**Abstract**

Due to its noninvasive nature, good spatial resolution and other advantages functional magnetic resonance imaging (fMRI) has become a tool of choice for investigating the brain mechanisms underlying psychological phenomena. Functional MRI studies have elicited substantial media coverage and this has led to increased public interest in neuroimaging. Having in mind enormous potential of this method as well as potential risks it is of crucial importance to be aware of ethical and practical challenges when conducting fMRI research, especially with children and adolescents.

In this essay we selectively review issues regarding informed consent and child’s capacity to withdraw from the study, importance of incidental findings and the problem of motion during image acquisition. Strategies how to deal with those problems are also addressed.

**Keywords:** functional magnetic resonance imaging, informed consent, incidental findings, motion

**Introduction**

The field of ethics, also called moral philosophy, involves systematizing, defending, and recommending concepts of right and wrong
behavior. Cribb (2004) argued that ethics exist as a characteristic of humankind and that laws are inadequate to create good behaviour. Similarly Singer pointed out that ethics must be suited to the ‘rough-and-tumble of everyday life’ (Singer, 1993). Also valuable insights into evolutionary origins of human altruistic behaviour and human capacity for moral behaviour have been offered in recent years (de Waal, 2008).

Unfortunately, atrocities committed during Second World War stand as a painful reminder that humans have equal capacity for unethical behaviour and that basic principles for ethical research with humans need to be defined.

Beauchamp and Childress (2001) identified treating and protecting participants as autonomous agents, maximizing possible benefits, minimizing potential harms and justice as four key ethical principles that should govern research with humans. As noted by Hinton (2002), the same ethical dilemmas that are related to research with adults are present in research in children, only exponentially magnified. Also introduction of a new technique for diagnostic as well as research purposes stresses the importance of careful evaluation of potential risks that might be one of the consequences of its usage.

Since its invention in the early 1990s, there have been more than 12,000 articles published to the end of 2007 that mention fMRI in the abstract or title and this number is now growing by roughly 30–40 papers every week (Poldrack, 2008). Functional magnetic resonance imaging (fMRI) has become a tool of choice for investigating the brain mechanisms underlying psychological phenomena (Cacioppo and Decety, 2009). Noninvasive nature of fMRI, the fact that it allows continuous collection of data and enable us to look at the mind at work (as indexed by brain function) without the distortion from conscious control, advances in fMRI technique itself are just some of the reasons for increasing frequency of the fMRI use (Cacioppo, Bernstein and Nusbaum, 2008).

However, use of functional brain imaging techniques, especially fMRI present new ethical challenges of a practical nature (Farah, 2005; Illes and Racine, 2005). In this essay we would like to address some of the problems related to conducting of neuroimaging research with children, most notably issues regarding informed consent and child’s capacity to withdraw from the study, importance of incidental findings and the problem of motion during image acquisition.
Informed Consent and capacity to withdraw

Adequate information, voluntariness and capacity to understand information are three main elements of informed consent. However, children’s consent raises difficult questions. Respect for persons includes respect for autonomous decision-making but as highlighted by many researchers (Hinton, 2002) applying autonomy theory in the fullest sense when working with children is not an easy task. Child’s parents or guardians must give consent for child to participate in research. However, in order to ensure that child is treated respectfully written consent by the child should be obtained. Assent is defined as the concept of providing agreement to participate in research where full consent is not possible by virtue of copromise one of main elements f consent (Kuthler and Posada, 2004) and while the term consent has both legal and ethical implications, assent is based entirely on ethical concerns. While study by Burke, Abramovitch and Zlotkin (2005) showed that children as young as six years are able to understand difficult and complex concepts associated with participation in biomedical research if appropriate modules of information are created, Ondrusek et al. (1998) found that children under 9 years have little ability to understand the study to which they had assented. Study by Ondrusek et al. (1998) showed that children’s freedom to act on knowledge that it is permissible to withdraw from participation can be limited. Most children felt that their parents would react negatively to their decision to withdraw from the study and that researcher would be ‘dissappointed’or ‘sad’.

Functional MRI studies have elicited substantial media coverage (Racine i sar, 2005). This has led to increased public interest in neuroimaging and its enormous potential. However, one particular problem with the popularization of neuroimaging data is that these data seem to have disproportionately strong persuasive impact (Weisberg et al., 2008) and since many media stories tend to emphasize sensationalism over accuracy this can create false hopes in parents. Also statements like ‘fMRI knows your secrets’ or ‘How brain scans could invade your private life’ and insistence that fMRI technique itself is dangerous and unreliable may intimidate parents. As a consequence this can bias parents decision and influence them to either uncritically push their children to become participants in various studies or refuse to give consent for their child’s participation and therefore not act in child’s best interest.
Incidental findings

Discovery of any abnormality, usually on a structural MR image, in an asymptomatic individual who was scanned for non-medical reasons represent incidental finding. The rate of incidental findings can be surprisingly high, even in healthy populations and what brings this subject to the forefront is above mentioned expanding role of fMRI for neuroscience research. Illes et al. (2004) invited investigators who conducted MRI studies in the United States and abroad to participate in web-based survey which asked questions regarding knowledge and handling incidental findings. They found that eighty-two percent of investigators reported discovering incidental findings in their studies. Study by Katzman et al. (1999) reported that in their cohort of 1000 subjects incidence of findings was 18%, age range in this study was from 3 to 83 years with mean age of 30.6. Kim et al. (2002) reviewed MR imaging studies in a cohort of 225 neurologically healthy children (age range 1 month – 18 years) and detected abnormalities in twenty-one percent. Although incidence reported by these two studies is similar, in study by Katzman et al. (1999) 15.1% of the findings detected required no referral, 1.8% routine referral and 1.1% urgent referral while in study conducted by Kim et al. (2002) almost 10% of subjects required at least routine referral. This double dissociation between age and severity underscores importance of unexpected brain anomalies in healthy child subjects and also raises important ethical questions.

Total brain size does not increase significantly after age five (Durston et al. 2001), different brain regions follow different developmental time courses. For example, while white matter volume increases significantly during childhood and into the adulthood cortical grey matter exhibits decrease in volume across this age span. Male brain is 10% larger than female brain and most structures display this trend with amygdala being disproportionately smaller and caudate and hippocampus being bigger in females. Also it has been shown that children may recruit different brain regions or larger areas than adults to perform the same task (Casey et al., 1997) and that brain regions termed as “social brain” (Brothers, 1990) undergo structural development including synaptic reorganization during childhood and adolescence which is paralleled by functional changes and changes in behaviour related to social cognition (Blakemoore, 2008). This dynamic interplay of simultaneously occurring progressive and regressive
events, brain plasticity and potential resilience of child must be taken into account when interpreting incidental findings. Also labelling apparently healthy child as developmentally delayed or under the risk to develop some form of neurobehavioural disorder can seriously affect the way the child is raised.

The problem of motion during image acquisition

One of the most damaging problems for fMRI studies is head motion (Huettel, Song & McCarthy, 2009). Very small movements of the head, on a scale of less than a millimetre, can be a major source of error in fMRI analysis if not identified and treated correctly. The basic assumption when analysing the image intensity at each voxel is that identical region of the brain is sampled at every point in an experiment and obviously head motion renders this assumption incorrect by moving samples of other, nearby, brain regions in and out of the voxel being studied. The effects of head motion can be minimized during preprocessing by using motion correction whose goal is to adjust the series of images so that the brain is always in the same position. However, as noted by Huettel, Song and McCarthy (2009) it is more easily prevented than corrected. Most laboratories use head restrains. A bite-bar, mask systems that use moldable plastic to create a mask around subject’s head, vacuum-pack systems are just some of the most common forms of head restrains. Head motion is especially acute problem in studies involving child participants. Closed space, loud sound produced by the scanner, long experimental session and tiring tasks can contribute to child’s motion and head restrains used in adult participants can make child feel more anxious and increase the likelihood that it will end a session prematurely.

Conclusion and some recommendations

Although the problems we have tried to describe in this review are necessarily selective, and there are many others that are important and worth considering, they illustrate how challenging conducting research with children is. Most researchers being limited in the amount of time that they can spend with both parents and child may overlook important issues related to consent to participate in research. However, informing the child about
every detail related to the study prior to scanning session should be prerequisite for every study. Adequate preparation can decrease if not eliminate anxiety. Use of MRI simulator where scanner noises can be played for added realism can significantly reduce child’s anxiety during actual scanning session. Making tasks age-appropriate and more engaging, separating long sessions into several shorter ones, the use of video/audio programs are also ways of reducing possible discomfort and by doing that minimizing problem of head motion and ultimately obtaining good data. Also, researcher should carefully explain to child that it can withdraw from the experiment at any time and should also pay attention to any signs of anxiety and discomfort that child may exhibit. The problem of incidental findings will certainly remain a topic in years to come. Some guidelines of how to deal with this problem have been put forward. Illes et al. (2002) proposed a minimum standard for consenting subjects in fMRI protocols, adding new anatomical sequences has been suggested by Huettel, Song and McCarthy (2009). Possible benefits as well as further practical and ethical dilemmas (subject confidentiality, authorship, increased cost of scans which could make an already expensive technique cost-prohibitive) of introduction of expert physician readers into research team have been discussed by several authors (Illes et al., 2002; Brown and Hasso, 2008). However, as suggested by Huettel, Song and McCarthy (2009) it is likely that no consensus will emerge in close future.

Despite all these issues research with children is rewarding and offers valuable insight into development of brain structures and functions in typical individuals as well as in individuals with neurobehavioural disorders, the most powerful tool for achieving this is not fMRI or any other technique but intelligence, creativity and ethics of investigators. As John Cacioppo noted ‘Just because you’re imagining the brain doesn’t mean you can stop using your head’ (Cacioppo et al. 2003).

References


PRAKTIČNI I ETIČKI IZAZOVI KOD SPROVODENJA ISTRAŽIVANJA SA DECOM I ADOLESCENTIMA

Apstrakt

Zahvaljujući neinvazivnosti, dobroj spacijalnoj rezoluciji i brojnim drugim prednostima funkcionalna magnetna rezonanca (fMRI) je postala metod izbora u istraživanju kognitivnih funkcija. Neke od ovih studija su zaokupile medijsku paznju i dovele do interesovanja za ovu metodu. Uzimajući u obzir veliki potencijal ali i potencijalne rizike važno je biti svestan etičkih i praktičnih izazova koji su vezani za upotrebu ove metode u istaživanju, naročito kada su ciljna grupa deca i adolescenti.

U ovom članku razmotrićemo probleme vezane za pravo deteta na dobrovoljni pristanak da učestvuje u studiji i da se iz nje povuče, za neočekivane potencijalno patološke nalaze kod dobrovoljaca u istraživanju i za problem neželjenih pokreta u toku eksperimentalne sesije. Neki od načina na koji se ovi problemi mogu potencijalno prevazići će biti razmotreni.

Ključne reči: funkcionalna magnetna rezonanca, neočekivani nalazi, neželjeni pokreti