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ARTICLE

Incidental Findings from Deep Phenotyping Research in Psychiatry: Legal and Ethical Considerations

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Abstract

Substantial advancement in the diagnosis and treatment of psychiatric disorders may come from assembling diverse data streams from clinical notes, neuroimaging, genetics, and real-time digital footprints from smartphones and wearable devices. This is called "deep phenotyping" and often involves machine learning. We argue that incidental findings arising in deep phenotyping research have certain special, morally and legally salient features: They are specific, actionable, numerous, and probabilistic. We consider ethical and legal implications of these features and propose a practical ethics strategy for managing them.

Keywords: deep phenotyping; smart phones; ethics; incidental findings; psychiatry; machine learning

Over the past decade, researchers in psychiatry have begun to look for new, clinically useful insights by integrating clinical and biological data with the digital data generated by our nearly constant interactions with digital devices through advances in computer science. This is often referred to as "deep phenotyping" research in psychiatry, which integrates an individual's real-time digital footprint (*e.g.*, texts, GPS, and wearable data) with their biomedical data (*e.g.*, genetic, imaging, and other biomarkers) to discover clinically relevant patterns, usually with the aid of machine learning.

For example, researchers in academic medicine are using digital footprints, audio-visual information (*i.e.*, how a person moves, behaves, and speaks), clinical information, and cognitive information to search for robust predictors of mania and psychosis.[1] In the private sector, a company named MindStrong provides a virtual health platform where those with serious mental illness can receive care from psychiatrists and therapists through an app-based platform that also enables remote monitoring "through AI-powered digital biomarker technology that can track changes in mental health symptoms. More importantly, the technology can also trigger alerts to a member's clinical team when these markers indicate their mental health may be at risk of deteriorating, outside of a therapy or psychiatry session." MindStrong has an active research and development division trying to identify new clinically useful features of their data.[2]

Whether in academic medicine or in research and development of a private sector company, findings that are incidental to a study's objectives but also potentially of great importance to participants will inevitably arise in deep phenotyping research.

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The legal and ethical questions these incidental findings introduce are interesting and complex. We aim to point out special features of incidental findings in deep phenotyping research in psychiatry to help frame the developing discussion of their legal and ethical implications.

Consider three hypothetical cases below of individuals who enroll in a hypothetical deep phenotyping research study designed to identify factors affecting risk of substance use relapse or overdose:

A 51-year-old woman with alcohol use disorder (AUD) is 6 months into sobriety. She is intrigued to learn that the study algorithm will track her proximity to some of her known triggers for alcohol relapse (e.g., bars and liquor stores), and asks to be warned with a text message when nearby so she can take an alternative route. Should the researchers share that data?

A 26-year-old man with AUD is 2 years into sobriety. Three weeks into the study, he relapses. He begins arriving to work inebriated and loses his job. After the study is over, he realizes the researchers may have been able to see from his alcohol use surveys, disorganized text messages, GPS tracking, and sensor data that he may have been inebriated at work. He wishes someone had reached out to him before he lost his job. Should they have?

A 35-year-old man with severe opioid use disorder experiences a near-fatal overdose and is discharged from the hospital. Two weeks later, his smartphone GPS is in the same location as his last overdose, and his wearable detects that his respiratory rate has plummeted. Should researchers call emergency medical services?

These vignettes highlight several unique features of incidental findings in deep phenotyping research. They are *specific* because events like inebriation are contextualized by where, when, and how long. They are *actionable*, because the observations are trackable in real-time. They are *numerous*, because they multiply with each data-stream. They are *probabilistic*, because they are deduced from multiple observations and by evolving algorithms.

In this article, we highlight examples of legal and ethical considerations of these features, as much has already been written about incidental findings generally.[3,4,5]

Legal Considerations: Mandatory Reporting Statutes, Duty to Rescue, and Tort Law

The specificity enabled by cross-linking multiple data streams may lead to certain specific situations (e.g., impaired driver and perinatal substance use) that could cause researchers to wonder whether mandatory reporting statutes apply. For example, with respect to substance use disorders, 25 states in the United States require healthcare professionals to report suspected prenatal drug use, 8 states require doctors to test for prenatal drug exposure if they suspect drug use, 23 states consider substance use during pregnancy to be child abuse, and 3 consider it grounds for civil commitment[6]. However, such obligations in most states apply specifically to members of certain professions acting in their professional capacity. It would be unlikely that researchers—even physician-researchers—acting in a research capacity would be within their scope. One exception might be mandatory reporting of child abuse, as 18 states require all persons to report suspected child abuse or neglect, regardless of profession.

The actionability of real-time data, sometimes of serious and urgent events like overdose, might cause researchers to wonder whether they have legal duty to rescue or to aid. Although affirmative legal duties to rescue exist in other countries, no such duty exists in the United States, and as researchers are not traditionally considered fiduciaries, no legal obligation to act in the participant's best interests (i.e., by disclosing[7]) would arise from the researcher-participant relationship. However, if the researcher is also a participant's physician (which can and does occur with frequency in clinical research contexts), this analysis would become more complex as the physician-researcher would have a fiduciary duty to the participant, and depending on the situation, would have a duty to disclose relevant and significant incidental findings.

The specificity of the incidental findings could potentially be brought forward to support a cause of action under the tort of ordinary negligence if a participant could prove that (1) the researchers owed a duty to report, (2) that duty was breached, and (3) failure to report was the "but for" cause of the participant's injury. To determine whether there was a duty that was breached, courts would look at what the standard of care is. The success of such a claim would likely ultimately depend on whether there is a consensus on the prevailing professional standard of care for the disclosure of incidental findings. No such consensus currently exists in deep phenotyping, and such standards currently vary even in well-established fields like genomics. There would also likely be much jurisdictional variation.

Finally, the duty to report depends not just on the identity of the event but also on the identity of the person who has suspicion of the event. Thus, the closer this research comes to the clinic and the more the mandatory reporters become involved in the research, the more serious the question of mandatory reporting incidental findings will likely become.

Ethical Considerations: How Good a "Fit" Are Guidelines on Incidental Findings from Other Forms of Biomedical Research?

An emerging consensus from the fields of genomics and medical imaging is that at minimum researchers have an ethical obligation to disclose when the participant consents to disclosure and the disclosure "offers clear medical benefits."[8] If we accept that premise, we see that applying this ethical minimum to deep phenotyping is challenging.

First, a single deep phenotyping study would not only have all the potential findings of a genomics and medical imaging study, but also a multiplication with each additional data stream, making anticipation and full consideration of incidental findings during an informed consent conversation unrealistic. Moreover, machine learning algorithms raise the potential for truly unforeseeable findings.[9] Though researchers could follow the example of biobanking and seek a "broad consent"[10] to both foreseen and unforeseen findings, the question of which incidental findings then merit action would remain.

Second, a "clear medical benefit" is often specified in genomics as depending on both the certainty of the result and the actionability of the result. Working groups in genomics have recommended winnowing reportable incidental findings based on (1) the certainty of the result, (2) the actionability, and (3) the time available for a person to action.[11] As the vignettes here illustrate, however (1) certainty of incidental findings is difficult to determine *ad hoc*, as it may be dependent on the sensitivity and specificity of an algorithm which the study itself seeks to establish (and may even differ between individuals), (2) actionability would hardly narrow the list of reportable findings, and (3) there is a moving window of time available for action that is by definition enabled by any research program with real-time collection and analysis.

The Future of Incidental Findings in Deep Phenotyping

The challenge of any new technology is identifying how well it can be handled by existing legal and moral structures. For deep phenotyping, the specificity, actionability, number, and uncertainty of incidental findings merit tailored consideration.

One possibly useful approach in handling these features would be to directly involve participants in the decision of how to handle incidental findings. Participants could be given a menu of options to create "if-then" rules tailored to their needs (such as that envisioned by the participant in the first vignette to warn herself of approaching triggering locations) and decide whether to involve third parties like family or physicians. Rather than anticipating specific incidental findings, researchers could anticipate broader categories of incidental findings (e.g., indications of relapse, geographic triggers, and indications of emergency) and allow participants to decide upon which categories of incidental findings they are interested in and specify course cutoffs of certainty that would be meaningful to them. One practical advantage of this approach would be that it follows a structure

amenable to computer programing language, and thus could potentially be carried out with a higher degree of automaticity. One moral advantage would be that subjective calls about usefulness or desirability of types of information would be personalized and thus more likely to be accurate than if these calls were made by researchers themselves and applied uniformly across the entire study population. This would maximize both respect for autonomy and a consequentialist approach to benefit. It would also have the benefit of enabling a clear conversation about the possibility of mandatory reporting of incidental findings, should such a situation be determined to apply.

Our practical solution presupposes that there will be some types of incidental information that *should* be returned. Although a defense of the position that it would be seldom (if ever) acceptable to adopt policies of returning *no* incidental information is beyond the scope of this piece, we believe it to be a reasonable position. A number of principles have been cited in support of an ethical obligation to report incidental findings to research participants, including the principle of beneficence, respect for persons, the duty of rescue, reciprocity, and the partial-entrustment model.[12] In particular, under the duty of rescue, which "obligates an individual to act when presented with an opportunity to alleviate the serious plight of another with minimal burden to oneself," researchers might have an ethical obligation to return incidental findings "if the level of effort to report is minimal and the possible benefit to a participant is great."[13] It is worth observing that as the automaticity of reporting increases, the level of effort to report decreases, and thus the appropriate threshold for returning results might be expected to decrease as the field of deep phenotyping matures (and with it, the technology for detecting and returning these sorts of results). Of course, as deep phenotyping efforts mature, there may be cases where some incidental information, if shared, could undermine a study objective (for example, by revealing a study group to which a person belongs) and it will be important in future work to consider when design limits to the sharing of useful incidental information are justified.

Notes

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