

Biomarkers for PTSD Susceptibility and Resilience

Citation for published version (APA):

Bassil, K., Rutten, B., & Horstkötter, D. (2019). Biomarkers for PTSD Susceptibility and Resilience: Ethical Issues . AJOB Neuroscience, 10(3), 122-124. https://doi.org/10.1080/21507740.2019.1632964

Document status and date:

Published: 01/01/2019

DOI:

10.1080/21507740.2019.1632964

Document Version:

Publisher's PDF, also known as Version of record

Document license:

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Please check the document version of this publication:

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Download date: 07 Oct. 2022



AJOB Neuroscience



ISSN: 2150-7740 (Print) 2150-7759 (Online) Journal homepage: https://www.tandfonline.com/loi/uabn20

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To cite this article: Katherine C. Bassil, Bart P. F. Rutten & Dorothee Horstkötter (2019) Biomarkers for PTSD Susceptibility and Resilience, Ethical Issues, AJOB Neuroscience, 10:3, 122-124, DOI: 10.1080/21507740.2019.1632964

To link to this article: https://doi.org/10.1080/21507740.2019.1632964

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Biomarkers for PTSD Susceptibility and Resilience, Ethical Issues

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Expanding on the International Neuroethics Society Emerging Issues Task Force comments on military neurotechnologies (Kellmeyer et al. for the Emerging Issues Task Force, International Neuroethics Society 2019), we elaborate on the ethical questions that arise when applying neuroscience findings of biomarkers to the prevention of posttraumatic stress disorder (PTSD) among members of law enforcement agencies.

PTSD is a highly debilitating mental disorder that impacts not only the health, social life, and economic situation of those affected, but also the well-being of their families. Occasionally, PTSD may also have an influence on the safety of the wider communities, particularly in cases where PTSD patients display aggression and/or violent behaviors toward others.

RESILIENCE AND SUSCEPTIBILITY IN PTSD

Being a stressor-related disorder, PTSD is closely linked to the exposure to shocking and/or life-threatening events. However, after being exposed to such an event, a substantial number of individuals do not develop PTSD or other mental disorders. Thus, substantial interindividual differences exist in the response to a traumatic exposure. Such differences are commonly differentiated in a dichotomized way between individuals who do not develop mental disorders and are considered "resilient," and those who do develop a mental disorder and are considered "susceptible" (Yehuda 2004). Members of law enforcement agencies, like the police or the military, are particularly at risk to develop PTSD, because of the nature of their profession, which is characterized by dealing with serious incidents such as traffic accidents, (mass) shootings, armed threats, or war combat. Incidence rates of PTSD in populations of military personnel and police officers are substantially higher (Weichselbaum et al. 2017) than in the general population.

Today, the underlying pathophysiology and etiology of PTSD are not yet completely understood, although it has become clear that PTSD is associated with alterations in multiple biological systems working in concert and impacting a range of brain and physiological functions (Daskalakis et al. 2018). A series of studies has explored the benefits of making use of potential biomarkers as identified by brain imaging, behavioral and cognitive measures, and measurements of molecules bathing in peripheral biofluids including blood, urine, and saliva, to better understand the occurrence of PTSD (Schmidt et al. 2013). Also, our research group has identified candidate biomarkers in a military cohort, including differentially methylated genes. We have also obtained evidence showing that changes in DNA methylation in certain genes may be linked with changes in clinical PTSD symptomatology, thus suggesting that distinct epigenetic marks may differentiate susceptible versus resilient individuals (Rutten et al. 2018).

While two of us (KB and BR) are engaging in the basic and translational neuroscience of PTSD, we all believe that this upcoming possibility to predict resilient and susceptible individuals even before the exposure to traumatic events can trigger a series of ethical questions. These should be addressed proactively, that is, before the very occurrence of actual applications, in order to guide responsible decision making and to raise awareness about salient ethical issues in biomedical PTSD treatment and prevention.

Today, ethical studies and discussions on biomarker research in trauma-related mental disorders including PTSD are rather sparse. Where they do exist, the scientific reports seem to mostly focus on research-related ethical questions (Jain et al. 2011), on questions that arise when treating PTSD patients (Yang et al. 2017), and on ethical issues relevant for the criminal justice system (Soltis et al. 2014). However, biomedical research on PTSD susceptibility and resilience furthermore raises ethical questions in the context of prevention that have been largely underrepresented in the scientific literature. Also, the INS Task Force focuses on different issues such as neuroweapons when considering neuroethics in the

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context of the military and law enforcement agencies (Kellmeyer et al. 2019).

Prior to setting the agenda, we acknowledge that despite the use of increasingly sophisticated techniques to differentiate between susceptible and resilient individuals, this is not a black-and-white issue. Absolute resilient or susceptible individuals are likely the exception rather than the rule, and most people will end up somewhere along this spectrum. Furthermore, the phenotype of resilience is dynamic and may change during life. Still, for the time being, we prefer to structure the ethical debate around the two dichotomized ideal types, because they allow us to structure a complex future reality and to facilitate clear ethical thinking.

PTSD SUSCEPTIBLE INDIVIDUALS: ETHICAL ISSUES

Moral Failure

The prevention of PTSD is particularly important, and a failure to apply and translate upcoming insights can be considered a moral failure, because we will be allowing the manifestation of avoidable harm and suffering. That is, as soon as biomarkers, with some accuracy, allow the identification of susceptible individuals even before exposure to any traumatic experience, we should reconsider how responsible and justifiable it would be to let these individuals run enlarged risks of experiencing traumatic events. While it might not be possible to avoid such experiences over a person's life span, it seems very possible to avoid enlarged risks to exposure, as in police or military contexts. Having such findings and not using them for risk prevention purposes could be considered an unethical practice, because it generates avoidable cases of PTSD.

Susceptibility-Informed Policies

In this sense, it should be considered whether and how these biomarker-based findings should influence legislation and policymaking. For example, should screenings for PTSD susceptibility precede military and police recruitment and deployment to war combat and crime scenes, respectively? Such strategies might prevent susceptible individuals from being presented with traumatic experiences. As such, biomedically informed recruitments could avoid, or at least reduce, the very occurrence of PTSD among members of law enforcement agencies. However, is this a desirable situation? Early identification of susceptible individuals—that is, before the very occurrence of situations that trigger the onset of the disorder-does also lead to some critical considerations. Would such screenings be obligatory during recruitment? How will susceptible individuals be governed? Will they also face stigmatization and social or professional exclusion or discrimination? Will they be denied job opportunities? But also, fundamentally, are

PTSD susceptible individuals, purely by underlying biological sensitivities, different from those with a different genetic and/or neurophysiological makeup? Will they come to perceive themselves differently? How will they be seen by their peers? To date, these are open yet fundamental questions, which we should ask and find answers to in order to proceed in ethically and socially responsible ways in our search for PTSD biomarkers and for our ultimate aim to render these clinically relevant.

PTSD RESILIENT INDIVIDUALS: MORE **ETHICAL ISSUES**

Dual Use

At this point, the potential application of biomarkerbased PTSD research also gives rise to specific concerns about dual use. The dual-use aspect of military neurotechnology holds true not only for neurotechnological arms race and what is termed "neuroweapons" as identified by the INS Task Force. Identifying PTSD-susceptible individuals necessarily goes together with detecting those who are resilient. Today, it is unclear what this knowledge might imply for those concerned, as well as for their current or future employers. What does it mean to know that you are resilient to PTSD, when being on a military mission or when visiting a highly-troublesome crime scene? What does it mean that your employee knows this about you? Will those who know that they are more resilient, be desensitized to real-life violence and the suffering of others? Will they be more willing to participate in more violent and de-humanizing behaviors? On the other hand, the situation might be that those considered PTSD resilient will more easily than others be sent to particularly dangerous situations.

The End of Guilt?

A final point relates to the feelings of guilt and shame, frequently reported by those who do suffer from PTSD, partly due to behavior committed by themselves, but later regretted. For example, Yang et al. (2017) report about an army reservist who later learned he had killed a young child among adult combatants. This soldier suffered from PTSD and had clear feelings of "guilt, shame, anger, irritability, intrusive thoughts and nightmares" (435). What does it mean to feel guilty about one's own behavior, or about unintended bad consequences of one's own actions? In a certain way, feeling guilty of some wrongdoing-in this case, killing a child during combat—is of significant ethical worth. At least, doing wrong and not feeling guilty can be considered to constitute a moral failure. But how will feelings of guilt change after identifying individuals as being PTSD resilient? Will they lose, or fail to have, the capacity to feel guilty or shameful for any wrongful behavior? This certainly requires further thought, particularly on the relationship of such moral emotions with psychiatric disorders (Fontenelle, de Oliveira-Souza, and Moll 2015).

CONCLUSION

The questions presented here are open and unexplored to date. However, as we go along, developing neurotechnologies that will enable us to differentiate between PTSD susceptible and resilient individuals on the basis of any (including genetic, neurophysiological, and/or clinical) markers, it is of great ethical value to think these issues through before the technologies become available.

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Neuroethics and the Naturalistic Fallacy

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Adina Roskies first identified two traditions within neuroethics, the neuroscience of ethics, and the ethics of neuroscience. The focus of the Emerging Issues Task Force report (Kellmeyer et al. for the Emerging Issues Task Force, International Neuroethics Society [INS] 2019) was on the ethics of neuroscience, wherein prescriptive theses are advanced about the development and deployment of neurotechnologies. This commentary suggests that perhaps the greatest potential for future work in neuroethics lies in the neuroscience of ethics, which uses advances in neuroscience to address traditional philosophical questions. Of special importance are problems of metaethics concerning the source and justification of moral claims as well as questions of normative ethics

regarding which moral principles ought to guide our ethical decision making.1 These questions are critical because although there can be little doubt that there is a great need for ethical reflection on current and emerging neurotechnologies, this reflection is hampered by the moral pluralism-if not moral chaos-so forcefully put to bioethics by such thinkers as Alasdair MacIntyre and Tristram Engelhardt (Engelhardt 1996; MacIntyre 1984). Moral pluralism has arisen, in part, by the failure of traditional philosophical methodologies to resolve these questions. Without resolution on these questions, bioethics has been forced to proceed by way of a tenuous "mid-level" approach to moral theory whereby moral reflection is encouraged to invoke some, but not too

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^{1.} The neuroscience of ethics is not limited to questions of moral theory, but also includes puzzles such as the nature of the relationship between the mind and the body/brain, and the existence of free will. Benjamin Libet's experiment attempting to shed light on the problem of free will is a classic example of the neuroscience of ethics.