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SHORT COMMUNICATION

Obstetric patients' perspectives on functional magnetic neuroimaging research in pregnant women

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Abstract

Magnetic resonance neuroimaging (MRI) studies of healthy pregnant women could identify key mechanisms of spontaneous health behavior changes observed in expectant mothers as novel intervention targets, but are currently unprecedented. As balancing potential benefits of research with unknown risks, including participant perceptions of risk, is foundational to ethical conduct, we surveyed a convenience obstetric sample to understand pregnant women's perspectives on this issue. Respondents were 76 pregnant women (modal age of 30–39 years; 64% multiparous) presenting for obstetric care from April to June 2016 at privately and publicly funded clinics at an urban academic medical center in the Midwestern USA. Following a written description about functional magnetic resonance neuroimaging (fMRI) and its known and unknown risks, women were queried on their willingness to participate in a hypothetical study involving fMRI during pregnancy, and specific concerns about doing so, if hesitant or unwilling. Willingness to participate was "yes" (28.4%, $n = 21$), "maybe" (28.4%, $n = 21$), and "no" (43.2%, $n = 32$). Among those responding "maybe" or "no" ($n = 53$, 73.6%), 11 women (20.7%) articulated concern about the fetus. Other concerns expressed were time commitment ($n = 11$, 20.7%) and discomfort being in an MRI machine ($n = 4$; 7.5%). Pregnant women may be open to participating in research involving MRI provided concerns about fetal health, time, and personal comfort are addressed.

Keywords Pregnancy · Plasticity · fMRI · Neuroimaging · Ethics · Survey study

Introduction

In the context of the urgent need to develop more effective and durable treatments for substance use disorders (Volkow 2014), it is ironic that *pregnancy exerts a more robust* (*temporary*) *protective effect on women's drug use than any intervention to date*, *independent of psychosocial and familial factors* (Kendler et al. 2017), *including intentions to raise the affected child* (Massey et al. 2011; Massey et al. 2012). Yet, due in part to the relative paucity of studies involving pregnant women, it remains unclear why.

Increased plasticity of the maternal brain (Sonuga-Barke 2017), putatively in preparation for caregiving, is supported by neuroimaging studies of mothers in the early postpartum period (Kim et al. 2010; Rutherford et al. 2017), and a recent within-individual design comparing pre- and post-pregnancy magnetic neuroimaging (MRI) scans (Hoekzema et al. 2017). Elucidating how changes in the expectant brain lead to long-observed positive health behavior changes among pregnant women (Crozier et al. 2009) could uncover novel targets for interventions aimed at changing health-related behaviors (Massey and Wisner 2018). The proportion of preventable morbidity and mortality caused by health-related behaviors in the USA (i.e., unhealthy diet, inactivity, and smoking/drug use) provides reasonable justification for studying the expectant brain (Massey et al. 2017).

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An important barrier, however, is the lack of certainty regarding the safety of high-resolution neuroimaging technologies for pregnant women and fetuses. Functional MRI (fMRI), for example, is a non-invasive technique for brain imaging developed in the 1990s (Voos and Pelphrey 2013) used to detect changes in blood oxygenation in different neuroanatomical areas during the execution of tasks designed to mimic real-life events. Attempts to link structure with function using fMRI have led to inferential models of brain function and impairment when healthy and diseased populations are compared. While cheaper and more portable modalities for neuroimaging such as electroencephalography (EEG) can provide similar information with excellent temporal resolution, spatial resolution is far superior with MRI. Non-contrast MRIs are routinely used for diagnostic purposes, including in fetuses (Griffiths et al. 2016). While there is no evidence that MRI during pregnancy is associated with adverse effects to the mother or fetus following over 20 years of routine use (Ray et al. 2016), fMRI has not been used for research studies on healthy pregnant women due to ethical concerns (Copel et al. 2016).

An equally important ethical issue concerns the *perception* of fMRI by pregnant women in the context of this uncertainty. Perception of risk by research subjects, and emotional reactions related to these perceptions, is always an important consideration in research involving human subjects. This is especially critical for populations who are historically underrepresented in clinical research due to distrust (Corbie-Smith et al. 1999). For example, Smith et al. (2007) found that African American women were reticent to participate in research due to concerns that research is biased to benefit White populations (Smith et al. 2007). Such perceptions can be an important barrier to the inclusion of representative samples, and must be adequately considered and addressed.

In this study, we surveyed a convenience sample of obstetric patients on their willingness to undergo an fMRI in a hypothetical research study and queried their specific concerns about doing so. We hypothesized that concern about safety to the fetus would be the overwhelming barrier to participation, and that African American women would express less willingness to participate compared to women from other racial groups.

Methods

Participants were 76 English-literate adult (age ≥ 18 years) pregnant women who completed anonymous questionnaires distributed to all new patients by staff at four obstetric clinics serving both privately and publicly insured patients at a large Midwestern academic medical center. The present data were collected from April to June 2016 as part of a larger survey on the prevalence of prenatal smoking and were thus collected following questions about demographic information and cigarette use. Potential participants were informed in writing that the questionnaire was part of a research study and that declining participation would not affect their access to care in any way. A written lay language description about fMRI (including the absence of evidence for risk but lack of absolute certainty about its safety in pregnancy) was provided (see Fig. 1) and followed by the questions:

> If you were compensated (paid) for your time and inconvenience for participating in a study that involved getting a brain fMRI during pregnancy, would you participate?
> If you answered "No," what are your concerns or objections about participating?
> Is there anything that would change your mind about participating?
> If you answered "Maybe – I need more information," what types of information would help you make this decision?

Completed questionnaires were returned to clinic staff and securely stored until collection by the research team. The study was exempt from formal review by the Institutional Review Board of Northwestern University. A two-sided chi-square test ($\alpha = 0.05$) was employed to assess differences in responses by race. Percentages were calculated for participants' willingness (yes, no, maybe), any narrative responses, and completed narrative responses using IBM SPSS Statistics Version 23.0. All percentages were tabulated using the number of respondents for each question.

Results

Nearly two thirds of women were 30–39 years of age (63.9%, $n = 46$) and the majority were multiparous (64.4%, $n = 47$). Racial characteristics were White ($n = 32$, 43.2%), Black/African American ($n = 30$, 40.5%), Asian ($n = 7$, 9.5%), Native Hawaiian/Other Pacific Islander ($n = 1$, 1.4%), and Other ($n = 4$, 5.4%). Eight women (13.1%) identified as Hispanic/Latina. Over half of participants ($n = 42$, 56.8%) responded "yes" or "maybe" regarding willingness to participate. Among women who responded "no" or "maybe" ($n = 53$, 73.6%), 35 (66.0%) provided narrative responses. Concern for the baby ($n = 11$; 31.4% of all narrative responses) and time commitment ($n = 11$, 31.4%) were the most commonly endorsed concerns, followed by general disinterest in the study ($n = 6$, 17.1%). Four participants cited discomfort with being inside an MRI machine. We did not find a

Fig. 1 Information about fMRI presented to survey participants

What is MRI and fMRI?
Magnetic resonance imaging, also called MRI, is a way of creating a detailed image of body tissues such as the brain or other organs using a strong magnet. Functional MRI, or fMRI, is a way to determine which areas in the brain are most active – this method is considered safe for use during pregnancy. In fact, fMRI is increasingly being used to study brain activity in the unborn child (the fetus) in research studies.

How can brain fMRI be used to improve the health of pregnant women and their children?
Many researchers suspect that the brain changes in important ways during pregnancy, but exactly how is still unclear. Using brain fMRI in pregnant women could help scientists understand how and why pregnant women experience new and different emotions during pregnancy.

What does fMRI of the brain involve?
A brain fMRI involves laying still for 15 – 45 minutes while the machine produces scans of your brain. You will be given headphones to listen to music since the machine can be loud. You would be required to remove any metal jewelry for this test. You cannot have an MRI if you have any implanted metal in your body.

significant difference in willingness among African American/Black women, relative to others ($p = 0.62$, $\chi^2 = 0.948$). Further details are shown in Table 1.

Discussion

This is the first study to our knowledge on pregnant women's perspectives on the use of fMRI in research studies of pregnant women. The majority of women surveyed (56.8%; $n = 42$) responded that they would participate, or would consider participating. "Concern about the baby" was cited among about a third of hesitant (maybe or no) respondents as hypothesized, though time commitment was a comparable concern. Concern about fetal health was articulated more frequently by women who responded "maybe," than by those who responded "no" (33 versus 12.5%, respectively), suggesting that additional information about safety might increase willingness. We expected that African American women would be less willing than others, particularly for a research study that lacked historical precedence, but did not find evidence to support this. Results in this small sample should be considered preliminary, may have been influenced by selection bias, and may be generalizable only to patients seeking care at a large academic medical center. Additionally, we do not have any information about concerns among women responding "no" or "maybe" who did not provide a narrative explanation.

Table 1 Willingness and concerns about hypothetical fMRI research study, total sample and by race

	Total $N = 74$	Black/African American $n = 29$	White $n = 32$	Asian $n = 6$	Other* $n = 7$
Willingness					
Yes	21 (28.4%)	10 (34.5%)	8 (25.0%)	0 (0%)	3 (42.9%)
No	32 (43.2%)	11 (37.9%)	16 (50.0%)	4 (66.7%)	1 (14.2%)
Maybe	21 (28.4%)	8 (27.6%)	8 (25.0%)	2 (33.3%)	3 (42.9%)
Provided any narrative response to why unwilling (no or maybe)	35 (66.0%)	11 (57.9%)	19 (79.2%)	5 (83.3%)	0 (0%)
Responses					
Time required	11 (31.4%)	2 (18.2%)	6 (31.6%)	3 (60.0%)	0 (0%)
Concern for the baby	11 (31.4%)	2 (18.2%)	7 (36.8%)	2 (40.0%)	0 (0%)
Not interested	6 (17.1%)	3 (27.3%)	3 (15.8%)	0 (0%)	0 (0%)
Discomfort about being in MRI	4 (12.1%)	2 (18.2%)	2 (10.5%)	0 (0%)	0 (0%)

*Includes Native Hawaiian/Other Pacific Islander ($n = 1$), as well as women who selected "other" ($n = 4$) or chose not to answer the question ($n = 2$)

In summary, considering the prevalence and magnitude of positive health behavior changes observed among expectant mothers (Kendler et al. 2017; Solomon and Quinn 2004), combined with the need for more effective interventions on health behavior change (Riddle 2015), we recommend further research on the feasibility of fMRI research in healthy pregnant women. Maternal behavior is the most proximal (and modifiable) determinant of a child's rearing environment, beginning at conception. In this way, research on pregnant women may be viewed as one of the best investments in disease prevention.

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Compliance with ethical standards

Conflict of interest The Department of Psychiatry at Northwestern University receives contractual fees for Dr. Wisner's consultation to Quinn Emanuel Urquhart and Sullivan, LLP (New York City), who represents Pfizer Pharmaceutical Company. Authors Newmark, Zaydlin, Yang, Kuchenrither, and Massey have no conflicts of interest to report.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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