Fatal Fate in Monoamine Oxidase A: Examining the Conflict of Free Will and Genetic Determinism through the "Warrior Gene"

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Introduction

The rise of genetic testing has empowered individuals to know more about their physical bodies and their predilections for certain diseases or conditions. Services like 23andMe, which takes a DNA sample from users' saliva to determine the user's chances of possessing certain traits (anything from the chances of exhibiting restless leg syndrome to Parkinson's), have enabled the regular consumer to plan ahead to avoid unpleasant or potentially fatal surprises (23andMe). While this seems harmless for the most part, the realm of genetic screening becomes much more morally muddled when it crosses the line of personal use onto the legal docket. In 2006, a self-confessed murderer received 32 years in prison, a slap on the wrist compared to the usual punishment for murderers—life in prison or death row. One of the largest mitigating factors in the case was evidence that the murderer possessed the "warrior gene," a gene that inhibits serotonin breakdown, and seems more likely to provoke uncontrollable bouts of rage and addictive behavior. Unfortunately, the "warrior gene" is at best a misunderstood scientific fantasy, and at worst an instance of postmodern hubris. This paper will examine the current scientific literature on variants of the monoamine oxidase-A gene (MAOA) more popularly known as the warrior gene, its history of controversy, and the legal and ethical implications of discriminating between free will and genetic "predetermination."

"Warrior" Gene

The Warrior Gene is perhaps better described as a variation of one enzyme—monoamine oxidase A—of a family of enzymes (monoamine oxidases). Monoamine oxidases, as a family, break down various dietary amines and neurotransmitters like serotonin, dopamine, and norepinephrine vital for normal mood regulation (Chen et al, 2004). MAOA is a mitochondrial enzyme coded in the X-chromosome, closely linked to another monoamine oxidase, MAOB

(OMIM). Researchers have pinpointed multiple variations in the genetic code that can affect patients' psychological conditions to induce "warrior"-like aggression. One such variation in the MAOA gene appears in the 30bp variable number tandem repeat (VNTR) repeated 2, 3, 3.5, 4, or 5 times 1200 bp upstream of the actual MAOA sequence. Alleles with 3.5 or 4 VNTR's produce MAO 2-10 times more efficiently than those with 3 or 5 VNTR's, and those with the decreased levels of monoamine oxidase (this group of individuals with low levels of MAOA are referred to as MAOA-L) then exhibit unusually aggressive behavior when threatened or provoked (Sabol, 273). Guo et al conducted a longitudinal study of anti-social behavior in youth, and found a significant association between the rare 2 repeat VNTR polymorphism and serious delinquency (626). As MAOA is sex-linked, most individuals who are MAOA-L are men (Gade, 50). McDermott et al also point out another cohort study that observed the unusually aggressive behavior of a "Dutch family with a repeated incidence of violent criminal behavior among males across several generations…*[with] a missense mutation of a single nucleotide of the [MAOA] gene*…" (2119, emphasis added). As the aforementioned studies show, while there is no one specific polymorphism to blame for any atypical aggression, there is evidence for a connection between certain MAOA variants and aggressive, anti-social behavior.

It is wise, however, to temper the genetic findings of these controlled studies and the few available observational studies with the understanding that human behavior and development is much more complex than the order of a series of nucleotide bases. Ferguson et al make clear that "The present findings [of greater likelihood of exhibiting anti-social behavior and violence in abused youth who are also MAOA-L] add to the evidence suggesting that there is a stable [gene-environment] interaction involving MAOA, … adverse environmental and personal factors, and

antisocial behaviour across the life course. These analyses also demonstrate the utility of using multiple environmental/personal exposures to test [gene-environment] interactions." (123)

Regardless of whichever MAOA gene variation that MAOA-L patients possess, the literature suggests that the aggression implied in the "warrior gene" results from a combination of multiple factors: both genetic (coding sequences that produce low levels of monoamine oxidase A) and environmental (abuse as a young child). McDermott et al note that MAOA-L individuals display enhanced reactivity in the amygdala and inhibited activity in the regulatory prefrontal lobe which can result in anti-social, violent behavior (2119). This connection between MAOA-L and antagonistic behavior has largely ignored the developmental aspect of the behavioral problem, which has led to a series of highly controversial conflicts, to be discussed below.

History of Controversy

In 2006, Dr. Rod Lea made the highly controversial statement that Maori men were twice as likely to possess a "warrior gene" or an MAOA-L polymorphism which the Maori people to risk-taking activities like gambling and smoking. That same year, Davis Bradley Waldroup, Jr. shot, beat, stabbed, then attempted to rape his wife. His wife survived, but her friend who had accompanied her did not. In the controversial court hearing in 2009, a pivotal part of his defense relied on the mitigating factor of Waldroup, Jr.'s possessing a "warrior gene." Waldroup, Jr. received a reduced sentence of 32 years in prison that would allow the 35 year old to leave prison within his lifetime.

Critique of Maori "Warrior Gene"

Dr. Lea's claim relies for the most part on established literature that made some kind of connection between MAOA-L patients and anti-social behavior. However, he extends the

research by testing a sample of 46 Maori men (men with at least one Maori parent). Within this super-small sample, which Dr. Lea admits "places uncertainty around [the statistic]," he takes an even smaller subgroup of 17 Maori men who have 8 Maori great grandparents (to "reduce European admixture") to establish that the Maori ethnic group exhibits significantly higher rates than Caucasian males of displaying the 3-R VNTR polymorphism of the MAOA gene (Lea and Chambers, 3). This, to Dr. Lea, constitutes data significant enough to make the sweeping generalization that Maori men are twice as likely to exhibit aggressive, risk-taking behavior than Caucasian males. Dr. Lea and Dr. Chambers later submitted a followup paper after the media firestorm surrounding their statements, in which they make the point that there is an ethnic group with even more occurrences of the 3-repeat VNTR polymorphism than either Caucasian or Maori males—Chinese males (Lea and Chambers, 3). Interestingly, Lu et al, the researchers who found the abnormally high allele frequency of 3-R VNTR's in Chinese males, conclude "the MAOA gene does not play a major role in increasing susceptibility to alcoholism in Chinese men" (460). While there are controlled experiments that establish the connection between MAOA-L mice and aggression, as well as a few observational studies that note the co-occurrence of MAOA mutations and aggression, there is insufficient scientific knowledge regarding the complex interplay of genes, environment, and race to convincingly argue that one gene can overwhelmingly predispose one ethnic group to risk-taking behavior or "warrior-like" acts.

Genetic Determinism in the Courts

What happens when genetic determinism spills over from the realm of science into personal affairs? Into a justification of crime and rage? On October 13, 2006, Davis Bradley Waldroup, Jr. brutally assaulted his estranged wife, Penny Waldroup, who had brought their

children for a visit, along with a friend of hers, Leslie Bradshaw, for support. According to the testimonies provided by Ms. Waldroup and Mr. Waldroup, Ms. Waldroup did not wish to discuss their marital problems at the time, but Mr. Waldroup took Ms. Waldroup's car keys and threw them into the woods. As he got increasingly agitated, blaming Ms. Bradshaw for his marital problems, he fired the .22 caliber rifle he had brought with him multiple times, killing Ms. Bradshaw. Ms. Waldroup fled, but he shot her in the back, then cut her pinky; she attempted to flee again, but Mr. Waldroup proceeded to attack her with a shovel, and then a machete. Afterwards, he took her to the trailer where the children were and told them to say good bye to their mother. According to Ms. Waldroup's testimony, Mr. Waldroup then tried to make her shower, so he could rape her (State of Tennessee v. Davis Bradley Waldroup, Jr.). Mr. Waldroup denies that he tried to make her shower, and the Waldroups' oldest daughter states that Mr. Waldroup was planning to take Ms. Waldroup to get help. Mr. Waldroup claims that "his ears were ringing and his head was roaring and the next thing he knew, he had started firing the gun. He said he did not recall shooting Bradshaw but was certain he did." (Mr. Waldroup is audible on the police dispatch radio background, when he tells the officer "I murdered her.") (Polk News Online). He said he did not have much memory of the events that came afterward and that his memories were like still pictures. "I don't know why I snapped, I don't know why the level of violence, I just know I wanted her and loved my kids." (Polk News Online).

Part of the defense for Mr. Waldroup included testimony from forensic psychiatrist Dr. William Bernet. Mr. Waldroup was genetically screened and Dr. Bernet testified that the tests showed that Mr. Waldroup possessed the "warrior gene" and with such abnormal serotonin and neurotransmitter levels, Mr. Waldroup had only a limited capacity to engage in the reflection and judgment necessary to premeditate the crimes (Polk News Online). Dr. Bernet said, "We didn't

say these things made him become violent, but they certainly constituted a risk factor or a vulnerability" (Hagerty). This mitigating factor of possessing a high-risk gene that predisposed him to murdering his wife saved Mr. Waldroup from the death penalty. Instead of receiving a charge for first-degree murder, he was charged for attempted second-degree murder, voluntary manslaughter (a Class C felony with a range of jail time from only 3-6 years), and especially aggravated kidnapping. Dr. Bernet further stated that, "A person doesn't choose to have this particular gene or this particular genetic makeup. A person doesn't choose to be abused as a child. So I think that should be taken into consideration when we're talking about criminal responsibility" (Hagerty). In this case, there is less sensationalism, as Mr. Waldroup did face child abuse in a broken family, and he did possess a variation of the gene, which would make him MAOA-L. These two factors, one genetic and the other developmental, both of which are completely out of Mr. Waldroup's control, culminated in that fateful night on October 13, 2006, leading to an exploration in whether genetics is becoming a shield for criminals or a smarter, more just legal system.

The Ethics of Genetics in the Legal System

The legal system rests on the assumption that each individual has a free will, and is thus fully responsible for his or her actions. The laws provide the lines within which a free will can exercise its power. When an individual's free will is abridged, and with this abridged will commits a crime, then the legal system takes that into account in determining how much the individual must bear the burden of the crime. For instance, when one is physically threatened and told to kill another person, he is not held responsible for the act, as his free will is completely overridden and his options are reduced to suicide and murder. Instead, the person threatening the other and forcing him to kill is held responsible and punished. Similarly, if it is true that one's

genes can predispose an individual to uncontrollable acts of rage, then the legal system must take into account the fact that while the individual has a semblance of a choice in choosing to commit the murder or assault, it is under considerably different circumstances than an act committed by a genetically "normal" individual's free will. Unfortunately, the legal system cannot punish the individual's genes. The genes are an inseparable part of our identity and existence, which conflicts with the assumption that an individual is born *tabula rasa* (like a blank slate), free to create for himself his own identity.

In a postmodern view of identity, there are additional biological laws of genetics overlaid the social laws we have constructed for the community's welfare. Just as we cannot fully ensure that individuals do not get away with breaking a society's laws (like child abuse in the case of Mr. Waldroup), which may then damage another individual, we cannot ensure the genetic "normalcy" of every individual (for example, mental retardation, or, more relevant to this paper, the abnormally high levels of serotonin which inhibited Mr. Waldroup's normal decision making) to act as a fully rational agent with a free will. So where do we draw the line? At what point do we consider the individual free, beyond just his genes or the circumstances of his upbringing? Further, at what point can we say someone is bad and deserves punishment or that the accused is not responsible for factors out of his control and thus deserves reduced punishment or none at all? While the conception of a binarized form of justice is appealing, where evil is punished and righteousness preserved, genetic screening adds just another dimension to the complexity of man, who is neither fully good nor fully bad. As with most important questions, there is no right answer we can find; in this case, it must rely on more than just the incompetent buckets of "right" and "wrong," and more on individual human judgment, or the jury.

Contrary to popular belief that genetics will usher in a new era where only the evil go to prison and the innocents are protected, I believe that the entrance of genetics necessarily requires a new, refined understanding of justice as an entity that is not always fair, but rather an imperfect construct to maintain a semblance of order for the majority of its constituents. "Justice for all" becomes meaningless when there are multiple dimensions of right and wrong, and when nobody is fully wrong nor fully right.

This kind of uncertainty, however, does not sit well with a justice system that must mete out punishment and protect its constituents. Genes should not have the power to reduce the gravity of a crime, and genes should not protect perpetrators from the justice of punishment following a crime. I have no answer for whether Mr. Waldroup is evil, even at the time of his murder, and I certainly cannot know his state of mind during the time of his crime. However, I do believe that the legal system should provide a firm infrastructure of rules that support the safety of the majority of its citizens rather than protect the shreds of innocence that may lie in a guilty man's heart. As stated before, society cannot always prevent individuals from harming others, but when the perpetrator is caught, and found to have faced uncontrollable factors (like child abuse) that made him act as an abnormal agent in later life, then it is up to the legal system to find a way to try to fix the wrongs committed in the past by a perpetrator that went unpunished, and similarly deliver a punishment to the current perpetrator. To allow the current perpetrator to walk free (or nearly free) only ensures that he may victimize another and spur on a vicious cycle of crime engendering reactionary crimes in their own victims.

Conclusion

Certain MAOA gene polymorphisms have been shown to increase the probabilities of individuals exhibiting aggressive, violent behavior, especially if the individuals have been

brought up in a broken family with a history of child abuse. This correlation between a gene and aggression has led to a misnomer of the MAOA gene as the "Warrior gene," resulting in controversial (and dubious) racial profiling of Maori males as more aggressive/risk-taking, and also an unsatisfying resolution to a murder case. The controversies around the MAOA gene's use in trying to decipher social issues is a reflection of a deeper social sensitivity to a conception of free will in conflict with the modern discoveries of biological hardwiring, and perhaps the first of many more conflicts of genomics and ethics in the coming years of this rapidly changing world.

Works Cited

Chapman, Paul. “Violence Is Blamed on “Warrior Gene” in the Maoris.” Daily Telegraph (U.K.), Aug. 10, 2006.

Chen H, Pine DS, Ernst M, Gorodetsky E, Kasen S, Gordon K, Goldman D, Cohen P. “The MAOA gene predicts happiness in women”. Prog Neuropsychopharmacol Psychiatry. 2013 Jan 10;40:122-5. doi: 10.1016/j.pnpbp.2012.07.018. Epub 2012 Aug 4. PubMed PMID: 22885141.

Chen K., Holschneider D. P., Wu W., Rebrin I., Shih J. C. “A spontaneous point mutation produces monoamine oxidase A/B knock-out mice with greatly elevated monoamines and anxiety-like behavior.” J. Biol. Chem. 279: 39645-39652, 2004.

Fergusson DM, Boden JM, Horwood LJ, Miller A, Kennedy MA. “Moderating role of the MAOA genotype in antisocial behaviour.” Br J Psychiatry. 2012 Feb; 200(2):116-23. doi: 10.1192/bjp.bp.111.093328. PubMed PMID: 22297589; PubMed Central PMCID: PMC3269651.

Gade R, Muhleman D, Blake H, MacMurray J, Johnson P, Verde R, Saucier G, Comings DE. “Correlation of length of VNTR alleles at the X-linked MAOA gene and phenotypic effect in Tourette syndrome and drug abuse.” Mol Psychiatry. 1998 Jan;3(1):50-60. PubMed PMID: 9491813.

Guo G., Ou X.-M., Roettger M., Shih J. C. “The VNTR 2 repeat in MAOA and delinquent behavior in adolescence and young adulthood: associations and MAOA promoter activity.” Europ. J. Hum. Genet. 16: 626-634, 2008.

Hagerty, Barbara Bradley. "Can Your Genes Make You Murder?" NPR. NPR, 1 July 2010. Web. 29 Nov. 2013. <http://www.npr.org/templates/story/story.php?storyId=128043329>.

Huang SY, Lin MT, Lin WW, Huang CC, Shy MJ, Lu RB. “Association of monoamine oxidase A (MAOA) polymorphisms and clinical subgroups of major depressive disorders in the Han Chinese population.” World J Biol Psychiatry. 2009;10(4 Pt 2):544-51. doi: 10.1080/15622970701816506. PubMed PMID: 19224413.

Krupp, Daniel B., and Sana Halwani. "The Genetic Defence: The Impact of Genetics on the Concept of Criminal Responsibility." Health law journal 12 (2004): 35-70. ProQuest. 28 Nov. 2013.

Lea, Rod, and Geoffrey Chambers. “Monoamine Oxidase, Addiction, and the “Warrior” Gene Hypothesis.” 120 N. Z. MED.NEW ZEALAND MEDICAL J., Mar, 2, 2007,

http://journal.nzma.org.nz/journal/120- 1250/2441/content.pdf.

Lu RB, Lee JF, Ko HC, et al. “No association of the MAOA gene with alcoholism among Han Chinese males in Taiwan.” Prog Neuropsychopharmacol Biol Psychiatry. 2002;26:457–61.

McDermott R, Tingley D, Cowden J, Frazzetto G, Johnson DP. “Monoamine oxidase A gene (MAOA) predicts behavioral aggression following provocation.” PNAS. 2009 106 (7) 2118-2123; published ahead of print January 23, 2009, doi:10.1073/pnas.0808376106.

Sabol SZ, Hu S, Hamer D. “A functional polymorphism in the monoamine oxidase A gene promoter.” Hum Genet. 1998 Sep;103(3):273-9. PubMed PMID: 9799080.

Sjöberg RL, Ducci F, Barr CS, Newman TK, Dell'osso L, Virkkunen M, Goldman D. “A non-additive interaction of a functional MAO-A VNTR and testosterone predicts antisocial behavior.” Neuropsychopharmacology. 2008 Jan; 33(2):425-30. Epub 2007 Apr 11. PubMed PMID: 17429405; PubMed Central PMCID: PMC2665792.

State of Tennessee v. Davis Bradley Waldroup, Jr. Criminal Appeals of Tennessee at Knoxville. 15 Aug. 2013. Web. 01 Dec 2013. <http://tncourts.gov/sites/default/files/waldroupremandopn.pdf> .

"Waldroup guilty, will not face death penalty." Polk News Online. Polk County News, 25 Mar. 2009. Web. 01 Dec. 2013. <http://www.polknewsonline.com/2009/03/25/Top_News/Waldroup_guilty,_will_not_face_death_penalty/4158.html>.