pp. 357–362
DOI: 10.1089/cap.2012.0076

Empirical Examination of the Potential Adverse Psychological Effects Associated with Pediatric fMRI Scanning

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Abstract

Background: Over the past decade, the number of functional magnetic resonance imaging (fMRI) studies has increased dramatically. As MRI scans may be anxiety provoking, performing them in a research setting, particularly with children already prone to anxiety, raises questions about ethics as well as methodological feasibility. It is essential to address these questions before expanding the use of this technique to clinical settings, or more widely in the context of pediatric psychopharmacology and biological psychiatry research. The current study investigates the psychological reactions of anxious and non-anxious children and non-anxious adults to an fMRI scan.

Methods: Eighty-seven anxious children, 140 non-anxious children, and 98 non-anxious adults rated their emotional reactions to an fMRI scan.

Results: Results indicated that anxious and non-anxious children reported no greater anxiety after fMRI scanning than did adults. In addition, no age-related differences in distress were observed. These data demonstrate that anxious children, healthy children, and healthy adults have similar emotional reactions to fMRI scanning.

Conclusions: The observed findings suggest that the potential for fMRI to produce anxiety should not impede its widespread use in clinical research, psychopharmacology, and biological psychiatry.

Introduction

Functional magnetic resonance imaging (fMRI) maps neural activity by monitoring the hemodynamic response to various events. Although MRI has been widely used clinically, its use in research has increased dramatically in recent years, allowing researchers to quantify the neural correlates of cognitive and affective processes (Perlman 2012). This noninvasive technique is particularly pertinent to the study of pediatric anxiety disorder patients, who exhibit disrupted neural circuitry function associated with attention, memory, and learning (Pine 2007). Moreover, for research on psychopharmacology and therapeutics more broadly, quantification of these neural correlates may be used to target novel anxiolytic therapies, or to better tailor existing treatments to particular patients, based on patterns of brain function.

Using MRI for research, especially in children, raises ethical concerns. Whereas MRI scans in a clinical setting are used to clarify medical issues and hence provide direct benefit to the patient, MRI scans in a research setting are not (King 2000). Therefore, application to healthy children is most easily justified when the technique poses no more than minimal risk. Although physical risks associated with MRI scans are minimal, less is known about whether such scans have negative effects at the psychological level. This is particularly relevant to fMRI studies examining emotional reactions by using aversive tasks. Such tasks could potentiate any adverse psychological effects related to the scan environment. Therefore, for widespread clinical application, it is important to quantify the level of psychological risk associated with fMRI. The current study examines psychological reactions to fMRI in healthy and anxious children, to determine the degree to which these reactions differ or resemble the reactions exhibited by healthy adults, a group for whom considerable data already exist.

Whereas fMRI has no known harmful physical effects, the procedure can be anxiety provoking, a conclusion emerging largely from research in adults. Research in medical settings suggests high levels of MRI-related anxiety, either prior to (Quirk, et al. 1989; Katz, et al. 1994) or during scanning (Kilborn and Labbe 1990; McIsaac, et al. 1998). Patients, who are typically left alone during scans, must remain still, often for >1hour, in a dark, physically restrictive space, while a scanner generates loud, potentially

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Funding: This research was supported in part by the Intramural Research Program of the National Institute of Mental Health (NIMH).

noxious sounds, during image acquisition. Most patients experience anxiety in the form of claustrophobia (Quirk et al. 1989; Eshed, et al. 2007), and to a lesser degree panic attacks, although other forms of anxiety also occur (Czarnolewski 2009). Patients report stress because of restricted movement, limited sight, loud noise, and fear of the unknown (Flaherty and Hoskinson 1989). As a result of some of these issues, ~10–15% of adults undergoing MRI for clinical purposes terminate the scan before completion (Melendez and McCrank 1993; Eshed et al. 2007).

Demographic variables and the portion of the body being scanned may affect a participant's response. For example, adult women tend to become more anxious than men (Katz et al. 1994, MacKenzie et al. 1995), and may be more likely to abort the procedure prematurely (Eshed et al. 2007). In addition, the highest rate of MRI termination from anxiety occurs during head and neck scans (Eshed et al. 2007), possibly because of the use of a head coil, a plastic cage-like device placed around the patient's head, and its effect on anxiety (Murphy and Brunberg 1997). Documentation of high discontinuation rates in adults raises questions about the psychological effects in children, a vulnerable population.

This concern has led researchers to use various methods to help children acclimate to the MRI environment. Familiarization with the MRI scanner, explanation of the fMRI procedure, orientation with the research team and, when necessary, implementation of relaxation techniques have all been found to alleviate anxiety (Davidson et al. 2003; Kotsoni et al. 2006). In addition, using a mock scanner provides the unique opportunity for the patient to experience the physical and auditory environment of the MRI scanner prior to data acquisition (Davidson et al. 2003; Kotsoni et al. 2006). Although children often require more simulation than do adults, undergoing a mock MRI scan is helpful for reducing anxiety in all age groups (Rosenberg et al. 1997). Prior training in a simulator could also reduce other developmental and methodological issues such as task noncompliance and motion (Perlman 2012). Considering all of these issues, the current study examines the psychological impact of an fMRI scan on anxious and non-anxious children and adults. Despite widespread research use, this study addresses lingering concerns about the overall degree of distress precipitated by fMRI scanning, particularly in anxious children.

Methods

Participants

Eighty-seven anxious children and adolescents (8–17 years old), 140 non-anxious age peers, and 98 healthy adults (18–53 years old) participated in the study. Anxious subjects had a current American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) (American Psychiatric Association 1994) diagnosis of generalized anxiety disorder, separation anxiety, specific phobia, or social phobia. Diagnoses were determined with the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children – Present and Lifetime version (K-SADS-PL) administered by a clinician. All clinicians were trained to an adequate level of reliability ($\kappa > 0.70$) for all disorders, and diagnoses were confirmed by a clinical interview with a senior psychiatrist. Healthy subjects were free of medical or psychiatric problems as determined by K-SADS (for children) and Structured Clinical Interview for DSM Disorders (SCID) (for adults). Data on subjects' age, gender, intelligence quotient (IQ), and socioeconomic status (SES) were collected. The study included healthy children, adolescents, and adults to provide a benchmark against which to compare data in anxious children and adolescents. Because most existing studies have examined MRI-related distress in adults only, the data from adults in the current study provide a context within the wider literature for considering elevated distress in anxious or healthy children and adolescents.

Table 1 summarizes the characteristics of the sample. Anxious and non-anxious children and adolescents scored lower on IQ

Table 1. Means and Standard Deviations for Sample Demographics and the Self-Reported Scales

	Anxious children/ adolescents	*Non-anxious children/ adolescents*	*Non-anxious adults*	*Statistics*	*Scheffé post-hoc*
Males	39	74	44	$X^2_{(2)} = 2.039$	
Females	48	66	54		
Age	12.11	13.45	25.64	$F(2,322) = 264.99$*	1 < 3, 2 < 3
	(2.72)	(2.78)	(7.23)		
IQ	111.47	111.57	118.33	$F(2,317) = 11.34$*	1 < 3, 2 < 3
	(12.06)	(12.50)	(9.88)		
SES	35.62	44.21	58.90	$F(2,246) = 21.02$*	1 < 2, 1 < 3, 2 < 3
	(14.74)	(19.70)	(26.10)		
Afraid	2.26	1.53	1.66	$F(2,322) = 12.96$	
	(2.25)	(2.32)	(2.21)		
Bored	5.63	5.06	5.73	$F(2,322) = 1.94$	
	(3.03)	(2.92)	(2.62)		
Grumpy	1.80	1.62	1.79	$F(2,322) = 0.19$	
	(2.30)	(2.60)	(2.48)		
Happy	5.27	5.88	4.94	$F(2,319) = 4.63$*	3 < 2
	(2.49)	(2.63)	(1.96)		
Tired	6.15	5.73	6.32	$F(2,319) = 1.30$	
	(2.79)	(3.15)	(2.48)		
State Anxiety	30.57	28.41	28.51	$F(2,131) = 1.58$	
	(5.64)	(4.94)	(7.33)		

1 = anxious children and adolescents; 2 = healthy children and adolescents, 3 = healthy adults.
*$p < 0.05$.
IQ, intelligence quotient; SES, socioeconomic status.

measures than the non-anxious adults, and anxious children and adolescents had lower SES than the two other groups. Before participation, informed consent was obtained from adult participants and parents of all child and adolescent participants; written assent was provided by all child and adolescent participants. All procedures were approved by the NIMH Institutional Review Board.

Procedure

Prior to scanning, participants were acclimated to the scan environment in a mock scanner, unless they viewed this as unnecessary because of their low level of fMRI-related fear. Then, all subjects performed an fMRI task used in one of our research protocols, which are generally designed to elicit some level of fear response. A range of techniques was employed, from fear conditioning and extinction tasks (Britton et al. 2012) to exposure tasks using threatening faces and contexts (Jarcho et al. 2013), with some tasks involving negative and positive feedback (Guyer et al. 2006). Immediately after scanning, subjects were asked to rate their emotional response to the fMRI experience, and their level of anxiety.

Questionnaires

Emotional response to fMRI experience. Distress associated with the fMRI scan was assessed with a six item questionnaire, derived from prior research on anxiety-provoking experiences with children (Pine et al. 2000). For the first question, subjects were asked to rate how they felt during the fMRI scan on three scales, anchored by the following adjectives: bored-interested, afraid-relaxed, and sad-happy (i.e., ''Doing the MRI test made me feel: Bored [0] – Interested [10]''). For the remaining five questions, subjects were asked to rate how afraid, bored, grumpy, happy, and tired they were during the scan on a 0 (not at all) to 10 (a lot) scale (i.e., ''How scared did you feel: Not at all [0] – A lot [10]''). For these scales, subjects were told that a score of ''0'' indicated they felt none of the emotion and a score of ''10'' indicated very high levels of the emotion, relative to their usual experience of these emotions in a typical day.

Anxiety measurements. Participants completed the adult or child version of the State and Trait Anxiety Inventory (Spielberger et al. 1970). Children and adolescents also completed the Screen for Child Anxiety Related Emotional Disorders- Child Self-Report (SCARED-C) (Birmaher et al. 1997), while their parents completed the parental version of this instrument, the SCARED-P (Birmaher et al. 1997). Clinicians rated the anxiety levels of the anxious children and adolescents using the Pediatric Anxiety Rating Scale (PARS) (Group 2002).

Data Analysis

Two sets of analyses were conducted. First, the five fMRI distress scales were compared across the three groups using ANOVAs. In addition, Spearman correlation coefficients were used to quantify the strength of associations between subjects' anxiety indices (SCARED-C, SCARED-P, PARS, and trait anxiety) and each of the five emotions comprising the fMRI distress scales. Second, differences between participants reporting high and low levels of distress were further assessed. This analysis considers whether or not subjects with high distress are unique, relative to subjects with lower distress. Discovering such differences might assist investigators in the future, as they attempt to identify individuals who may be more prone to MRI-related distress prior to undergoing a scan. While this analysis might at first be considered redundant with an analysis comparing anxious and healthy subjects, such redundancy would only emerge if there was a strong correlation between anxiety status and high distress following MRI, a finding that did not emerge in the current data set.

To perform the analysis comparing subjects with high and low distress, the MRI scales were dichotomized. This group assignment was performed by dividing each of the fMRI distress scales into low and high scores, such that all values ≥ 7 were considered *high* and all values <7 were considered *low*. A value of ''7'' was selected as a cut point to separate subjects based on the objective features of the scale, thereby identifying subjects who rated their experienced distress during MRI, relative to their other distressing experiences in life, as falling above a mid-point value on this scale, which was indicated by a score of ''5.'' With this approach, subjects were classified based on their usual experiences with distress, rather than relative to their peers. The current study is more concerned with the former than the latter. As most subjects rated their distress as extremely low, a data-driven approach would not identify highly distressed subjects. For example, a median split merely would have contrasted two groups of subjects with low as opposed to very low distress. It is of note that a slightly lower score, of ''6,'' generated similar results.

With this dichotomous approach, every participant had a score ranging from 0 to 10 on each of the five emotions, and accordingly was categorized into either the low- or high-scoring group for that emotion. Chi-square tests were used to examine the effects of gender (male, female) and diagnosis (anxious, non-anxious) on high and low levels of distress between anxious and non-anxious children and adolescents. In addition, five multi-analyses of variance (MANOVAs) were used, with demographic (age, IQ, and SES) and anxiety indices (SCARED-C, SCARED-P, PARS and trait anxiety) as the dependent variables, and the fMRI distress scales divided into low and high as the independent factors. To control for multiple comparisons, we restricted our analysis to emotions that yielded a significant omnibus MANOVA.

The analysis includes data from participants who completed the scan regardless of whether their data was useable. In addition, post-scan questionnaires were also collected from participants who aborted the scan.

Results

Spearman correlations between anxiety indices and the five fMRI distress scales across all children and adolescents are presented in Table 2. Overall, the relationship between anxiety and fMRI-related distress was weak. However, given the large sample size, significant correlations emerged. Correlations between all anxiety indices and fear during the scan were low (all $rs < 0.295$, $ps < 0.05$). Significant correlations were also found between trait anxiety and ratings of boredom, grumpiness, and happiness. Subjects with higher scores on trait anxiety reported to be more bored and grumpy and less happy during the scan. It is of note that all correlations were low (all $rs < 0.289$).

Group differences in high and low emotional distress post-scan ratings are presented in Table 3. As evident, very few subjects ($n = 10$) reported being very afraid during the fMRI scan, based on the >7 criteria. No differences in fear were found between boys and girls, $X^2_{(1)} = 0.44$, $p > 0.05$, or between anxious and non-anxious children and adolescents, $X^2_{(1)} = 1.49$, $p > 0.05$. Similarly, no gender (boys, girls) or diagnosis (patients, healthy) effects were found for the other emotions.

Table 2. Spearman Correlation Between Anxiety Indices and the Self-Reported Scales

	Afraid	*Bored*	*Grumpy*	*Happy*	*Tired*
SCARED-C	0.294**	0.114	0.134	−0.100	0.087
SCARED-P	0.195*	0.030	0.096	−0.087	0.003
PARS	0.112	−0.152	0.043	−0.119	−0.121
Trait anxiety	0.289**	0.140*	0.283**	−0.230**	0.110

* < 0.05; ** < 0.001.

SCARED-C/P, Screen for Child Anxiety Related Emotional Disorders Child/Parent; PARS, Pediatric Anxiety Rating Scale.

The omnibus MANOVAs revealed significant differences for those with high and low fMRI-related distress for each of the following emotions: Afraid, $F(6, 162) = 2.21$, $p < 0.05$; bored, $F(6, 162) = 3.20$, $p < 0.01$; grumpy, $F(6, 162) = 2.99$, $p < 0.01$; and happy, $F(6, 159) = 3.44$, $p < 0.01$. Participants with high levels of fear during the scan were younger than those with low levels of fear, $F(1, 167) = 5.41$, $p < 0.05$. However, only 10 subjects (~4%) reported high levels of fear during the scan. Participants with high levels of boredom during the scan were older $F(1, 167) = 8.57$, $p < 0.01$, and scored higher on the SCARED-C, $F(1, 167) = 4.96$, $p < 0.05$, than their counterparts with low levels of boredom. Participants with high levels of grumpiness had higher SES scores than those with low levels of grumpiness, $F(1, 167) = 11.05$, $p < 0.01$. Finally, participants with high levels of happiness during the scan were younger, $F(1, 164) = 10.01$, $p < 0.01$ and reported being less anxious as indicated in lower SCARED-C scores $F(1, 164) = 3.92$, $p < 0.05$, and trait anxiety scores $F(1, 164) = 5.23$, $p < 0.05$, than those with low levels of happiness. None of the demographic or anxiety measures predicted tiredness.

Discussion

The current study investigated psychological reactions to an fMRI scan among children and adolescents with and without anxiety disorders, as well as among healthy adults. The vast majority of participants tolerated the MRI well, and no significant differences in distress were observed across the three groups. These data suggest that healthy adults are less happy during scanning than healthy children or adolescents.

Several significant differences were observed between children and adolescents with high and low levels of fear, boredom, grumpiness and happiness. Age effects were observed for fear, boredom, and happiness. Highly fearful and highly happy subjects were younger than those with low levels of fear and happiness. These two results seem contradictory at first. However it is important to note that only 10 subjects were highly fearful, whereas the highly happy group was composed of 78 subjects. Age differences were also observed for boredom, with younger children reporting to be less bored than their older counterparts. Some anxiety-related differences were observed for those with high levels of boredom and happiness. Subjects who were less happy and more bored during the scan tended to have higher levels of trait anxiety. Finally, subjects with high levels of grumpiness during the scan had a higher SES background than those with low levels of grumpiness.

Table 3. Frequencies, Means and (Standard Deviations) for Groups High and Low on Self-Reported Scales

	Afraid		*Bored*		*Grumpy*		*Happy*		*Tired*	
	Low	*High*	*Low*	*High*	*Low*	*High*	*Low*	*High*	*Low*	*High*
Males	107	6	101	66	160	7	116	50	90	76
Females	110	4	112	76	166	22	132	54	79	107
Patients	85	2	66	51	105	12	86	30	52	64
Healthy	132	8	147	91	221	17	162	74	117	119
Age	13.02 (2.83) $n = 217$	11.01 (2.00) $n = 10$	12.62 (2.82) $n = 146$	13.50 (2.77) $n = 81$	12.87 (2.81) $n = 212$	13.93 (2.93) $n = 15$	13.46 (2.76) $n = 146$	11.99 (2.69) $n = 78$	12.61 (2.83) $n = 115$	13.31 (2.77) $n = 109$
IQ	111.79 (12.43) $n = 215$	106 (7.72) $n = 10$	112.12 (12.46) $n = 144$	110.49 (12.04) $n = 81$	111.92 (12.42) $n = 210$	106.13 (9.34) $n = 15$	110.74 (11.86) $n = 144$	112.58 (12.99) $n = 78$	113.65 (12.66) $n = 114$	108.99 (11.42) $n = 108$
SES	41.10 (18.57) $n = 191$	34.00 (11.06) $n = 10$	40.46 (19.79) $n = 127$	41.24 (15.59) $n = 74$	39.68 (16.83) $n = 187$	54.93 (29.66) $n = 14$	41.05 (19.65) $n = 131$	39.81 (15.88) $n = 67$	38.56 (15.08) $n = 101$	42.77 (21.23) $n = 97$
SCARED-C	18.44 (13.79) $n = 194$	16.60 (9.69) $n = 10$	16.49 (11.38) $n = 130$	21.61 (16.41) $n = 74$	18.12 (13.13) $n = 190$	21.50 (19.36) $n = 14$	19.14 (14.17) $n = 135$	16.55 (12.56) $n = 66$	17.07 (12.58) $n = 100$	19.49 (14.66) $n = 101$
SCARED-P	14.35 (15.04) $n = 193$	15.49 (19.22) $n = 9$	13.73 (14.68) $n = 126$	15.51 (16.05) $n = 76$	14.70 (15.33) $n = 188$	10.57 (13.05) $n = 14$	15.46 (15.7) $n = 132$	12.28 (13.95) $n = 67$	14.89 (16.22) $n = 94$	13.95 (14.24) $n = 105$
PARS	14.31 (4.59) $n = 65$	17.00 (4.24) $n = 2$	14.83 (4.55) $n = 41$	13.69 (4.62) $n = 26$	14.33 (4.70) $n = 63$	15.25 (1.89) $n = 4$	14.26 (4.67) $n = 47$	14.68 (4.58) $n = 19$	15.06 (3.73) $n = 32$	13.74 (5.28) $n = 34$
Trait Anxiety	32.39 (9.07) $n = 183$	35.56 (6.98) $n = 9$	31.53 (8.17) $n = 125$	34.42 (10.15) $n = 67$	32.22 (8.81) $n = 181$	37.73 (10.66) $n = 11$	33.52 (9.29) $n = 126$	30.73 (8.24) $n = 63$	31.94 (8.80) $n = 93$	33.23 (9.25) $n = 96$

IQ, intelligence quotient; SES, socioeconomic status; SCARED-C/P, Screen for Child Anxiety Related Emotional Disorders Child/Parent; PARS, Pediatric Anxiety Rating Scale; High score ≥ 7.

The results suggest that, on average, MRI scans are associated with low levels of psychological distress among anxious and healthy children and adolescents, and, therefore, are tolerable and feasible in widespread use, if suitable clinical applications could be found. These results are in line with previous results indicating low levels of anxiety among general pediatric patients undergoing MRI scans for clinical reasons (Marshall et al. 1995). Undoubtedly, the training procedures used in the current study may have contributed to these findings. Most participants underwent training in a mock scanner, which allowed them to acclimate to the scanner environment. In addition, a clinician was present during scans to minimize the likelihood of any untoward reactions. Finally, subjects were equipped with devices that allowed them to communicate with the researcher during the scan. A positive scanning experience not only reduces attrition rates but also improves the quality of the imaging data acquired. Similar recommendations for preparing participants for an MRI scan and their ability to reduce anxiety has been reported by others (Quirk et al. 1989; Rosenberg et al. 1997; Davidson et al. 2003; Perlman 2012).

United States regulations limit non-therapeutic research that carries more than minimal risk (Wendler 2009). The current data are consistent with MRI being a minimal risk procedure, at least based on the psychological reactions to the procedure. These data might also be helpful to research teams working with families, as both parents and children typically are willing to participate in non-beneficial pediatric research, as long as risks are negligible (Wendler and Jenkins 2008).

Limitations

Some limitations of the present study should be mentioned. First, some participants aborted the MRI procedure, whereas others completed the entire scan. Similarly, the subjects included in the current sample are those who agreed to at least attempt to undergo an MRI scan at the time of consent. Further, some participants completed two tasks in one session; therefore, duration of the scan, and the attentional state of participants, may have varied. Unfortunately, data are not available to allow particular aspects of the procedures to be linked to the ratings reported here. Therefore, these data that are reported here apply generally to an fMRI study, rather than to specific fMRI manipulations. Second, measures were collected immediately after participants completed scanning but not during the scan. Therefore, conclusions apply to subjects' reactions upon finishing an fMRI study. Finally, self-reported answers may be biased, participants may be uncomfortable disclosing embarrassing details, and various biases, such as social desirability, may affect the results.

Conclusion

The current study suggests that fMRI scans are associated with relatively little psychological distress in healthy and anxious children and adolescents. These results suggest that even among vulnerable subjects, diagnosed with psychopathology, fMRI scanning does not appear to exacerbate their symptoms or to produce increased distress. Therefore, the emotional reaction to scanning procedures should not limit the use of fMRI in further research applications and also, potentially, in clinical applications.

Clinical Significance

This knowledge may increase the willingness of parents and children to undergo fMRI scanning in a research setting that does not have direct benefits for the participant. Moreover, continued research advances in this area will support understanding of the brain and its variations in mental illness. Ultimately, this may lead fMRI to generate clinically relevant tools.

Disclosures

No competing financial interests exist.

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