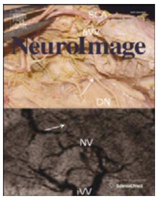
NeuroImage 82 (2013) 671–676

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Review

The ethics of secondary data analysis: Considering the application of Belmont principles to the sharing of neuroimaging data

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ARTICLE INFO

Article history:
Accepted 14 February 2013
Available online 4 March 2013

ABSTRACT

The sharing of data is essential to increasing the speed of scientific discovery and maximizing the value of public investment in scientific research. However, the sharing of human neuroimaging data poses unique ethical concerns. We outline how data sharing relates to the Belmont principles of respect-for-persons, justice, and beneficence. Whereas regulators of human subjects research often view data sharing solely in terms of potential risks to subjects, we argue that the principles of human subject research require an analysis of both risks and benefits, and that such an analysis suggests that researchers may have a positive duty to share data in order to maximize the contribution that individual participants have made.

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Introduction

The sharing of data has become important across many different fields of science, and in some cases (such as molecular biology and genomics) has radically transformed the pace of scientific progress. It has long been hoped that the sharing of neuroimaging data could provide a similar benefit to the field of cognitive neuroscience (cf. Poline and Poldrack, 2012; Van Horn and Gazzaniga, 2012). However, the sharing of human neuroimaging data poses potential ethical issues that are not encountered when sharing data from non-human samples. Researchers have unique responsibilities to ensure that subjects are protected, including by following the principles of respect of persons, justice, and beneficence. Researchers also have a responsibility to use data to produce "knowledge, products, and procedures to improve human health" (National Institutes of Health, 2003). The core argument of this article is that sharing data for secondary data analysis aligns with the Belmont principles that underlie the protection of human subjects. In this paper we will outline some of the potential

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http://dx.doi.org/10.1016/j.neuroimage.2013.02.040

ethical issues that can arise in the context of secondary analysis of human subject data. We will provide some context for currently proposed changes to regulations that researchers must follow, then lay out some basic principles that underlie human subject protection, and discuss how each of these interacts with data sharing and secondary data analysis. To provide support for the public trust, researchers have an obligation to share research data with other scientists; human subject ethics do not conflict with this obligation but rather provide added support for it.

In this paper, we will focus on the sharing of data from nonclinical studies, which are those in which subjects are individuals who are not receiving treatment from any personnel associated with the research or from that institution. That is, these research subjects are not also patients of the researcher. Data collected in the context of treatment are subject to more restrictions than data collected solely for research, such as the U.S. Health Insurance Portability and Accountability Act (HIPAA) (42 USC §, 1320d-2) or the U.S. Patient Safety and Quality Improvement Act of, 2005 (Pub.L. 109–41, 119 Stat. 424–434), as well as FDA regulations (21 C.F.R. 50, 56, 312 and 812).

The 2011 ANPRM and the principles of human subject research

In 2011, the US Office of Human Research Protections (OHRP) released an Advanced Notice of Proposed Rule Making (ANPRM) outlining proposed changes in regulations on human subject research (OHRP, 2011a). This ANPRM was created to solicit opinions and information about potential changes in human subject regulations from the public at large, including IRB members, research administrators, and investigators. One of the areas of change is how the secondary use of biospecimens will be regulated and generally, the ANPRM treats using existing *data* and the use of existing *biospecimens* as one issue, implying the same regulatory controls would apply to both. OHRP has described the reforms to biospecimen research as "reforms would require written consent for research use of biospecimens, even those that have been stripped of identifiers" (OHRP, 2011b). Because the ANPRM links the use of previously collected data and the use of previously collected biospecimens, this should be of concern for any researcher who uses shared data. The official comment period for the ANPRM has closed, but the next step for OHRP will be releasing a draft of the potential revised rules in the form of a Notice of Proposed Rule Making which will again seek comments from the community of researchers that will be impacted. If and when this happens, it will provide another opportunity for researchers to ensure that a distinction is made between biospecimens and research data and to ensure that OHRP considers the ethical arguments in favor of increased data sharing and decreasing the administrative burden of doing so.

This paper relies on a set of fundamental concepts underlying human subject research, which were laid out in the Ethical Principles and Guidelines for the Protection of Human Subjects Research (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978), better known as the "Belmont Report". While the Belmont Report was specifically developed and used in the US, the principles it espouses are important ethical guidelines that reach beyond national boundaries.

The Belmont Report outlined three fundamental ethical principles for human subject research: justice (the equitable distribution of benefits and burdens of research), respect for persons (in which people should be able to make autonomous decisions and people with limited autonomy should be protected), and beneficence (the obligation to not only "do no harm" but to actively maximize benefits and minimize harms to subjects) (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978).

The tension between the doctrine of informed consent for participation (from the principle of respect for persons) and the need to minimize risk and increase the benefit of research (from the principle of beneficence) as well as the need for scientific validity and generalizability of results (from the principles of justice and beneficence) are at the heart of the changes requested in OHRP's 2011 ANPRM. The principle of respect for persons as applied to informed consent would seem to require that subjects be asked to consent to the future use of their data and that, without specific information about what that future use will entail, providing truly "informed" consent is not possible. However, the principles of beneficence and justice may lean towards a different conclusion; if researchers do not use the data they are given to extract the most knowledge possible, they risk requiring individuals to bear burdens of research without providing the maximum benefit. There is a natural tension between the three principles. Each should be explored and then balanced with the others when examining how they should be applied to a specific topic or question.

After first discussing the concept of the research/treatment divide, we introduce each of these principles and discuss their application in the context of data sharing and secondary data analysis.

The research/treatment divide and the responsibility of researchers

The research/treatment divide is also known as the "therapeutic misperception" or "therapeutic misconception." In a clinical setting, the subjects of research often have an established relationship with the institution or even the investigative team that is collecting the data. Without a clear delineation, it can be difficult for subjects to appreciate that the time and information they are providing to researchers will not benefit their specific care. Ethically, the subjects enrolled in clinical studies are more vulnerable to blurring the lines between what is research and what is treatment. These subjects may also have a hard time understanding that there is no or very minimal benefit for participating in an imaging study (Kirschen et al., 2006). The concept of the research/treatment divide is more apparent in the collection of data from patients or in a clinical setting, but the same principles apply in the nonclinical setting. In a nonclinical setting, it can still be difficult for subjects to overcome the idea of treatment (for example, in expecting brain abnormalities to be detected as part of research imaging) (Kirschen et al., 2006).

This divide can become important in understanding the subjects' perceptions of what happens to the information they provide. Subjects may inaccurately believe that fMRI scans become part of their permanent medical record, available for physician review either at the time of participation or later. Subjects may inappropriately believe that because health care data are generally protected at a very high standard that the research data will be protected and shared only at that level. Studies should be designed to consider the therapeutic misperception and to consider it at both the time of initial data collection. At the time of secondary data analysis, researchers should be confident that the research subjects allowed the type of analysis that the researchers are conducting.

While not something that is specifically outlined in the Belmont report, the concept of the research/treatment divide encompasses the special relationship that develops between even a non-medical or non-clinical researcher and the participant. When a person agrees to participate in a research study, he or she forms a "fiduciary relationship" with the researcher. A fiduciary relationship means that there is an unequal balance in knowledge or training between two people, thus requiring that one party put faith in the other to act in their best interest. In Grimes v. Kennedy Krieger Institute (2001), the highest state court of Maryland described this "special relationship" as existing between research subjects and researchers in the case where the researchers were not physicians and the research was expressly nontherapeutic. In that case, public health researchers measured the effectiveness of different levels of lead abatement in housing. The researchers collected children's blood samples to test for lead levels. Parents sued for a variety of causes, including that researchers had become aware of a hazardous condition during the analysis of the samples and the researchers did not report that condition to the parents. The