



Return of Results in Pediatric Behavioral Prevention Research Involving Predictive Genetic Testing

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January 25, 2018

Case Example

Brody et al (*Pediatrics*, 2009)

- You are an African American mother living below the poverty line in rural Georgia
- Your child's school provides researchers with contact information for all 11 year old African American children
- You are contacted by the Center for Family Research to participate in a study
- The purpose of the study is to test whether a new parent education program called *The Strong African American Families Program* (SAAF)
 1. *Will increase the ability of African American mothers to communicate with their 11 year old child*
 2. *Reduce the possibility that their child will engage in high risk behaviors (drug use and sexual behavior) when they are 12 measured by the child's self-report*

Nature of Study

- You will be assigned to the SAAF or control group based on randomization based on your county
- If you are in the SAAF group, the program will last 7 weeks and is conducted at a community center with sessions for parents and for children.
- The success of the program will be assessed when the child is 12 years old
- You will be paid \$100 for the pre-test and \$100 post-test conducted in your home.

Participation Choice

- What are reasons you would or would not want to participate in this study?
- Would you expect the researchers to share the general results of the study with you (e.g. comparison between intervention and control group)?
- Would you expect researchers to share your child's self-reported risk behaviors with you?
- If the researcher explained that sharing that information might limit the honesty of the child's report, would you be OK with the researcher keeping that information confidential?

Genetic Susceptibility Follow-up Study

- You are told that the SAAF (compared to the control group) was found to increase family communication and lower initiation rates of risk behavior.
- You are asked to participate in a follow-up study when your child is 14 years of age
- The purpose of the study is to test whether:
 1. The effects of the SAAF continued between 12 – 14 year
 2. Your child's genetic makeup (5HTT: a specific gene associated with risk behaviors gathered through saliva) influenced whether or not participation in the SAAF or control group reduced his/her initiation of risk behaviors

Participation Choice

- Would you agree to have your child participate in this study? Would you feel differently if you were in the control or SAAF group?
- Would you expect or want to know your child's self-reported risk? His/her genotype results?

Study Results

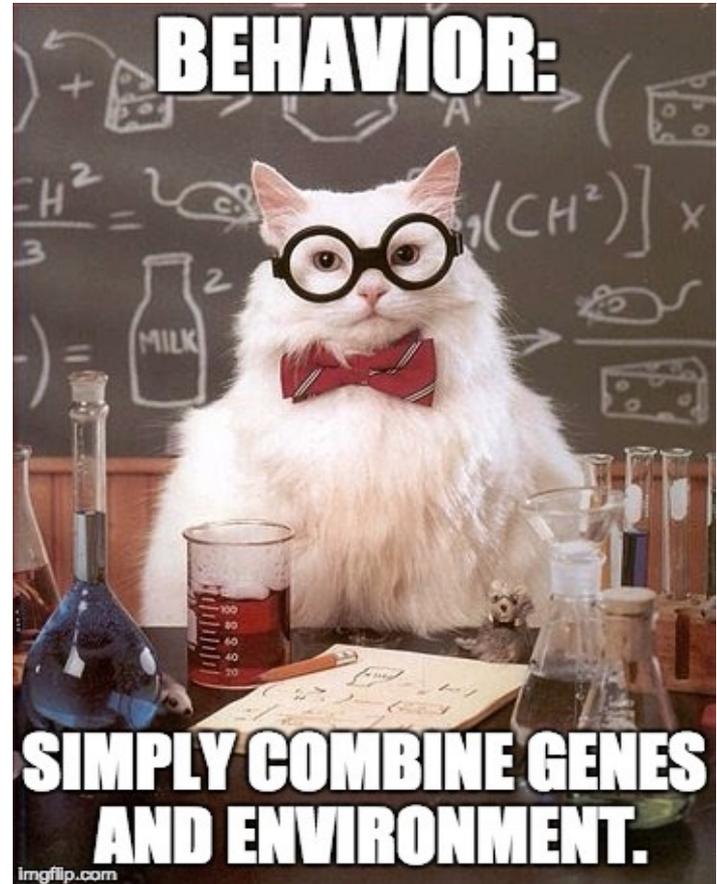
- Youth at “genetic risk” (e.g. carrying the 5HTT gene) in control condition reported more risk behaviors than youth at “genetic risk” in the SAAF condition *and youth in either condition without the 5HTT*
- How would you feel as a parent learning about these results?

Predictive Genetic Testing for Behavioral Problems: The New Frontier

- **Non-intervention studies:** Relative contribution of genes & environment on development of behavioral problems
- **Intervention studies:** Relative contribution of genes & environment on responsiveness to programs to prevent behavioral problems
- Studies are conducted at schools or after-school programs and often involve asymptomatic children

PGT: New Solutions to Preventing Old Problems?

- HTR2A gene [M] maternal education on academic problems (Keltikangas-Järvinen et al, 2010)
- 5-HTTLPR polymorphism [M] childhood abuse on adolescent depression (Pingault et al., 2013)
- BDNF gene [M] school intervention on conduct problems (Banducci et al., 2014)
- DRD4 repeat allele [M] family intervention on adolescent alcohol use (Cleaveland et al., 2015)



Genetic Bases of Behavioral Problems: What do We Know

Studies indicate behavioral problems....

- Derive from multiple genetic and non-genetic factors
- May be the result of 100s of different genes that independently influence the same behaviors
- Genetic effects account for only a small proportion of individual differences (heritability)
- Test results lack individual utility because currently gene-intervention effects are probabilistic

How Are Results Shared?

- **Directly** through individualized feedback to parents
- **Directly** through aggregated feedback to parents
- **Indirectly**, simply through assignment of child to intervention implemented in schools or community-based programs
- **Indirectly** through publication or media dissemination of research results

“Toddler’s Aggression Strongly Associated with Genetic Factors”

Science News



Lacourse et al (2014)
Psychological Medicine

Risks of Sharing Results: Genetic Determinism

- Asymptomatic children may be treated differently by parents, schools and practitioners
- Negative self-identification
- Misuse of genetic findings for psychiatric diagnosis, criminal justice decisions, educational placement
- Shift from educational, health or social policy solutions to individual or family responsibility



“Child’s Right to an Open Future”

Feinberg 1980

- Sharing may violate the child’s right to withhold information from others that may be detrimental to their self-interests
- Parents, school personnel and others have access to private information of which the participant him/herself is unaware
- Results can create an irreversible risk to child’s self-concept, social standing, educational or other opportunities

REMEMBER

In school-based prevention studies the child’s genetic “risk” may be *indirectly* shared simply through study inclusion

Sharing Results: Risk of Shifting Roles

Social-behavioral scientists *are not*
clinicians or genetic counselors

- There is no evidence based guidance for whether or how information should be shared with children
- Difficult to predict how parents will react to results shared
- Parents may have unrealistic expectations regarding the value of such information
- The probabilistic nature of genetic influences → sharing individual results → over or underestimation of risk

Sharing Results: Who Decides?

The science establishment has traditionally determined appropriate human subjects protections

- Societal trends toward transparency and self-determination rights in research, healthcare and consumerism
- As research moves out of the lab and into the community scientists & IRBs have less control over indirect dissemination and misconceptions

Informed Consent “Genetic Literacy”

Are guardians familiar with and can they apply information about the use of genetic data to make appropriate research participation decisions? (Fisher, 2017; Fisher & McCarthy, 2013)

Genetic literacy is necessary for parents to make an informed participation decision whether or not the researcher and IRB have decided the child’s individual genetic information will be shared

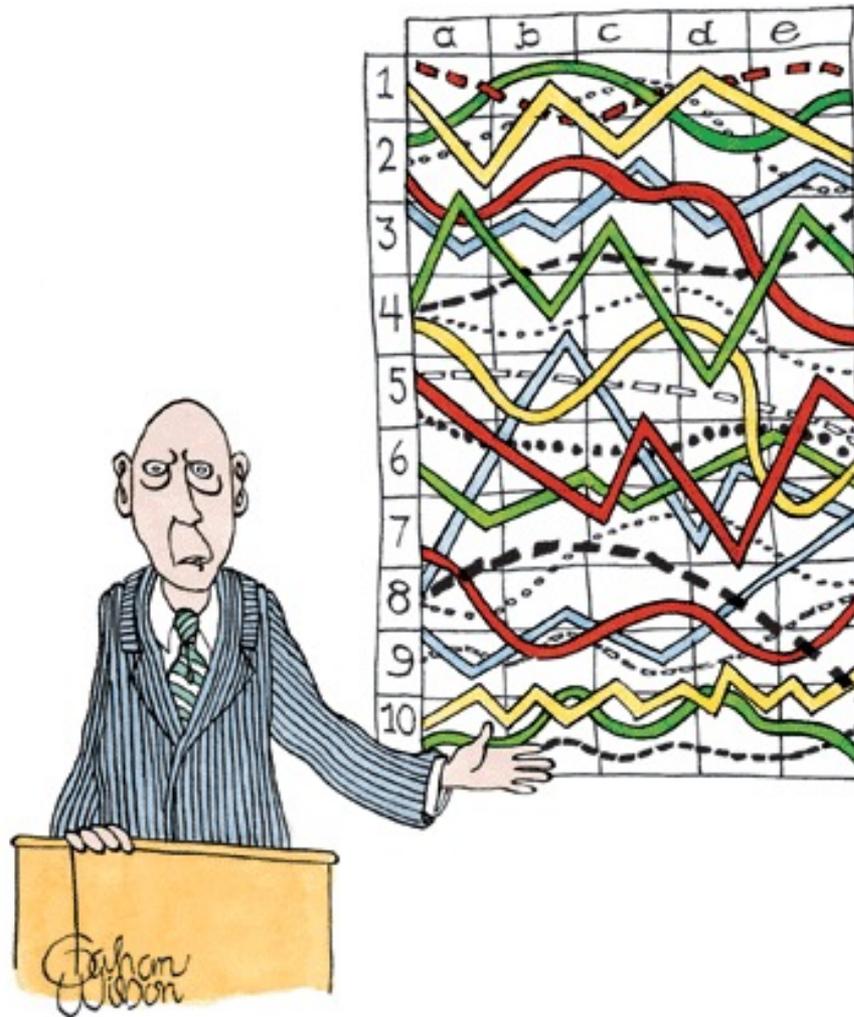
Informed Consent and Genetic Literacy

What Parents Need to Know

- Evidence supporting the role of genetic factors for both predicting risk and intervention responsiveness
- Multifactorial and probabilistic nature of genetic and environmental influences
- Genetic effects account for only a small proportion of individual differences (heritability)
- Lack of predictive ability for individual children

Informed Consent: Risks & Rights

- How genetic information may qualify or disqualify child from participation---including non-verification of paternity
- Possibility of incidental findings during genetic analysis--and if findings will be shared
- Risks of genetic determinism
- Clarification of role of researcher
- Availability of adequate genetic counseling
- Right to receive or not to receive results



"I'll pause for a moment so you can let this information sink in."

Sharing of Results: Research Ethics Questions

- Have sufficient efforts been made to ensure genetic literacy during consent?
- Is there evidence that sharing genetic information has predictive utility for individual children?
- If not shared directly, are there adequate protections against indirect sharing of results?
- Is debriefing and dissemination adequate to address individual needs or to reduce parental, school, or societal misconceptions?

BIG DATA, BROAD CONSENT AND INDIVIDUAL AND GROUP RIGHTS AND HARMS

Big Data and Broad Consent

Perceived Benefits of Big Data



Inclusion of Identifiable Biospecimens as Human Subjects



Ability of IRBs to waive consent for use of identifiable biospecimens



Broad Consent

What is Broad Consent?

§ __.116 (d)

In changes to Common Rule participants consent to:

- **Future** use of **identifiable** information/biospecimens
- For a range of **specified or unspecified future research**
- Subject to **a few content and/or process restrictions** overseen by an IRB.

Big Data & Broad Consent: The New Ethics Frontier

A prolonged life course of identifiable data use by researchers

- who were not the originator of the data,
- are not regulated by the original IRB,
- who are studying issues that may be far removed from the original research questions and
- who may not be subject to traditional oversight.

Criteria and Ethical Challenges for Broad Consent

Types of Future Research

§__.116 (d)2.

A *general* description of the

- **Types of future research that may be conducted** with identifiable info/biospecimens
- **Sufficient** such that a **reasonable person would expect** the type of future uses

What-If-Whom

§ __.116 d(3)

- **Type of data** that might be used in research,
- Whether **sharing** might occur
- **Types of institutions or researchers** that might conduct research with the IPI/IB;

Time Period

§ __.116 d(4)

For how long will the data be

- **Stored and maintained** (which could be indefinite) and
- **Used for research purposes** (which could be indefinite)

Disclosure of Future Use

§ __.116 d(5)

A statement that

- They will not be informed of the details of any future studies using their identifiable I/B
- They might have chosen not to consent to some of those specific research studies

Challenges for IRB Approval of Broad Consent Language

- What is “sufficient” information to make a decision regarding “types” of future research use?
- Who is the “reasonable person” and what type of information “would they expect”?
- What are the types of institutions and researchers permitted to use the data in the future?
- Should participants be given opportunity to list types of future research they would or would not give approval to?

Ethical Challenges for IRB Approval of Secondary Use of Data

How will investigator and IRB access the original broad consent?

Did the original broad consent provide “sufficient” information?”

What are criteria for determining secondary use is “consistent” with broad consent?

How does consistency relate to advances in privacy risks and protections?

Does the study meet the participant’s “reasonable expectations”

- For the purpose of study?
- For qualifications of institution or investigator?

Ethical Justification for Broad Consent

Scientific and social benefits of future big data research should be privileged over the burden of continually requiring consent....but

- Government regulates both big science and ethics oversight.
- **What happens when there is a blending of agendas?**



Assumptions of Science Establishment

- Knowledge gathering is a fundamental good
- The scientific method is objective and should be value free
- Scientists are not responsible for the potential goods and harms of how others may use data in the future



The Scientific Pluralism Fallacy

- Science is not conducted in a socio-political vacuum.
- Science goes where the money is and majority of research \$\$ controlled by the gov't or industry.
- Funding priorities (or their absence) driven by political or economic concerns of the majority
- Priorities may not reflect participant values or may produce policies disadvantageous to marginalized populations

Consent by Others

- Broad consent is consent for governance of the use of one's private information by others.



- This works when the “others” share participants’ values and are knowledgeable about and motivated to protect the participants best interests.
- How can IRBs fulfill that role?

If it can be studied, should it?

Genetic Research and Social Justice

The NIMH Violence Initiative

- Inner city youth with a genetic predisposition to violence (an older sibling with a criminal record) would receive biomedical psychiatric intervention to prevent future delinquency (Goodwin, 1992)

- To be of benefit, an “experiment should be such as to yield fruitful results for the good of society”

Nuremberg Code, 1946, Principle 2

Whose Benefit? Who Decides?

Method: 100 racially and economically diverse teens and parents participated in focus group discussions about use of genetic testing in research on behavioral problems involving ethnic minority youth

Funding: National Science Foundation #SBR 9710310; PI. C. B. Fisher

Reference: Fisher, C. B., & Wallace, S. A. (2000). Through the community looking glass: re-evaluating the ethical and policy implications of research on adolescent risk and psychopathology. *Ethics & Behavior*, 10, 99–118. PMID: 11841105.

Socio-Political Bias

- *They do “research in the school about [white] students who do good and about crimes they only talk about black people”*
- *“ “They know the reason why [there is violence]...ghettos...racism...and prejudices may still exist, but they don’t want to say that. They want to say it’s in their genes...to make a cover story.”*

Scientific Validity: Implicit Race-Based Inferences

- *I think it might be possible for it to be biological, but its not one race... look at white Hitler... and South Africa apartheid...Why don't they study white suburban serial killers or the KKK?"*
- *My Moms and Pops spoil me...and...I'll still be a bitch...I will still fight. Why? Because it's already in me. I guess it probably is genetic. Hey, I'm Puerto Rican, Black Dominican, Italian, and Cuban. You pick a race where it came from."*

Social Value vs. Social Harms

- Such research “promotes supremacy of the races...that one race is better than the other.”
- “So they take...an honor student...the kid’s been doing great and then you’ve got that violent gene and we’re going to start treating you for this gene problem when the problem is not there”
- “I think we’ve been duped to think that any of the results will be used to improve the African community...because too much has been used against us”

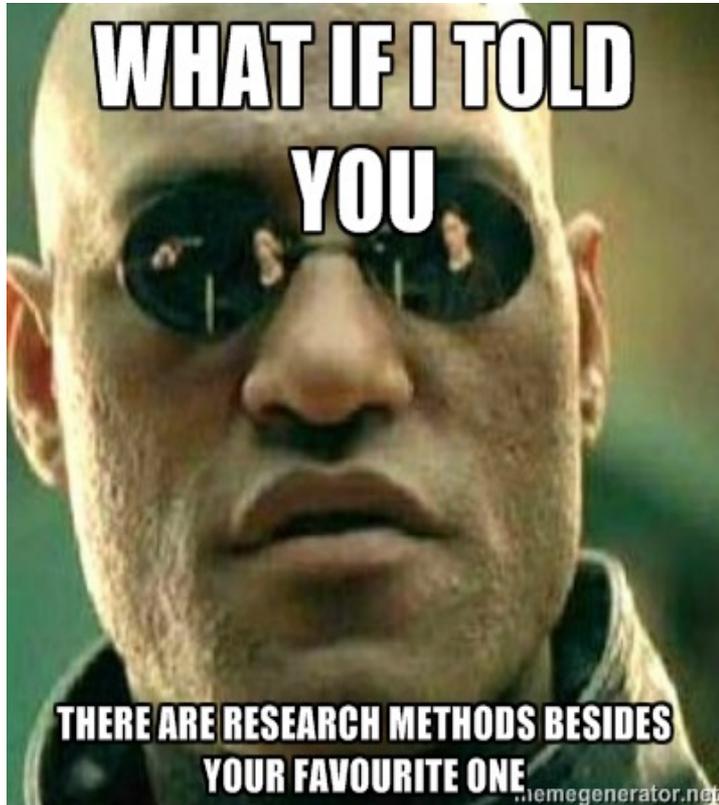
Will Research Contribute to Morally Sound Social Policies?

- Funding for genomic research is often driven by economic and political concerns of the majority
- These may have little to do with or are antithetical to the concerns and social circumstances of participant groups
- New “genetized” diseases may be created for behaviors resulting from social inequities
- Potential for genetic stereotyping → racial/ethnic segregated interventions

Sharing Results: Assessing Scientific & Social Value

- Is there sufficient evidence that genetic factors play a significant role in targeted behavioral problems?
- Is the design sufficient to adequately assess non-genetic factors influencing future behaviors?
- Is subject selection equitable, or based on convenience or social bias?
- Have investigators drawn on stakeholder opinion to ensure the research goals and human subjects protections reflect the values and merit the trust of those we ask to participate in research?

If it can be studied, should it?



"The key is Dr. Fisher, that when you...talk to your counterparts...ask yourselves what will others do with this research?"

No matter what role that you have played to make this happen, you could have the purist intention, but if it gets into the wrong hands then it becomes a weapon"

Thank You

