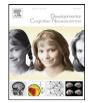
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Review Considerations for imaging the adolescent brain

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ABSTRACT

In recent years the number of functional neuroimaging studies on adolescence has exploded. These studies have led to important new insights about the relation between functional brain development and behavior. However, special consideration is warranted when working with adolescents. In this review, we review variables, including pubertal stage, sleep patterns and pregnancy, which are particularly relevant for developmental cognitive neuroscience studies involving adolescents. Consideration of the unique challenges associated with adolescence will help the growing field of developmental neuroimaging standardize procedures and will eventually facilitate interpretation across studies.

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1. Introduction

Adolescence is characterized by risk-taking (Steinberg, 2008), reward seeking (Galván, 2010) and particular

interest in social relationships (Pfeifer and Blakemore, 2012). Neuroimaging techniques, including structural magnetic resonance imaging (sMRI) and functional MRI (fMRI) have helped identify neurobiological changes that partially explain these behaviors. In particular, these studies have helped illustrate three main points that are relevant to understanding adolescent behavior: (1) in some domains (e.g. reward processing), there is a non-linear change in neurodevelopmental trajectories, with



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adolescents showing heightened or dampened brain activation compared to children and adults (Galván, 2012); (2) regulatory regions, such as the prefrontal cortex, lag behind regions implicated in affective processing, such as the amygdala and striatal regions (Somerville and Casey, 2010); and (3) contextual factors, such as peer influence and emotion, influence neural functioning in adolescence (Chein et al., 2011; Richards et al., in press). However, there is still much to learn about the adolescent brain and disparities across studies that remain to be resolved (e.g. Galván, 2010).

Because the field and the number of studies on adolescent brain development are growing at such a rapid rate (Blakemore, 2011), it is important to review areas for improvement. The goal of this paper is to review important variables to consider when using neuroimaging to study the adolescent brain. We begin by providing a rationale for studying neurobiological development during this developmental period, highlight some issues that are specific to adolescents (as compared to children and adults), and provide some suggestions for acquiring high-quality data from this population. We close by presenting preliminary data suggesting that, across development, scanner-related anxiety can be reduced by implementation of subtle practices. Overall, our goal is to provide an overview of approaches commonly implemented by pediatric neuroimagers. We hope this review will be helpful to those who are relatively unfamiliar with adolescent neuroimaging and also to launch a conversation between those of us who are already scanning adolescents to arrive at a consensus of best practices.

A number of reviews have described conceptual and methodological issues associated with pediatric neuroimaging. These issues include adequate ways to address age-related differences in hemodynamics, vasculature, neural structure and variance in behavioral abilities/performance (Poldrack et al., 2002; Kotsoni et al., 2006; O'Shaughnessy et al., 2008; Church et al., 2010; Luna et al., 2010; Poldrack, 2010; see Samanez-Larkin and D'Esposito, 2008 for a review). Practical considerations when scanning prepubertal children, including how to restrict head motion, minimize attrition and anxiety, and increase participant compliance, have also been reviewed quite extensively (Burgund et al., 2002; Poldrack et al., 2002; Davidson et al., 2003; Kang et al., 2003; Wilke et al., 2003; Kotsoni et al., 2006; O'Shaughnessy et al., 2008; Thomason, 2009). We will not reiterate these issues here and instead focus on factors that may present novel challenges when working with adolescents.

1.1. The importance of understanding adolescent neurodevelopment

In recent years, interest in the adolescent brain has grown (Blakemore, 2011; Casey et al., 2008; Dahl, 2004; Galván, 2010; Galván et al., 2006; Giedd and Rapoport, 2010; Hare et al., 2005; Luna et al., 2001, 2010; Reyna and Dougherty, 2012; Sowell et al., 2003; Van Leijenhorst et al., 2010a, 2010b), reflecting the growing appreciation that there are considerable physical, behavioral, social, and neurological changes in the second decade of life. This developmental period thus provides an ideal model in which to study intriguing developmental questions.

By studying adolescent brain development we have the opportunity to address questions that cannot be answered with children and adult populations alone, including questions regarding developmental change and puberty. By including adolescents in neurodevelopmental studies, we can obtain a better snapshot of developmental change from childhood through adolescence and into adulthood. Thus, adolescents help 'fill in the gap' between childhood and adulthood to examine changes in system-level organization that accompany changes in an array of cognitive functions. For instance, our understanding of how the brain anatomically changes from child- to adulthood has been revolutionized by acquiring brain scans in participants from a broad age range using sMRI. Data from the NIMH longitudinal study, the largest study on anatomical brain development to date with over 800 scans from 387 participants ages 3-27 years, show that total cerebral volume follows an inverted U-shaped trajectory that peaks at age 10.5 in girls and 14.5 in boys (Lenroot et al., 2007). White matter volume, in contrast, generally increases throughout childhood and adolescence (Lenroot et al., 2007). This and other sMRI studies (Colby et al., 2011; Sowell et al., 2003) have demonstrated the utility of including a wide age range that spans adolescence. By taking this approach, Sowell et al. (Sowell et al., 1999, 2003) found that the most significant anatomical changes in the brain occur in frontostriatal circuitry, which is critically involved in affective processing; these findings served as an important point of departure for fMRI studies that examined reward and emotion systems.

The handful of published longitudinal fMRI studies show interesting changes around adolescence (Koolschijn et al., 2011; Pfeifer et al., 2011). In a 3-year longitudinal study, Koolschijn et al. (2011) tested participants, ages 8–27, while they performed a child-friendly rule switch task and received an fMRI scan. They found that change in brain function was most variable in children, compared to adults and adolescents and that task performance, rather than age, was a better predictor for change in brain function over time (Koolschijn et al., 2011). A separate longitudinal study showed that neural responses to affective facial displays changes considerably between late childhood (10 years) and early adolescence (13 years) (Pfeifer et al., 2011). Interestingly, their data suggest that increased activation in the ventral striatum correlates with decreased susceptibility to peer influence and risky behavior (Pfeifer et al., 2011). Despite the logistical challenges associated with longitudinal studies, both of these studies show promise in the utility of this approach and the coming years will undoubtedly see a wave of longitudinal studies.

Second, the study of adolescents presents an opportunity to probe the relationship between puberty and neurodevelopment. There is a wealth of evidence from nonhuman studies showing that the hormonal events of puberty exert significant effects on brain maturation and behavior (Spear, 2000; Sisk and Foster, 2004; Blakemore et al., 2010). The diverse stages of pubertal development in adolescence can be used to examine how hormonal changes influence brain development in humans. However, in order to appropriately study pubertal effects in human brain development, careful methodological procedures are warranted. This task will continue to be challenging until there are sufficient sample sizes and standardization across reporting modalities (for comprehensive reviews on this topic by experts in the field, see Dorn, 2006; Blakemore et al., 2010; Forbes and Dahl, 2010). Most importantly, studies that are designed to (a) explicitly disentangle puberty and age effects. (b) use accurate and reliable measures of puberty, and (c) are replicable (Blakemore et al., 2010) are necessary. Only a handful of neuroimaging studies have attempted to examine the role of puberty in brain development (Bava et al., 2011; Blakemore et al., 2010; Bramen et al., 2011; Forbes et al., 2010, 2011; Moore et al., 2012; Mueller et al., 2009; Neufang et al., 2009). Using sMRI, a recent study found positive associations between pubertal stage and grey matter volume in the amygdala (Neufang et al., 2009). A different group reported significant interactions between sex and puberty on brain volume: in boys, increasing pubertal stage was associated with larger volumes in right amygdala and hippocampus while the opposite was observed in girls (Bramen et al., 2011). In a recent fMRI study. Moore et al. (Moore et al., 2012) report that self-reported puberty was positively associated with activation in the amygdala, thalamus and visual cortex in response to affective faces. This finding is in contrast to previous findings showing less activation in the amygdala and ventrolateral prefrontal cortex when viewing emotional faces (Forbes et al., 2012) and in the ventral striatum during reward processing (Forbes et al., 2010) with increasing pubertal stage. Differences in how puberty was assessed (self-report and by a trained nurse in the former and latter study, respectively) may have contributed to these divergent results. Collectively, the dearth of studies on this topic and the conflicting results suggest that there are many opportunities for exploration of this important question. At the very least, reporting pubertal stage for descriptive purposes is warranted.

Third, adolescent participants provide the possibility of probing more sophisticated questions about the relationship between changing social roles and neurodevelopment. Adolescence constitutes a period of significant changes in social roles and identity (Choudhury, 2010). As such, studies with adolescent participants can be used to examine how the progression from dependence to autonomy is subserved by changes in brain function. Last, adolescence is a developmental period in which there is an increase in onset of psychiatric disorders (Paus et al., 2008). Converging evidence suggest that changes in underlying neural systems, particularly those involved in processing emotional or affectively-charged information and in behavioral regulation, contribute to this phenomenon (Paus et al., 2008). A better understanding of brain development in both typically developing and clinical populations could provide opportunities for treatment or prevention (see Nelson et al., 2005 for a review on this topic). In the current review we do not discuss the important factors that must be considered when scanning clinical populations but refer the reader to an informative review on this topic (Kotsoni et al., 2006).

2. Adolescent-specific challenges in developmental neuroscience

2.1. Defining adolescence

A significant challenge associated with adolescent participants is how best to define adolescence (Luna et al., 2010). Adolescence is often defined as the transition form childhood to adulthood, roughly corresponding to the second decade of life (Spear, 2000; Steinberg and Morris, 2001; Dahl, 2004), starting with the onset of puberty (Dahl, 2004). However, this definition is influenced by age, sexual maturation, puberty level, and grade in school (Blakemore et al., 2010). As a consequence, the age range of individuals characterized as adolescents varies widely among fMRI studies. While some groups define adolescence as high-school aged individuals (Galván et al., 2006; Geier and Luna, 2009), other researchers include age-restricted groups as adolescents (Gunther Moor et al., 2010; Van Leijenhorst et al., 2010b). These methodological differences likely reflect differences in research goals, the complexity in defining developmental groups and to the inherent variability in this developmental period (Dorn et al., 2006). To help interpret results across different studies, it would be helpful if investigators made a concerted effort to report how the age groups were defined, and give a justification for the selected definition. Researchers might include discrete age groups with participants of a particular age, pubertal level, or factors that may contribute to socioemotional development, such as year in school (e.g., inclusion of only high school students, or grouping youth in primary school, middle school, and high school as children, early-mid adolescents, and late adolescents, respectively). A second approach is to treat age continuously and recruit participants who are between the ages of approximately 7-30 years old, which allows examination of developmental change without imposing investigator-biased age gaps. Alternatively, age groups could be defined based on performance on the task of interest (Luna et al., 2010) or on pubertal stage (e.g. Dorn et al., 2006 for review). While no one method is better than another, whichever one is implemented should be justified, and described in sufficient detail for replication purposes.

2.2. Sleep

From childhood to adolescence, there is a significant change in sleep and circadian function. In general, adolescents sleep less than children or adults (Gradisar et al., 2011), exhibit more variability in sleep patterns across the 7-day week, with school-night sleep shorter than sleep on weekends (Gradisar et al., 2010), and report greater daytime sleepiness (National Sleep Foundation, 2006). A U.S. national survey of 1602 adolescents found that 20% of adolescents reported at least one problem with daytime sleepiness every day, or almost every day (e.g., fell asleep in school, while doing homework, too sleepy in general, too sleepy for sports, overslept) (National Sleep Foundation, 2006). These sleep patterns, which may be associated with pubertal onset (Sadeh et al., 2009), influence adolescents' cognitive functioning and behavior during daytime hours (Wolfson and Carskadon, 1998). Sleep deprivation also has adverse consequences on affect (Talbot et al., 2010), which is particularly relevant to the numerous studies on affect processing and socio-emotional development conducted in adolescents. Although mounting evidence from fMRI studies suggests that sleep deprivation alters brain function in adults during numerous cognitive operations, including reward processing and value computation (Benedict et al., 2012; Gujar et al., 2010, 2011; Libedinsky et al., 2011; Venkatraman et al., 2007, 2011), resting state (De Havas et al., 2012; Gujar et al., 2010), directed attention (Chee et al., 2011; Jackson et al., 2011), and emotion processing (Chuah et al., 2010; Sterpenich et al., 2009; Yoo et al., 2007), surprisingly few studies have examined how decreased sleep during adolescence influences brain function. One adolescent sleep study found that during reward processing, brain activation is diminished following a night of poor sleep (Holm et al., 2009) and is influenced by a single nucleotide polymorphism in a circadian-related gene (PER2) (Forbes et al., 2012). Preliminary work has also suggested that sleep-restricted adolescents require more neural activation to maintain accurate performance on a working memory task than well-rested peers (Beebe et al., 2009). These studies underscore the need to document and study the effects of sleep on neurodevelopment. Sleep is an understudied area in developmental cognitive neuroscience that undoubtedly has a significant influence on adolescent brain function. As such, collecting information about sleep quality and duration from adolescents may shed insight into neuroimaging results and interpretations.

2.3. Pregnancy

There is currently no known risk to a developing fetus of scanning at 4T or less and no known mechanism of potential risk under normal MRI operating procedures (Nagayama et al., 2002; De Wilde et al., 2005). Nonetheless, the possibility that risks may be discovered in the future cannot be ruled out. Based on Federal protection regulations, pregnant females are not knowingly scanned for research purposes unless the pregnant mother and/or fetus are the subject of the research question. Thus, the general policy in many neuroimaging centers is to screen participants for pregnancy and to exclude anyone who is or may be pregnant. This procedure poses a particular challenge when the participants are adolescents under age 18 because of confidentiality concerns and privacy conflicts that may arise between adolescents and parents. Below, we outline some current practices regarding pregnancy as noted by the NIMH and provided by investigators across the U.S. in personal communication with AG. We recognize that variations in state confidentiality laws as well as different perspectives on teenage pregnancy preclude generalizing approaches to pregnancy screening. Nonetheless, this topic is absent from the literature and warrants attention.

A variety of approaches are implemented across institutions to screen for and exclude pregnant participants. As noted in the "MRI Research Safety and Ethics: Points to Consider" Report (2005), sponsored by the NIMH Council Workgroup on MRI Research Practices, there are no standard guidelines across institutions regarding pregnancy screening: 'Some sites simply note, during the consent/assent process, that the individual should not participate if there is a possibility she may be pregnant. Other sites use questions that include the date of the last menstrual period and/or whether there is any chance the potential subject might be pregnant. Still others use pregnancy tests for all females who have begun menstruation and are not yet post-menopausal. Pregnancy testing eliminates the possibility of scanning a female who is unknowingly pregnant. However, this approach potentially poses a disclosure and confidentiality issue when the potential participant is an adolescent. For example, having a parent first learn of an adolescent's sexual activity and/or pregnancy during the consent or screening process may be harmful for the adolescent girl and her family; further, sensitivity to cultural factors is warranted in these circumstances.'

Investigators at different institutions handle this potential dilemma in different ways, often based on institution-specific IRB requirements. To minimize the risks of placing underage females in a potentially problematic situation at the time of testing, one approach is to inform potential participants, at the time of recruitment, that there will be a pregnancy test should she choose to enroll in the study. This information allows the participant to decline participation without providing specific reasons for doing so. Some investigators screen the minor privately and explicitly state in the consent and assent forms that parents will not be informed of test results to protect the minor's confidentiality; others disclose the information to parents. As noted in the NIMH Report (2005), 'Sites testing for pregnancy should consider in advance how participants and/or parents will be informed of results, and whether there are personnel on site who are adequately trained to provide counseling. Such considerations should be discussed with the local IRB(s) in advance.' However, implementation of these procedures will vary by state. For instance, some states (e.g. California), parents do not have the right to access medical records regarding their child's pregnancy in some cases, raising another issue/complication of this procedure: 'Irrespective of who consented for the care, a health care provider is not permitted to share information or records regarding the prevention or treatment of a minor's pregnancy with a parent or legal guardian without the minor's written authorization. Cal. Civil Code 56.10(a), 56.11(c); Cal. Health & Safety Code 123110(a), 123115(a)(1).

As an additional precaution, we and others note in our consent and assent forms, under the "Potential Risks" section, that the requirement of a urine pregnancy test and its result may be considered to be a risk, especially with minor volunteers. At the initial phone screening and during the consent process, we make clear that the results will only be shared with the minor, and that learning of a positive result from these tests may be a risk. We will also inform them that we will provide a medical or psychological referral if needed. Last, we give participants who learn of their pregnancy through our screening test the option to remain in the testing area for what would have been the duration of the experiment to preclude parents from asking why she was excluded from the study (*Note*: This approach needs to be heeded with caution as it may lead to unintended consequences.) While these privacy issues are specific to adolescent girls, other sensitive subjects such as drug and alcohol use are applicable for all adolescents.

3. Recommendations

Thus far we have reviewed issues that may bias neuroimaging data in adolescent samples. In the remainder of the paper, we suggest strategies to ensure high quality data collection that have proven successful in our own laboratory (summarized in Table 1). The guidelines that follow are specific to fMRI but can be applied to other types of methods with youth, including electroencephalogram (EEG), eye-tracking and behavioral studies.

3.1. Preparation

Previous studies have shown that the more information a participant has about upcoming (medical) procedures, the less anxiety they experience about that procedure (Mahajan et al., 1998; Gursky et al., 2010). In Table 1, we list procedures that have proven effective in our lab to prepare participants. First, we review consent and assent forms and MR screening forms carefully with participants and parents when they first visit the lab to ensure that both participants and parents understand what taking part in the study will involve. We also place significant importance on building rapport with the adolescent. For instance, participants visit our lab twice and during both visits, they interact with the same study team (e.g. RAs, graduate students). At the first visit, we obtain consent, introduce the mock scanner and administer questionnaires and an IQ test. The second visit is strictly reserved for the scan, which helps preclude subject burden and fatigue.

Another helpful tip is to avoid relying on the parent for information, as s/he may be a less reliable source of information than the adolescent. For example, parent-report Tanner ratings (Tanner and Whitehouse, 1976) may be less accurate than teen self-report ratings (Blakemore et al., 2010), and parents might not be aware of body piercings, sexual activity and drug- or alcohol use. Building trust, ensuring our commitment to confidentiality to the adolescent (even between the teen and his/her parent) and being explicit about study procedures is, in our experience, critical for successful data collection.

3.2. Sensitization to MRI scanner

Mock scanners are effective in improving participants' ability to lie still and optimize data quality in children (Poldrack et al., 2002; de Amorim e Silva et al., 2006; Kotsoni et al., 2006; de Bie et al., 2010). An MRI simulator looks like a real MR scanner but does not have a magnetic field, which facilitates demonstration of study procedures to participants and parents. Little is known about its effectiveness in adolescence, and whether or not one is used is not always clearly reported (but see Eatough et al., 2009). We would recommend that when a mock scan is available, older adolescents should be given the same opportunity to experience it as children. Sufficient time should be reserved to allow for flexibility and to tailor the experience to the needs of the participant and parent. In our lab, participants and their parents are shown a mock scanner as well as pictures of the real MRI scanner, and are played the sounds the different scans sequences (e.g. EPI, DTI) will make. Participants are told how long they will be in the scanner, and we explain that the MRI scanner is a big magnet that we use to take pictures of their brain. To ensure they understand the importance of staying still, we explain that the scanner is analogous to a regular camera: when a picture is taken of a moving object with a regular camera, the resulting image is blurry. Similarly, if s/he moves during the scan, the pictures we take of her/his brain will be blurry. We also explain that if they move their head more than a few millimeters, we may not be able to use their pictures and that it is very important for them to help us get good results by trying to keep as still as possible. In addition, we explain that because the scanner is a magnet it may attract metal and that it is very important that no metal enters the room. This information is also sent to participants and their parents in an email.

3.3. Adolescent-friendly fMRI tasks and incentives

Acquiring meaningful data rests entirely on ensuring that participants comprehend, and are engaged in, the fMRI tasks they are asked to perform. Therefore, it is imperative that researchers implement tasks that are motivating to participants. Creating tasks with stimuli that are interesting to adolescents (e.g. faces) and/or that they are familiar with (e.g. creating tasks that look like a video game) (Galván, 2010), rather than implementing tasks that were originally designed for use with adult populations (Bjork et al., 2004) is a good first step. Other suggestions include making the task as straightforward as possible without multiple conditions and rules that the adolescent needs to hold in working memory. For instance, the monetary incentive delay (MID) task requires participants to remember the meaning of each of seven cues (Knutson et al., 2001), which is reasonable for adult participants but probably more challenging for children and adolescents. Using the MID task, Bjork et al. (Bjork et al., 2010, 2004) report that adolescents in their studies do not exhibit increased mesolimbic activation, findings that are divergent from other studies on reward processing (Ernst et al., 2005; Galván, 2010; Geier and Luna, 2009; Van Leijenhorst et al., 2010b). Bjork et al. (2010) note that these differences may have arisen because the MID requires "unusual vigilance" and attentional capacity, is not very entertaining, and uses relatively mundane visual stimuli (as compared to other incentive tasks that used pirate cartoons (Galván et al., 2006) and slot-machine wheels (Van Leijenhorst et al., 2010b; Bjork et al., 2010).

While it is challenging to create tasks that do not become boring or tedious throughout the experiment, choosing age-appropriate forms of compensation is another way to help motivate participants (Schlund et al., 2011). In most fMRI studies, researchers use rewards to encourage motivation and maintain task compliance.

Table 1

Suggestions for working with adolescent participants.

Participant preparation:

- 1. Direct questions at the adolescent, not the parent.
- 2. Explain the goals of the experiment is (e.g. "the brain grows as you grow and we want to study it. The MRI scanner helps us take pictures of your brain").
- 3. Avoid using negative language, such as referring to the scanner as big, dark, and scary. Instead focus on the positive (e.g. "your participation is helpful to research", "we want you to have fun while you are in the lab with us", "you get to see your brain").
- 4. Sensitize participants with a mock scanner.
- 5. Explain why keeping still is important and what exactly that means (e.g. no head nodding).
- 6. Explain to participant what will be happening when and why (give an overview of the whole session, the step-by-step procedures, and the duration of each step to minimize anxiety).
- 7. Be clear about what you expect from the participant (e.g. "your job will be to keep your head still and play the games/watch a movie").
- 8. If a pregnancy/drug test is a component of the protocol, administer it in private, away from parents/guardians. Remind the adolescent that all pregnancy test results will remain confidential.

Data collection:

- 1. Allow ample time to explain/practice the task before the participant enters the scanner.
- 2. When positioning the participant in the scanner explain the procedures. Remind them that they will be spoken to through a microphone from the main control room.
- 3. Ensure that participants are always engaged/entertained (e.g. play video from the moment they enter the scanner room).
- 4. Speak to the participant between each scan acquisition. Give positive feedback on their effort and remind them to keep their head still.
- 5. If possible, break scans up into shorter runs with time in between to talk to participant. Do not make separate runs too long.
- 6. Limit the amount of time in scanner. While 1.5 h may yield good enough data in adults, this is usually too long for children/teens.

Data reporting:

- 1. The criteria used to determine age range/age distribution.
- 2. The definition of adolescence used for subject recruitment and the method(s) used to assess pubertal development.
- 3. The methods used to prepare participants for the scan (e.g. mock scan, practice task outside of scanner) as well as possible differences in the approach for different ages.
- 4. Report if parents/siblings/friends were present in the scanner room.
- 5. The methods used to minimize motion.
- 6. The mean and maximum motion for different age groups and the methods used to correct for it.
- 7. The scan duration (e.g. was the task part of a larger battery, were functional data collected first or at the end of 1.5 h scan?).

With younger children (Raschle et al., 2009) or special populations (e.g. drug using participants), researchers sometimes give small prizes (e.g. stickers, pens) or gift certificates, respectively, as rewards. However, monetary compensation, either as a standard amount or earned directly as a result of task performance, is perhaps the most commonly used reward. In an informative paper, Schlund et al. (2011) describe recent evidence suggesting that subtle manipulations in how money is awarded or earned can influence task compliance. They note that some rewards (such as a sticker or trinket), 'may fail to maintain task compliance [because the reward] does not have the capability to function as a reinforcer, which strengthens or makes a behavior more likely to occur (e.g., completing an fMRI task). Thus, while a subject may report that they 'like' or 'want' a preselected reward, it may simply not encourage or maintain a target behavior' (Schlund et al., 2011). They empirically test the efficacy of alternative approaches to help maintain motivation in child and adolescent participants and identify several useful tactics: (1) the use of preference assessments to determine which prizes/incentives are most attractive to each participant; (2) increasing reinforcement rates during the scan such that the participant earns a reward for each scanning run; and (3) presenting a 'visual road map' during the imaging session so that participants can keep track of their progress and earnings (Schlund et al., 2011). By implementing these approaches, they found significantly greater task compliance (e.g. completion of, and engagement, in fMRI tasks) compared to when participants received a

standard reward at the end of the experiment (Schlund et al., 2011).

Neural circuitry underlying motivation undergoes maturational changes during adolescence (Bjork et al., 2011; Ernst et al., 2011; Gladwin et al., 2011; Padmanabhan et al., 2011). It is thus unsurprising that when adolescent participants are motivated by incentives they find enticing, their performance during an experiment changes. The Luna Lab recently published data showing that both behavioral (Geier and Luna, in press) and neural responses (Padmanabhan et al., 2011) change in adolescents when they are motivated to perform a task. In the behavioral study, rather than simply informing the child, adolescent and adult participants that they would receive a set amount of money upon completion of the study, they were allowed to choose the type of gift card (e.g. specialty store versus music) they would earn: this simple manipulation yielded more engagement and better performance on an antisaccade task in adolescents than in conditions where they were not given the opportunity to select the reward (Geier and Luna, in press). Using fMRI, the same group recently showed that performance on an antisaccade task improved significantly (e.g. participants made less errors) on rewarded versus neutral (non-rewarded) trials and that this behavioral change was paralleled by increased activation in motivational neurocircuitry (i.e. ventral striatum) uniquely in the adolescent group but not in the children or adults (Padmanabhan et al., 2011). Collectively, these studies highlight the important role that motivation plays in obtaining meaningful data.

| Table 2 | |
|-----------------------------|----|
| Participant characteristics | 5. |

| I | | | | | |
|----------------|--------------|------------------------------|-------------------------|--|--|
| Age group | Age, M (SD) | Tanner stage, M (SD) | Ν | | |
| 8-12-year-old | 10.56 (1.30) | 1.5 (.76), pre/early puberty | N=14 (6 female) | | |
| 13-15-year-old | 14.29 (1.23) | 3.07 (.92), mid puberty | <i>N</i> =14 (7 female) | | |
| 16-18-year-old | 17.05 (.82) | 3.85 (.55), late puberty | N=13 (5 female) | | |
| 22-30-year-old | 25.51 (2.53) | 5 (0), post puberty | N=14 (6 female) | | |

3.4. Motion and anxiety in adolescence

The primary practical challenges associated with neuroimaging studies in developmental populations are related to reducing motion and anxiety. To date, most papers on pediatric neuroimaging emphasized the need to minimize motion and anxiety during MRI scanning in children (e.g. Poldrack et al., 2002; Davidson et al., 2003; Kotsoni et al., 2006). While most studies report more motion in children compared to adults, a few studies have also reported greater anxiety in children compared to adults during fMRI scanning (Rosenberg et al., 1997; Davidson et al., 2003). However, to our knowledge there is no empirical study examining motion and anxiety in adolescence. To test whether the recommendations mentioned above reduce motion and anxiety in adolescents, a controlled study in which different methods of preparation and different durations of scan sessions are used would be needed (see for example a study on the preparation of pediatric patients in a medical setting (Westra et al., 2011)). Unfortunately, this type of controlled study is not logistically practical.

We conducted a preliminary study to determine whether scanner-related anxiety differs across development. Fifty-five participants, ranging in age from 8 to 30 years, who took part in an fMRI study on decision-making in our lab (greater experimental detail in Van Leijenhorst, McGlennen, Galvan, in preparation) were asked to provide ratings (1=not nervous at all, 2=a little nervous, 3 = very nervous, and 4 = extremely nervous) about the MRI experience. The ratings were completed after the scan. Participants were categorized into four groups (see Table 2 for participant characteristics): a group of 8-12-year-olds, 13-15-year-olds, 16-18-year-olds, and 22-30-year-olds. We collected imaging data using a 3 T whole body Siemens Trio MR scanner with a 12-channel head-coil. Participants viewed a movie or computerized game through MRIcompatible video goggles. All scans started with a reference scan of approximately 2 min and were followed by two 7-min functional runs and collection of high-resolution structural images.

A One-way Analysis of Variance (ANOVA) was conducted to examine participants' rating of nervousness upon first seeing the scanner immediately before the fMRI experiment began. As expected, the ANOVA revealed less anxiety in older participants (F (3, 55)=3.52, p < .05); on average, 8–12 year olds (M=2.11, SD=.46), 13–15 year olds (M=2.00, SD=.21) and 16–18 year olds (M=1.77, SD=.23) rated feeling a little nervous before the scan, while 22–30 year olds (M=1.38, SD=.14) did not feel nervous at all. Post hoc Tukey tests revealed that the youngest participants were significantly more nervous than the oldest

participants. Most participants (62%) reported they no longer felt nervous as soon as they heard the researcher speak to them through the headphones, 28% reported their nervousness had disappeared before they started playing the games, and only 10% reported they felt nervous throughout the scan. The distribution of these answers did not differ significantly between the four age groups (χ^2 (6)=5.46, p > .05).

These preliminary findings indicate the importance of communicating with participants of all ages while they are in the scanner. In our lab, we break up the scan into short duration runs and talk to the participants between each scan. When speaking to participants we avoid negative language (e.g. "Are you doing OK in the machine", or words such as, "big", "dark" and "scan"); instead, we focus on giving them positive feedback (e.g. "you are doing a great job", "have fun"), tell them how long the next series of "pictures" will take, and remind them to keep still. While we did not collect data on positive experiences with the scan experience, most participants mentioned they thought it was fun to participate (see Thomason, 2009 for a discussion of this topic).

To test motion in our participants we examined maximum rotational and translational motion over the course of two 7-min functional runs in the same 55 participants described above. For some participants (N=15), a foam insert was placed on their forehead; others only had support on the sides of their head (grey circles, N=40). We did this to test differences in motion with and without additional support on the forehead. Maximum motion was low (<2.5 mm) in all directions for every participant, and no participants had to be excluded from the analyses due to excessive motion. Nevertheless, additional padding on the forehead nearly eliminated rotation movement, and reduced translation to less than 1 mm in participants of all ages, and age-related change was no longer significant (p > .05). This illustrates that a relatively small and non-invasive method can drastically improve the quality of acquired data.

4. Conclusions

Although the field of developmental cognitive neuroscience has made significant strides in understanding neurobiological changes during adolescence in recent years, there is still opportunity for growth in this area in terms of methodological refinement. To acquire meaningful and informative fMRI data, issues specific to adolescents must be addressed. We have focused on practical considerations that are particularly important when studying adolescents, including questions related to defining adolescence, pregnancy issues, sleep changes, and pubertal development, and have provided suggestions for how to reduce anxiety and motion in adolescents who participate in fMRI studies. We have suggested ways to address these issues and described procedures that we use in our lab to optimize participants' experience and performance while minimizing anxiety and motion (summarized in Table 1). We have found that the use of appropriate procedures increases the likelihood that high quality data can be obtained.

In addition to reporting information about the technical specifications of the scanner and software used to analyze the data when presenting research, sufficient detail about the preparation of participants, characteristics of the sample (e.g. age range and distribution, pubertal development) and descriptive factors (e.g. pubertal stage, sleep quality or problems) should be provided. This information will make findings more clear and informative, both within and across studies. While the issues discussed here are particularly important in fMRI studies that include youth, we believe neuroimaging research that examines other age groups or special populations can benefit as well. In sum, we hope this paper serves as a helpful reference for researchers interested in using neuroimaging methods to study the adolescent brain.

Conflict of interest

The authors report no conflicts of interest.

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