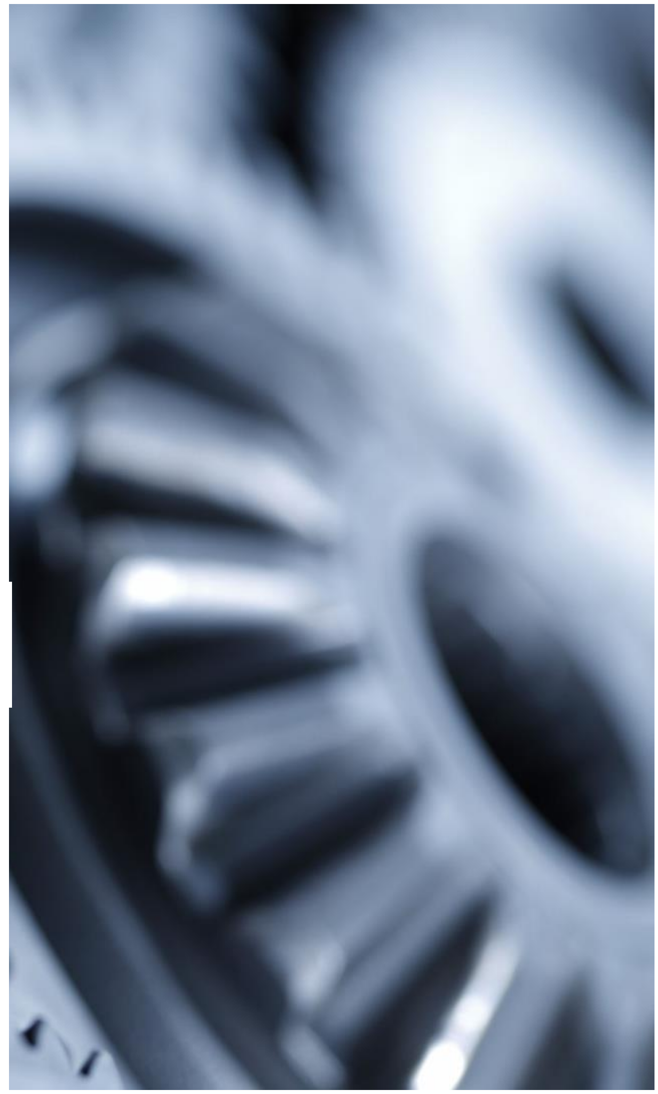
Emerging Neuroscience and Technology (NeuroS/T): Current and Near-Term Risks and Threats to US—and Global—Biosecurity



A STRATEGIC MULTILAYER ASSESSMENT Invited Perspective Paper

MAY 2021

Authors: James Giordano, PhD, Georgetown University; US Naval War College &
Diane DiEuliis, PhD, National Defense University
Series Editor: Ali Jafri, NSI Inc.

James Giordano, PhD, Georgetown University

James Giordano, PhD, MPhil, is Professor in the Departments of Neurology and Biochemistry; Chief of the Neuroethics Studies Program; Director of the Cyber-SMART Center's Program in Biotechnology, Biosecurity and Ethics; Co-director of the Program in Brain Science and Global Law and Policy; and Chair of the Sub-program in Military Medical Ethics at Georgetown University. He is Senior Fellow of the Project on Biosecurity, Technology, and Ethics at the US Naval War College, Newport, RI and Bioethicist-in-Residence of the US Defense Medical Ethics Center. He is also Senior Science Advisory Fellow of the SMA Branch, Joint Staff, Pentagon, and Chair Emeritus of the Neuroethics Program of the IEEE Brain Initiative. Prof. Giordano has previously served as Donovan Senior Fellow for Biosecurity at US Special Operations Command (USSOCOM); as an appointed member of the Neuroethics, Legal and Social Issues Advisory Panel of the Defense Advanced Research Projects Agency (DARPA); as Research Fellow and Task Leader of the EU-Human Brain Project Sub-Program on Dual-Use Brain Science; as an appointed member of the Department of Health and Human Services Secretary's Advisory Committee on Human Research Protections (SACHRP); and as Senior Advisor to the Organisation for Economic Cooperation and Development (OECD).

A Fulbright scholar, Prof. Giordano was awarded the JW Fulbright Visiting Professorship at the Ludwig-Maximilians University in Munich, Germany and is currently Distinguished Visiting Professor of Biotechnology, Health Promotions, and Ethics at the Coburg University of Applied Sciences in Coburg, Germany. He was previously an International Fellow of the Centre for Neuroethics at the University of Oxford, UK.

Prof. Giordano is the author of over 325 papers, 7 books, 22 book chapters, and 25 government white papers on brain science, global biosecurity, and ethics, and he serves as Associate Editor of the *Artificial Intelligence Ethics Journal* (Springer) and Editor-in-Chief Emeritus of *Philosophy, Ethics, and Humanities in Medicine* (BMC/Springer).

Prof. Giordano is a former US Naval officer, holding designations as an aerospace physiologist, research physiologist, and research psychologist, and he served with the US Navy and Marine Corps. In recognition of his achievements, he was elected to the European Academy of Science and Arts and was named an Overseas Fellow of the Royal Society of Medicine (UK).

Diane DiEuliis, PhD, National Defense University

Dr. Diane DiEuliis is a Senior Research fellow at National Defense University. Her research areas focus on emerging biological technologies, biodefense, and preparedness for biothreats. Specific topic areas under this broad research portfolio include dual-use life sciences research, synthetic biology, the US bioeconomy, disaster recovery, and behavioral, cognitive, and social science as it relates to important aspects of deterrence and preparedness. Dr. DiEuliis currently has several research grants in progress, and guest lectures in a variety of foundational professional military education courses.

Prior to joining NDU, Dr. DiEuliis was the Deputy Director for Policy, serving as Acting Deputy Assistant Secretary for Policy and Planning in the Office of the Assistant Secretary for Preparedness and Response (ASPR), US Department of Health and Human Services. While there, she coordinated policy in support of domestic and international health emergency preparedness and response activities, including implementation of the Pandemic All-Hazards Preparedness Act, the National Health Security Strategy, and the Public Health Emergency Medical Countermeasures Enterprise (PHEMCE).

From to 2007 to 2011, Dr. DiEuliis was the Assistant Director for Life Sciences and Behavioral and Social Sciences in the Office of Science and Technology Policy (OSTP) in the Executive Office of the President. During her tenure at the White House, she was responsible for developing policy in areas such as biosecurity, synthetic biology, social and behavioral science, scientific collections, ethics, STEM education, and biotechnology. Dr. DiEuliis also worked to help coordinate agency response to public health issues such as the H1N1 flu.

Prior to working at OSTP, Dr. DiEuliis was a program director at the National Institutes of Health (NIH), where she managed a diverse portfolio of neuroscience research in neurodegenerative diseases. She completed a fellowship at the University of Pennsylvania in the Center for Neurodegenerative Disease Research and completed her postdoctoral research in the NIH Intramural research program, where she focused on cellular and molecular neuroscience.

Dr. DiEuliis has a PhD in biology from the University of Delaware in Newark, Delaware.

Emerging Neuroscience and Technology (NeuroS/T): Current and Near-Term Risks and Threats to US—and Global—Biosecurity

James Giordano, PhD, Georgetown University[1]
Diane DiEuliis, PhD, National Defense University

There is increasing interest and effort in developing improved tools and methods through which political, military, and intelligence operations can influence the cognitive, emotional, and behavioral patterns of peer competitors and adversaries.

The brain sciences are affording new techniques and technologies to assess and affect human cognition, decisions, and actions. Global peer competitor nations and non-state actor groups are already invested in engaging these approaches.

Therefore, we argue that it is important, if not necessary, to fully define the capabilities and limitations of these neurocognitive tools, so as to (1) best evaluate their operational viability and value; (2) develop a neurocognitive "toolkit" that is fieldable and scalable for human terrain, psychological operations (PSYOPS), military information support operations (MISO), and both non-kinetic and kinetic military and intelligence missions; and in these ways (3) remain apace and ahead of current strategic competitors' neurocognitive sciences' enterprise that could be used to influence and affect global balances of power.

This IP addresses the current and near-term state of this science and technology (S&T), provides understanding about human cognition and behavior afforded by these methods, and offers recommendations for using a neurocognitive S&T toolkit for achieving and sustaining US tactical and strategic capability and hegemony in global influence operations.

[1] *Contact Information*: james.giordano@georgetown.edu

"The key to victory or defeat in war is people…the key to people lies in the brain"[2]

Introduction: Advances in Neuroscience and Technology (NeuroS/T)

Neuroscience employs a variety of methods and technologies to evaluate and influence neurologic substrates and processes of cognition, emotion, and behavior. In general, brain research can be either basic or applied. Basic research is aimed at furthering understanding of structures and functions of the nervous system; applied research explores and develops translational approaches to directly understand and modify the physiology, psychology, and/or pathology of select organisms, including humans. Neuroscience and technology (neuroS/T) methods and tools can be categorized as those used to assess and those used to affect the structures and functions of the nervous system. Note that these categories and uses are not mutually exclusive. For example, certain drugs, toxins, and probes can be employed to both elucidate and alter functions of the nervous system.

As a natural/life science, there is intent, if not expectation, to develop and employ neuroS/T capabilities in medicine. Thus, neuroS/T research is conducted with aims of achieving definable "benefit" and reducing incurred harms. However, absence of harm cannot always be assured for the use of research findings and/or products. This latter point has become somewhat contentious and is the focus of this report regarding the potential and actual uses of neuroS/T research that are distinct from intended applications and/or specifically intended to incur demonstrably threatening consequences to individual and public health and/or environmental integrity. Such applications of scientific and technological research are referred to as "dual use."

Working Definition of Dual-Use[3]

Axiomatically, dual-use research refers to findings or products of scientific and/or technological studies that can be employed for more than one purpose. According to this definition, neuroscientific techniques, technologies, and information could be used for medical as well as non-medical (educational, occupational, lifestyle, military, etc.) purposes. Of particular note is that this formal, albeit general, definition of dual use does not indicate or suggest that such secondary uses incur burdens, risks, or harms beyond those anticipated for primary intent. Nor is it particularly useful, since everything that could be employed for more than one purpose would fall under "dual use." To reduce ambiguity, increase specificity, and highlight potential risks and threats of harm, the United States' National Institutes of Health Office of Science Policy (OSP) established the classification of "Dual Use Research of Concern" (DURC) that entails life science research that can be anticipated or expected to

[2] See Jin et al. (2018).

[3] For further discussion on dual-use research, consult Giordano & Evers (2018).

afford information, technologies, and/or products that can be engaged to incur deleterious consequences to public health and safety, agriculture, animals, environment, and/or national security. Intrinsic to this definition is the possibility, if not likelihood, that such research outcomes could be usurped to elicit harm. Additionally, classification of DURC includes the use of tools and technologies that may pose risk and threat of harm as a consequence of inadvertent misuse (e.g., through laxity in laboratory containment, or contamination, etc.). Of note is that although military and national security applications are certainly implied by, if not constituent to the OSP definition, and thus would warrant consideration and address, they are not specifically explicated.

A still more focused definition, which more stringently identifies such applications and aims, is provided by the European Commission, which classifies dual-use goods, products, and technologies as those "…normally used for civilian purposes, but which may have military applications." However, this definition does not specify precisely which types of uses within the military would pose particular concerns that might be different from other occupational applications (e.g., cognitive, emotional, or behavioral alterations) that could pose risk or threat of harm. So, for example, would off-label use of neuropharmaceuticals or forms of non-invasive brain stimulation (NIBS) to optimize performance of military personnel elicit different concerns given their potential engagement in national security, intelligence, or warfare operations? Here, while performance optimization represents a proximate goal, it could also be viewed as means instrumental to warfare.

Of course, it could also be argued that such uses, performance enablements, and resulting capabilities could (and perhaps should) be used in intelligence and/or diplomatic operations to mitigate and subvert aggression, violence, and conflict. This remains a topic of ongoing debate. Of more focal concern are uses of research findings and products to directly facilitate the performance of combatants, the integration of human-machine interfaces to optimize combat capabilities of semi-autonomous vehicles (e.g., drones), and development of biological and chemical weapons (i.e., neuroweapons). The potential for such uses is sustained by historical examples of military adoption of scientific and technological developments, dating at least to the middle of the nineteenth century.

The increasing role of governmental support in both academic and industrial scientific enterprises during the early twentieth century fortified the establishment of unambiguous programs of military and intelligence use(s) of science and technology, inclusive of iterative developments in chemistry and biology that could be used to affect the nervous system. Furthermore, given that a formal definition of a weapon is "a means of contending against others," it becomes difficult to specify whether and which neuroS/T, when employed in military contexts, can and should be regarded as weapons. Moreover, if a broad definition of dual use or DURC is exercised, then the criterion of individual or public safety or harm might necessitate a more granular address and analysis of offensive or defensive applications, questions of protection versus harm, and a more thorough exploration of means and ends, writ large. Absent such conceptual clarification, categories of dual use and DURC could be considered vague and construed as either too broad or too narrow. This could incur practical as well as philosophical implications.

More sober efforts have been reflected in advisory reports from the US National Research Council commissioned by agencies, including the United States Army and Defense Intelligence Agency during the early-mid 2000s. These reports included recommendations for the military and intelligence community to identify and pursue neuroS/T that could be developed for operational use. This was prescient; for a while, a 2008 US National Academies Report, "Emerging cognitive neuroscience and related technologies," was somewhat cautious in its view of the operational utility of brain science. Subsequent reports, including a number of Pentagon white papers, have acknowledged that neuroscientific techniques and technologies have high potential for operational use in a variety of security, defense, and intelligence enterprises. These papers also advocated the need to address current and near-term ethical, legal, and social issues generated by such use. A subsequent report by the National Academies in 2014, "Emerging and readily available technologies and national security: A framework for addressing ethical, legal and societal issues," reflected this view and emphasized the importance of ethical engagement. At present, operationally viable products of brain science include microbiological agents, toxins, drugs, devices, and data. Certain microbiological agents, toxins, and chemicals are regulated and restricted by international policies, conventions, and treaties (such as DURC policies; the Biological and Toxin and Weapons Convention [BTWC]; and the Chemical Weapons Convention [CWC]); however, other substances (including novel agents that can be created using new tools of molecular biology), devices, and data, are not. Thus, neuroS/T are not wholly regulated and governed and is therefore viable for use in military, intelligence, and political initiatives and operations.

Military and Intelligence Use of NeuroS/T[4]

There is current and growing use of neuroS/T for military and intelligence purposes. Illustratively, as previously noted, the 2008 National Research Council's *ad hoc* Committee on Military and Intelligence Methodology for Emergent Neurophysiological and Cognitive/Neural Science Research in the Next Two Decades claimed that neuroS/T, while possessing potent capabilities, were not as yet demonstrably employable in military operations. However, by 2014, the Committee's subsequent report asserted that neuroS/T had matured considerably and were being increasingly considered, and in some cases evaluated, for operational use in security, intelligence, and defence operations. This evaluation reflected a 2013 Nuffield Council Report and a series of white papers by the Strategic Multilayer Assessment (SMA) Group of the Joint Staff of the Pentagon that illustrated the viability and value of the brain sciences to security, intelligence, and military operations.[5]

---

[4] Further discussion on military and intelligence uses of neuroscience and technology is available in Giordano (2015).
[5] For overviews of and access to reports, see: http://nsiteam.com/sma-publications/.

In large part, the iterative recognition of the viability of neuroS/T in these agendas reflects the pace and breadth of developments in the field. Although a number of nations have pursued and are currently pursuing neuroscientific research and development for military purposes, inclusive of efforts conducted by the United States Department of Defence, with the most notable and rapidly maturing research and development conducted by the Defence Advanced Research Projects Agency (DARPA) and Intelligence Advanced Research Projects Activity (IARPA). To be sure, many DARPA projects are explicitly directed toward advancing neuropsychiatric treatments and interventions that will improve both military and civilian medicine (e.g., Systems'-based Neurotechnologies for Emerging Therapies [*SUBNETS*]; Restoring Active Memory [*RAM*]; Next Generation Non-invasive Neuromodulation [*N3*]; etc.).[6] Yet, as represented by Table 1, it is important to note that prominent ongoing—and expanding—efforts in this domain by trans-Pacific and trans-Atlantic strategic competitor nations may pose serious threat to US' (and its allies') enterprise and capabilities in this space.

Table 1: Representative Competitive Research Programs in NeuroS/T for Military/Intelligence Applications: China and Russia (Giordano, 2015; Tennison et al., 2017)

Country	Major Research Institutions and Funding Resources	Research Themes
China	• National Natural Science Foundation of China • Ministry of Science and Technology (MOST) • Institute of Neuroscience (ION) of the Chinese Academy of the Sciences (CAS) • Chinese Society for Neuroscience • Second Military Medical University • Third Military Medical University • Fourth Military Medical University in Xi'an o Institute of Neurosciences • Zhujiang Hospital, Institute of Neuromedicine Partners • Beijing Society for Neuroscience • Neuroscience Research Institute, Peking University • IDG/McGovern Institute for Brain Research at Peking University	• "Bio-chips" and biotechnology • Trauma • Neuro-degeneration • Tumor biology • Pain and analgesia • Drug abuse and addiction

[6] See: www.darpa.mil for overview.

	- Beijing Normal University, National Key Laboratory of Cognitive Neuroscience and Learning - East China Normal University—School of Psychology and Cognitive Science - The Translational Neuroscience Center of West China Hospital of Sichuan University	
Russia	- Russian Foundation for Advanced Research Projects - Laboratory of Neurotechnology Perception and Recognition with focus areas - Russian Academy of the Sciences - Institute of Higher Nervous Activity 30th Central Scientific Research Institute, Ministry of Defense - State Research Center of Virology and Biotechnology (VECTOR)	- Integrated Biotechsystems - Memory, perception, and recognition - Public health and safety - Neurotrauma

As stated in the 2008 National Research Council report, ". . . ability to better understand the capabilities of the . . . brain could be exploited for gathering intelligence, military operations, information management, public safety and forensics" (National Academies of Sciences, Engineering, and Medicine, 2008). To fully acknowledge and address this reality, we propose the following premises.

- NeuroS/T will be ever more utilized in national security, intelligence, and (aspects of) military operations.
- This will enable leverageable power within militaries, against competitors and adversaries, and/or to control a government's/nation's populace (or selected individuals or groups).
- At present, several countries are dedicated to neuroS/T research that can be incorporated into military operations (see Table 1).
- These multinational enterprises establish the basis for a "neuroS/T race" to develop, counter, and/or improve upon competitors'/adversaries' achievements.

Any attempt to establish guidelines (and/or policies) to regulate neuroS/T research and development must recognize—and be responsive to—the potential for and trajectories of such escalation.

Performance Optimization of Military and Intelligence Personnel: Historical Background[7]

Drugs

Warfighters have long used myriad substances both to fortify performance of military tasks and to cope with operational stressors. Alertness, wakefulness, and focus—key decision-making capacities of a warfighter—have been enhanced for centuries. An ephedrine-containing herb stimulated the senses of guards on China's Great Wall, just as coca leaves did for Incan fighters. Bavarian soldiers used cocaine during the First World War, amphetamines were widely used by the German armed forces during World War II, and other stimulants, referred to as "go pills", have been utilized—in varying degrees—by military and intelligence personnel in several operations thereafter.

Warfighters have even used hallucinogens and intoxicating combinations of psychoactive herbs to enhance their combat effectiveness, or at least the appearance of ferocity. Turks reportedly used opium to enhance wartime bravery in the 1500s. Consumption of *amanita muscaria*, a psychoactive and hallucinogenic mushroom, reportedly facilitated the "berserker" rage characteristic of Viking raids. South African tribal warriors smoked dagga, a type of cannabis, in combination with the consumption of other herbs to enhance fearlessness and insensitivity to pain. A powerful amphetamine called fenithyllin (*Captagon*), which provides similar effects and can be produced via synthetic biological methods, is currently being employed in the Syrian conflict.

Not only have warfighters used substances to enhance capacities to *engage* in combat, the history of warfare is rich with examples of warriors using substances to *disengage* from combat. In this latter regard, US warfighters have recently used "no-go pills" to induce rest in preparation for, or in recovery from, combat. These interventions foreshadow ongoing research on drugs like propranolol, which could ultimately enable warfighters to disengage from combat without having formed traumatic memories.

Devices

The history of neuromodulation via electricity and magnetism also dates back centuries, if not millennia. Scribonius Largus, the ancient Roman physician, wrote the earliest known account of neurostimulation, and described the apparent benefit of application of an electric fish to the scalp as a remedy for headache. More recently, 18th century scientists demonstrated the therapeutic potential

[7] Refer to Tennison et al. (2017).

of transcranial electric current and the electrical stimulation of muscle contractions. For the following two centuries, researchers attempted to treat a number of physical and mental conditions with electric current, with varying success. Electroconvulsive therapy (ECT) was used to treat depression from the 1930s through the present. And deep brain stimulation (DBS) emerged in the 1980s as a treatment for Parkinson's and other movement disorders. Iterative advances in the hardware, placement, and control of DBS systems have prompted applications of this technique in the treatment of other neurological and psychiatric conditions. Additionally, ongoing research aimed at developing less or non-invasive methods of implantation of indwelling devices and systems (such as DARPA's N3 project) is establishing a basis for broader consideration of using DBS to affect cognition, emotion, and behavior in order to optimize task performance (inclusive of those tasks focal to military and intelligence operations).

As the 20th century came to a close, researchers rediscovered the potential of applying low-level electrical current through the skull to affect the brain and its functions. Types of transcranial electrical stimulation (e.g., direct, alternating, and/or pulsed current stimulation [tES]) have been used to modulate cortical excitability. In contrast to DBS, tES does not "stimulate" neurons by forcing or blocking their action potentials; rather, it "modulates" neurons by increasing or decreasing their threshold to fire. Studies have focused on tES's effects on neuroplasticity and the neurological substrates of cognition and motor activity. Although the safety of tES has been demonstrated, the current understanding of its efficacy for enhancement is incomplete. Some studies suggest that tES "can enhance cognitive processes occurring in targeted brain areas," but other scientists have failed to replicate this finding. Recent analyses reveal that "context matters," and the type(s) and extent of effects that can be elicited by tES strongly depend upon setting and the neuro-cognitive state of the subject. As well, recreational tES devices are available on the consumer market, and both clinical and direct-to-consumer tES technologies are of growing interest and potential utility to the military.

Magnetic current (e.g. Transcranial magnetic stimulation [TMS] is also used to modulate neurological functions. Approved to treat major depression and potentially promising for the treatment of post-traumatic stress disorder, TMS may have additional applications for cognitive and physical performance enhancement. In 2009, the US National Research Council identified TMS as a wakefulness enhancement for the US Army. Similarly, DARPA- and US Army-funded studies of wearable, helmet-borne devices have been dedicated to evaluating and operationalizing delivery of patterned ultrasound pulses to modify neurocognitive performance.

Brain-machine interfaces (BMIs, also known as brain-computer interfaces, or BCIs) constitute another major area of military neuroS/T research. BMIs can translate neurological signals into inputs for computers or machines, or vice versa. BMIs have potential for therapeutic breakthroughs in civilian and military medicine, as well as military and intelligence operational applications. BMIs attached to robotic arms have been employed to articulate prostheses using neurological output. Current DARPA research focuses upon fortifying feedback between the brain and prostheses to afford tactile feedback, such as pressure and temperature, from sensors in the prosthesis.

The DARPA AugCog (i.e.- “Augmented Cognition”) sought to fully integrate neurocognitive capacities and sensory perceptions with yoked input and control from combat vehicle environments. As computers monitor working memory, attention, executive function, and sensory input, military and intelligence personnel can sustain real-time information about cognitive load in order to more effectively manage and direct neurological functions and capabilities. Although the titular AugCog program has ended, similar and more capable, sophisticated research continues.

The 2014 National Academies’ report asserted that the research, development, and use of brain science in international military and security scenarios represent a significant and growing concern. In the United States and most Western nations, governmentally funded neuroscience programs adhere to dual-use research of concerns (DURC) policies, in keeping with the general constructs of the BTWC and CWC. But such control can also create a dilemma: It certainly creates parameters for the conduct of brain science in participatory states. Yet, at the same time, it can create opportunities for other nations or even non-state actors to take advantage of these constraints to gain a competitive edge toward attaining power. To be sure, international policies and treaties don’t guarantee cooperation, and studies and applications of brain science need not be clandestine or covert. As previously noted, the current BTWC and CWC do not restrict pharmaceutical formulations of neurotropic drugs for medical use or neurotechnologies (e.g., neurostimulatory or modulatory devices); exemptions for biomedical experimental purposes and/or shields of commercial proprietary interests and intellectual property can subvert inquiry into the dual-use or military applications of brain science.

Military Medicine: “Bench-to-Bedside” Applications

There is considerable literature addressing and describing evaluations and applications of neuroS/T to sustain vigilance, increase coordination, improve memory and learning, decrease fatigue, and reduce stress. This has fostered steadily increasing interest in, desire for, and use of such approaches to affect performance in certain occupational settings. Additionally, there is growing interest in employing neuroS/T for educational as well as avocational/lifestyle (e.g., gaming, athletic) purposes. At present, most such applications are administered in supervised laboratory and/or clinical settings (inclusive of “off-label” medical uses) and are characteristically well-controlled and monitored, in that distinct regulations apply for off-label use in research and medical practice.

For example, in research settings involving human subjects the use of any/all drugs and devices, must comply with the mandates of the Declaration of Helsinki and must entail and obtain:

- approval by an institutional review board (IRB) and, if the research engenders potential for serious risk to the health, safety, or welfare of a subject, approval of an investigational drug or device exemption (in the European Community, this approval comes from the European Medicines Agency);
- informed consent from all patients;
- labelling of the drug and device for investigational use only;
- monitoring of the study; and
- requisite records and reports.

In medical practice, the European Medicines Agency and Heads of Medicines Agencies defines off-label uses in 2017 as:

> Situations where a medicinal product is intentionally used for a medical purpose not in accordance with the terms of the marketing authorisation.
>
> Examples include the intentional use of a product in situations other than the ones described in the authorized product information, such as a different indication in terms of medical condition, a different group of patients (e.g. a different age group), a different route or method of administration or a different posology. The reference terms for off-label use are the terms of marketing authorisation in the country where the product is used. (p. 21)

This definition establishes that drugs and devices that have European marketing authorization will eventually be considered “off-label,” while those products without this authorization will be regarded as “unlicensed.” These definitions and existing regulations presume that any and all off-label use represents a matter of medical judgment and occurs in a conscientious manner with regard to good clinical practices.

Direct-to-Consumer Applications

An expanding industry that provides agents and devices directly to consumers (DTC) may warrant concern about public health and safety. In general, research supporting the development of neuroscientific drugs and devices that are made available to the DTC market is conducted either in academic laboratory settings or directly by the commercial entity. In the former case, published studies of mechanisms and effects of neurotropic agents and devices may be simply utilized by a commercial entity for the development, substantiation, and/or marketing of their product(s). As well, some commercial entities will directly subsidize academic research to investigate putative mechanisms of and potential outcomes of a particular product, which is then used to advance claims of process and effect, safety, and value that can be leveraged for both regulatory approval and marketing. In the latter case, a commercial entity will conduct research in laboratory and/or restricted field settings using in-house resources and personnel.

In the United States, EU, Canada, Australia, and New Zealand, research and development (R&D) of these drugs and devices can be regarded as dual-use in that they are explicitly not intended to diagnose or treat a medical condition. Furthermore, the provision and use of these products are not supervised by a physician, and therefore responsibility for appropriate use is shared, to some extent, by the commercial manufacturer and the consumer. To the extent that research studies are contributory to an understanding and explanation of these products' mechanisms, actions, and effects, there is also some degree of ethical (if not legal) enfranchisement of the participating researchers, although the nature and extent of these responsibilities remain a matter of discourse.

Here, key issues center upon if, and to what extent, studies of mechanisms and effects are directly focal to a specific product or represent mere generalizations. There are also concerns about the translation of findings generated under controlled laboratory settings to variable uses-in-practice, provision of information (and/or lack thereof) regarding effects, possible side- and adverse effects, and thorough definition and description of protocols for use. In the US, product claims are regulated by the Federal Trade commission, and in the EU, both the European Trade Commission and national agencies within member countries provide oversight to product claims. While these bodies define criteria for product labelling, there have been calls for an increased level of conformity in standards for research, marketing, and labelling of neuroscientific agents and devices that are offered DTC.

Do-It-Yourself/Neurobiohacking

There is also a growing do-it-yourself (DIY)/biohacking community that is dedicated to modifying commercially available DTC products to perform different functions and/or creating new products capable of affecting neurobiological functions. Biohacking typically implies modifications for benevolent ends (i.e., "white-hat" hacking), inclusive of development of agents and devices to improve human cognition, emotion, and behavioral performance. However, there is also a "black-hat" hacking community that engages DIY approaches to modifying neurobiology to produce pathogens or to incur other disruptions in individual or community stability and safety. Biohacking can be articulated in three research domains: synthetic biology (e.g., genetic and molecular editing); biotechnology (human-machine interfaces, technological implants, and prosthetics); and biochemistry (e.g., development of neurotropic agents that can be used either singularly or in chemical cocktails). These categories and their products are not mutually exclusive.

DIY scientists/biohackers often work in coordination within an informally organized community, and much of their research is made publicly available through open access databases and websites of community laboratories. The spirit of the DIY/biohacking community reflects a movement to make biology “easier to engineer” and more publicly accessible and available. In part, this is constituent to an expanding trend toward “open source” biology that has influenced both research institutions and the public. Additionally, “open source” biology has captured an economic market niche: engineered and modified organisms, drugs, and devices can be sold; community laboratories can be purchased (by conventional commercial entities); and both community laboratories and individual DIY biohackers can be subsidized through venture capital. With manuals and methods available online, along with components and devices that can be easily purchased on (eBay or other) internet platforms, it is relatively easy to establish and run a laboratory, and interested individuals and groups can obtain guidance on producing and/or manipulating a variety of neurobiological techniques and technologies. This community is reinforced and encouraged by public reports of success with these types of enhancements—e.g., the use of stimulation to improve batting and fielding performance in baseball players and reports of enhanced ability through “microdosing” of both (psychedelic) pharmaceuticals and device-delivered (electric and/or magnetic) currents.

These same opportunities also pose potential regulatory, health, and security risks. Independent laboratories and researchers do not always abide by the comprehensive policies that academic and industrial research entities must follow. Further, there is increasing use of the “dark web” (i.e.- covertly accessed Internet) by both “white-hat” and “black-hat” biohackers to facilitate exchange of information in ways that impede surveillance.

This community presents particular dual-use research concerns in that:

1. Outcomes and products may be used or misused in ways that adversely impact individual and public health and safety, as well as the integrity of flora and fauna in the environment.
2. Limitations and/or lassitude in research practices and/or laboratory conditions may incur accidental release of information or products that can pose health and environmental risks and harms.
3. Activities may be subsidized and outcomes and products utilized by national and non-state venture capitalists with explicit intent toward disrupting public safety, stability, and health.

These possibilities evoke security concerns on local, national, and international scales and have warranted involvement of crime prevention and public safety agencies (e.g., the United States Federal Bureau of Investigation) to establish dialogue with and provide insight to the DIY biohacking community. What is important to note is that neuroscientific and neurotechnological research and development is occurring on a variety of levels (from large-scale academic and industrial laboratories to individual DIY experimenters) and is international. In this latter regard, it has been estimated that a significant and growing percentage of neuroscientific and technical research and development will be engaged outside of the West by 2025. This increases the possibility for dual-use research and DURC and generates questions about what constitutes research for security purposes (i.e., preparatory defense) versus military/warfare (i.e., offensive capability) purposes.

Intelligence, Training, and Operational Applications[8]

Research in cognitive and computational neuroscience is being engaged to improve:

- **human cognitive performance** – through improved understanding of basic processes involved in memory, emotion, and reasoning to support and enhance intelligence analysis, planning, and forecasting capabilities.
- **training efficiency** – by using knowledge and tools of cognitive neuroscience to enable more rapid acquisition and mastery of knowledge and skills with more durable retention.
- **Team process performance** – via engagement of systems engineering of human/brain interfacing to enhance information processing capability of individuals, organizations, and surveillance and weapons systems (drones). Research in this domain generally employs a technology readiness/technology transfer approach that utilizes a nine-level assessment and articulation scheme (from observation of basic principles, through evaluation and validation in a relevant environment, to full operational readiness) to advance research, development, testing, and evaluation toward rapid use. At present, a number of human/brain-machine interfaces are transitioning from development through test and evaluation stages toward operational readiness within a five-year cycle.

Neurocognitive studies employing various forms of neuroimaging, neurogenomics, proteomics, and biomarker assessment are being used to identify and define neural networks involved in several dimensions of operational performance of military combat and support personnel. These approaches seek to identify and isolate neural structures, systems, and functions that can be "targeted" for interventions utilizing non-invasive brain stimulation, pharmacological agents (e.g., stimulants, eugeroics; nootropics), or cognitive-behavioral training to facilitate, sustain, and/or improve performance capability and reduce dysfunction. An overview of these approaches is provided by Table 2.

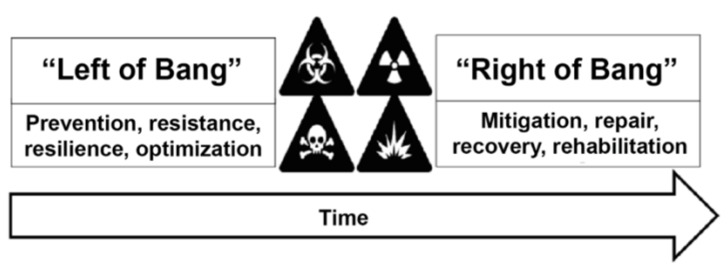
[8] Refer to Giordano & Wurzman (2014) and DeFranco et al. (2019).

Table 2: NeuroS/T Approaches to Personnel Performance Optimization (Giordano & Wurzman, 2014; DeFranco, et al., 2019)

Pharmacologic Agents	Types	Effects
Stimulants	Amphetamines (e.g., dextroamphetamine)	Facilitated attention, focus, and arousal; decreased fatigue; improved memory
	Substituted phenylethylamines (e.g., methylphenidate)	
Eugeroics	modafinil; armodafinil	Increased wakefulness; decreased fatigue; facilitated reasoning
Racetams	piracetam, oxiracetam, aniracetam	Putative general "nootropic" effects; increased focus
Neurotechnologic Methods	**Types**	**Effects**
Neurofeedback	• Electroencephalography (EEG)-based • Neuroimaging-based	Increased vigilance; directed attentiveness; improved concentration
Transcranial Neuromodulation	• Transcranial electrical stimulation (tES) • Transcranial magnetic stimulation (TMS)	Improved vigilance; increased focus; improved cognitive reaction time
Brain-Computer Interfacing (BCI)	EEG-based	Facilitated signal-noise/object recognition and discrimination

These assessments and interventions have been and could be regarded as components of preventive military medicine (i.e., to be used "left of bang", where "bang" is regarded as any inciting event; see Figure 1). Moreover, studies conducted within and/or directly funded by the military have been utilized for their "reverse dual-use" applications in civilian occupational and preventive medical contexts. However, these techniques and technologies also raise concerns about creating "super soldiers" (i.e., "super-sailors", "mega-Marines," and/or

Figure 1



“amped-airmen”) and intelligence operators (i.e., “super-spooks”) that obtain fortified cognitive, emotional, and behavioral characteristics that maximize their combat capabilities. A contrary position posits that such methods could and arguably should be engaged to instead produce soldiers who possess improved decision-making, interpersonal, and perhaps even empathic characteristics and skills. These contrasting views fuel current discussion and debate.

Weaponization of NeuroS/T[9]

The weaponization of neuroS/T in military/warfare contexts (e.g., combat) seeks to alter functions of the nervous system to affect physical and/or cognitive capabilities required for military operations. As noted, the weaponized use of neuroscientific tools and products is not new. Historically, such weapons have included nerve gas and various drugs. Weaponized gas has taken several forms: lachrymatory agents (e.g., tear gases), toxic irritants (e.g., phosgene, chlorine), vesicants (blistering agents; e.g., mustard gas), and paralytics (e.g., sarin). Pharmacologic stimulants (e.g., amphetamines) and various ergogenics (e.g., anabolic steroids) have been used to augment performance of combatants, and sedatives (e.g., barbiturates) have been employed to enhance cooperation during interrogation. Sensory stimuli (e.g., high intensity sound, prolonged flashing lights, irritating music or noise) have been applied as neuroweapons to incapacitate the enemy, and even sleep deprivation and distribution of emotionally provocative information in psychological operations (i.e., PSYOPS) could rightly be regarded as forms of weaponized applications of neuroscientific and neurocognitive research. The 2013 conflict in Syria involving the use of nerve gas, as well as the use of the neuroactive agent VX to assassinate Kim Jong-nam, estranged half-brother of North Korean leader Kim Jong-un, demonstrate the ongoing relevance of nervous system targets. Indeed, North Korea affords a prime example of a state resorting to chemical weapons in order to gain advantage when their military is out-competed by other nations’.

Moreover, computational neuroscience and neuropharmacologic research could be more indirectly utilized to optimize human functions modulating brain activity instrumental to signal detection and integration, so as to bio-engineer aspects of “human weak links” out of the chain(s) of military and intelligence operations. There is additional interest in employing neurotechnology to augment the role, capability, and effects of PSYOPS in military and political missions. Programs such as *Sociocultural Content in Language* (SCIL) and the *Metaphor* program at IARPA were directed toward improving insight into cultural linguistic and emotional norms, and DARPA’s *Narrative Networks* entailed a neurocognitive approach to understanding and modelling narratives in socio-cultural contexts. As noted in several SMA reports to the Pentagon, the intent and desired outcome of this research is an improved understanding of neural bases and effects of narratives that can afford insights to influences

[9] See Wurzman & Giordano (2015); Giordano (2017a); and DeFranco et al. (2019).

and processes that affect brain development, function, and behaviorwhich can be operationalized to mitigate violence on a variety of scales.

Additionally there is ongoing neuropharmacologic, neurotoxicologic, neuromicrobiologic, and neurotechnologic research that has potential to develop non-lethal or lethal weapons in combat-related and/or special operations' deterrence operations. Weaponizable products of neuroscientific and neurotechnological research can be utilized to affect 1) memory, learning, and cognitive speed; 2) wake-sleep cycles, fatigue, and alertness; 3) impulse control; 4) mood, anxiety, and self-perception; 5) decision-making; 6) trust and empathy; and 7) movement and performance (e.g., speed, strength, stamina, motor learning, etc.).

As summarized by Table 3, non-lethal and lethal neuroweapons include various categories and classes of psycho-neuroactive drugs, a variety of microbial agents (e.g., bacterial and viral strains) that act directly or exert effect upon the central and/or peripheral nervous system; organic toxins; and neurotechnological devices (e.g., sensory and brain stimulation approaches) and products (e.g., nanotechnologically derived substances). Additionally, brain-machine interfacing and neural network-derived computational decision systems could be employed to develop remote control or autonomous/semi-autonomous capability for unmanned aerial, ground, and marine (surface and subsurface) vehicles that could function as weapon platforms. The use of unmanned vehicles as weapons is not novel, and the realization of fully autonomous capability is iterative. Such progression and integration of neurotechnologically-enabled capabilities render these weapons increasingly viable and therefore a source of trepidation about near-term future developments that could be generated from ongoing research in neural architectures and human-machine systems.

Table 3: Weaponizable NeuroS/T (Wurzman & Giordano, 2015; Giordano, 2017; DeFranco et al., 2019)

Pharmacologic Agents	
Tranquilizing agents	benzodiazepines; barbiturates; neuroleptics; etc.
Mood altering agents	monoamine agonists and re-uptake blockers
Affiliative agents	methylenedioxymethamphetamine-MDMA; oxytocin
Dissociative agents	ketamine; phencyclidine
Psychedelics/Hallucinogens	lysergic acid diethylamide; tryptamine derivatives; psilocybin
Cholinergic agents	pilocarpine; physostigmine; (RS)-propan-2-yl-methylphosphonofluoridate (sarin)
Microbial Agents	
Viruses	*Togaviridae:* Equine encephalitis; *Flaviviridae*: flavivirus

Bacteria	*Bacillis anthracis*: anthrax; *Clostridium botulinum*: botulism; cyanobacteria; *Gambierdiscus toxicus*: cinguatoxin
Organic Toxins	
Bungarotoxins	krait snake toxin
Conotoxins	cone snail toxins
Dendrotoxins	mamba toxin
Maculotoxin	Blue-ringed octopus symbiotic bacteriotoxin
Naja toxins	cobra toxins
Saxitoxin	shellfish toxin
Tetrodotoxin	pufferfish toxin
Neurotechnologies	
Directed energy devices	Microwave (and other radio frequency) output systems to evoke neurocognitive disorientation/discomfort/dysfunction
Transcranial neuromodulating devices	Neural network stimulators for use in in-close operations against individual actors/targets
Nano-neuroparticulates	High CNS aggregation lead/carbon-silicate nanofibers (CNS network disrupters)
	Neurovascular hemorrhagic agents (for in-close and population targeted use)
Neurodata	See below

Neurodata[10]

The conjoinment of the physical, social, and computational sciences and concomitant "technique and technology sharing" has synergized the pace and breadth of discoveries and developments in the neurosciences. Such advanced integrative scientific convergence (AISC) paradigmatically de-silos disciplines to establish and sustain complementary knowledge and skills to create new methods and tools to (1) foster innovation and (2) further understanding and **capability**.[11] The AISC approach relies upon computational (i.e., big data) systems to allow the level(s) and scope of multi-tiered informational acquisition, processing, assimilation, and synthesis required for neuroS/t research and its translational applications. Taken together, the capabilities of computational and brain sciences have biosecurity and defense implications. While much of weaponizable neuroS/T (e.g., chemicals, biological agents, and toxins) are addressed in and by extant forums, treaties, conventions, and laws,

[10] See Giordano (2014); DiEuliis & Giordano (2016); and DiEuliis et al. (2018).
[11] For a comprehensive discussion, refer to Vaseashta et al. (2012).

newer techniques and technologies—including neurodata—have not. "Neurodata" is defined as the gathering and use of multi-scalar information to (1) establish increasingly detailed assessment of brain structure and function and (2) develop large-scale databases to enable (descriptive and/or predictive) evaluative metrics (for clinical medicine, law, socio-economic, and potentially political uses).

Of note is that the rapidity of such advances can—and often does—outpace securitization, and the uniquity of brain science and its applications—and meanings—render particular security vulnerabilities. Namely, the fact that the brain is regarded as the "source of the mind," and all of the functions and implications arising therein, establishes a normative aspect to neurodata. Simply put, neurodata can afford bases of what constitutes "normality" of brain structure, and functions (viz., thought, emotion, and behavior). Access to such information can enable insertion of data (e.g., in medical records, databases, registries, etc.) to alter the normative stature of targeted individuals (e.g., developing data profiles that depict them to have, be premorbid for, and/or predisposed to neurological and psychiatric conditions). Access and use of this information could impact national security by affecting (1) the type of medical care that is (or is not) provided to both civilian and military populations; and (2) ways that individuals and groups are socially, economically, legally, and politically regarded and treated.

Neurodata can also afford genotypic and phenotypic information that can be used to develop "precision pathogens" capable of selectively affecting specific targets (e.g., individuals, communities, domestic animals, livestock, etc.). Recent development in gene editing tools and techniques, such as CRISPR-Cas 9 (when employed with other, existing molecular biological methods), can facilitate both the modification of extant agents to be more viable, durable, and/or virulent, as well as the development of novel bacteria and viruses that have unique properties, specific affinities, and/or no known treatment. The COVID-19 pandemic has put into stark relief those ways that public reaction—and public health preparedness, readiness, and **response**(s)—could be engaged by the use of "precision pathologies" and disseminated misinformation to incur multi-domain and multi-dimensional disruptions within society (and military and intelligence communities) to incur and exploit weak elements of public health, social stability, and **national security**.[12]

Thus, we argue that digital biosecurity—the effective prevention or mitigation of current and emerging risks at the intersection of computational systems and biological information—is increasingly important and necessary. Given that several countries that are currently strategically competitive with the US and its allies are dedicating effort(s), resources and funding to neuro- and cyber-S/T research

---

[12] For more information on the nature of the COVID-19 response, refer to Besser (2020). A discussion on the national security implications of such phenomena can be found within Giordano (2017c).

and capabilities, there is increasing likelihood of attempts to engage neurodata for leverageable informational, social, legal, and military power advantage(s).

Therefore, we posit that an integrative approach to digital biosecurity is required that can effectively and efficiently address present and future challenges. The integration must occur in the domains and dimensions that are most relevant and crucial to surveillance, oversight, and direction of neurocognitive and other types of biodata. Such an approach would necessitate: (1) an integrative scientific convergent paradigm; (2) at least a whole-of-government, if not whole-of-nation dedication[13]; and (3) a multi-national re-address to more effectively guide and govern the ways that neurodata—and other bioinformation—are and can be used in both non-kinetic and kinetic engagements[14].

NeuroS/T Commercialization and Growth: Economic Hegemony/Global Power [15]

Neuro-data, coupled to and synergizing (other) advancements in neuroS/T, has contributed to much growth in the neuro-bioeconomy. To be sure, as current assessments and predictions from the Neurotechnologies Industries Organization and Organisation for Economic Cooperation and Development reveal, there is—and will continue to be—an evident and expanding market opportunity for neuroS/T development and production. In a 2016 analysis of data from 195 countries, the Global Burden of Diseases, Injuries, and Risk Factors Study Group (GBD) found that neurological disorders are the second leading cause of death worldwide (with approximately 9 million deaths, constituting 16.5% of global fatalities). Additionally, neurological disorders are the leading cause of disability, incurring approximately 276 million disability-adjusted life-years. Assessments by the GBD also illustrate the magnitude of neuropsychiatric illnesses, with current estimates that these disorders account for one-third of worldwide disabilities. A report by the *Lancet Commission* estimates that between 2010 and 2030, the fiscal productivity loss incurred by neuropsychiatric conditions could be as high as $16 trillion (USD). The increased prevalence of these diseases in an aging population is placing significant burdens on healthcare systems and generating substantial expenses in economic and social welfare.

When considering recent demographic trends and continuity of aging populations, neurological disorders may likely have a more significant impact in the near future. Current estimates project that the global population of people over the age of 60 years will increase from 800 million today to 2 billion in 2050 (accounting for ~22% of the world population). This percentage is disproportionately greater

[13] Discussions on whole-of-government approaches can be found in DeFranco, et al. (2019).
[14] Refer to Gerstein & Giordano (2017). Additionally, one can find further context in DiEuliis et al. (2018).
[15] See DeFranco et al. (2020).

in developed nations. For example, dementing disorders (i.e., pathologies that present with a progressive decline in memory, emotion, and executive behavior) currently affect 50 million people, and it is projected that 152 million people will be affected by 2050. These disorders are—and are predicted to remain—a primary focus of global brain science. In China, for example, the ever-growing aging population, at risk for neurodegenerative diseases, has been explicated as a driving force for current and near-future biotechnology research, development, and translation.

While the search for improved diagnostics, treatments, and potential prevention of neuropsychiatric disorders are principal drivers of brain research, there is a growing commercial interest in developing applications of neuroS/T in direct-to-consumer (DTC) healthcare, education, information and communication technology, law enforcement, and military markets. For example, in the past ten years, the number of patents for DTC neurotechnologies has more than doubled, and the worldwide market for neurotechnology products is forecasted to increase from $8.4 billion (USD) in 2018 to $13.3 billion in 2022. Moreover, in 2019, several neurotechnology startups disclosed annual funding ranging from $1 million–$50 million (e.g., *Thync, Halo Neuroscience*), to $50 million–$100 million (e.g., *Dreem, Kernel*), to $100+ million (e.g., *NeuroPace, MindMaze*). Such financial success can be demonstrated by the size and relative growth of the global deep brain stimulation device market, which is projected to reach $2.3 billion by 2025, increasing 16.1% in compound annual growth rate between 2019 and 2025.

Interactive developments in neuroS/T and computational biology have enabled the leveraging of neuropsychiatric data (i.e., "neurodata"). The convergence of diverse approaches and disciplines, including the physical, social, and computational sciences, and intentional "technique and technology sharing," has been crucial to the number and rapidity of recent advances in the brain sciences. Concerted efforts in neuroinformatics are producing new computational tools that can aggregate, organize, synthesize, and employ neurodata for uses in research and varied applications, inclusive of clinical medicine, law, and national security and defense.

As shown in Table 1, several countries have initiated programs in brain research and innovation (see Table 1). These initiatives aim to: (1) advance understanding of substrates and mechanisms of neuropsychiatric disorders; (2) improve knowledge of processes of cognition, emotion, and behavior; and (3) augment the methods for studying, assessing, and affecting the brain and its functions. New research efforts incorporate best practices for interdisciplinary approaches that can utilize advances in computer science, robotics, and artificial intelligence to fortify the scope and pace of neuroscientific capabilities and products. Such research efforts are strong drivers of innovation and development, both by organizing larger research goals and by shaping neuroS/T research to meet defined economic, public health, and security agendas.

In an attempt to coordinate goals and projects, the International Brain Initiative (IBI) was established in 2017 with specific intent toward "catalyzing and advancing ethical neuroscience research through international collaboration and knowledge sharing, by uniting diverse ambitions to expand scientific possibility, and disseminating discoveries for the benefit of humanity." Current constituents of the IBI include Australia, Canada, China, the EU, Japan, Korea, and the United States. While the intent is notable, it remains to be seen if and to what extent (1) the IBI will operate in partnership with other extant organizations (e.g., Organisation for Economic Cooperation and Development, Institute of Electrical and Electronics Engineers, World Health Organization, etc.) that are dedicated to similar, if not identical aims; and (2) the formation and addition of another group devoted to these purposes will facilitate these means and ends or merely become an example of "too many cooks ruining the broth."

Security Challenges of the Neuro-bioeconomy

The US National Academies of Science, Engineering, and Medicine has identified the need for the US and its allies to recognize dual obligations to the emerging bioeconomy. First is a responsibility for prudent direction and oversight, as failure to promote progress in/by biological and technological industries could result in losing leadership of the international community. Meeting this obligation could include adequately funding research and development in key areas, implementing appropriate research oversight, and educating the research workforce. Second is the need to protect the bioeconomy from deliberate adversarial acts that could impede biotechnological progress and allow other international individuals, groups, or countries to gain power advantage. Engaging this responsibility could entail developing more rigorous methods of proper handling and oversight of biologicals and/or technology, affording ample protection of biological data and digital infrastructures, and the development and implementation of (more effective, and globally relevant and responsive) intellectual property laws.

Additionally, it is important to note that although the US National Academies of Science, Engineering, and Medicine report briefly mentioned recent developments in brain-controlled robotics and brain-machine interface (BMI), neuroS/T, writ large, was not a core aspect of their address. At present, a majority of countries do not yet identify the brain sciences as a principal economic focus. Of the 41 nations that pursued specific political strategies to expand and promote their bioeconomies in 2018, only 10 included neuroS/T research and development objectives.[16] So, while there may be little doubt that neuropsychiatric disorders are a significant public health problem, brain research is relatively costly, and the perceived return-on-investment for those countries that do not have substantial neuro-epidemiological burdens may not be sufficient to justify pursuing dedicated neuroS/T initiatives. However, while *intra*national human capital and socio-political agendas of a given nation may not

[16] The countries or multi-national organizations that include neuroscience, neurotechnology, and/or brain science objectives in their bioeconomy strategies are Australia, Brazil, China, France, the EU, India, Japan, South Korea, Thailand, and the United States.

prompt investment and engagement in neuro-bioeconomics, the relative economic—and perhaps cultural and political—hegemony afforded by leveraging global neuroS/T (and overall biological) markets might prove influential to changing perspectives, postures, and participation. To be sure, due to the current lack of emphasis on brain science in national bioeconomic strategies, those countries that initiate policies and programs to invest in neuroS/T may achieve significant financial successes and economic power, and thereby direct future (ethical, technical, and legal) standards of research and use.

This power can be engaged in kinetic and non-kinetic operations, as evidenced by multinational interest and effort in brain science in military and intelligence agendas. Notable in this regard is that current treaties (e.g., the BTWC and CWC) do not specifically address neurotechnologies and neuroinformatics.

Furthermore, several aspects of the brain sciences make them particularly problematic for the biosecurity community. First, the field has become increasingly interdisciplinary and strives to integrate several sciences and technologies (e.g., biology, chemistry, psychology, physics, computational sciences) to address neuroscientific questions and forge innovative discoveries and interventions. For instance, state and non-state actors can use novel neurotechnologies (e.g., BMIs and transcranial neural stimulation devices) and advances in neuroinformatics (i.e., analyzing neuroscientific data to better assess, access, and affect the nervous system) for WINS applications. At present, the development and use of these devices are underregulated and not included in dual-use export safeguards, thus making effective oversight of potential dual-use research of concern (DURC) difficult. Second, these neurotechnologies are as yet underexplored for their augmentative and destructive capabilities and uses. In contrast to other conventional biological and chemical weapons (e.g., microbes, toxins, chemicals), devices that affect the nervous system are relatively new and have only recently been engaged for their WINS potential. This combination of “blank slate” and “unknown ground” dimensions of neurotechnology creates difficulties in realistic biosecurity forecasting and preparedness.

For the last two decades, publications in the brain sciences have steadily increased. Yet, for the aforementioned reasons oversight remains a problem, as surveillance of potential WINS applications is complexified by persistent challenges in tracking and evaluating (any) neuroS/T research and product development. Thus, the potential for dual- or direct-use of neuroS/T for disruptive or destructive purposes becomes increasingly viable.

Moreover, as previously stated, much of neuroS/T is reliant upon and force multiplied by big data and computational approaches. In this light it is important to note that the rapidity of advances in cybertechnology and data analytics often outpaces securitization. The term “cyberbiosecurity” has been proposed to describe the intersection of computational systems, biological information, and the processes required to effectively mitigate and/or prevent new and emerging risks and threats.

Clearly, brain science has become a multinational enterprise. And as previously noted, although some nations have not committed investments and resources to escalate neuroS/T initiatives, others most certainly have, and with ardent intent. Therefore, it is important to note (1) the distinct influence(s) that neuroS/T capabilities can exert within and between developed, developing, and non-developed nations; and (2) the differing cultural and political values that can affect the ethical codes that guide and govern the conduct of scientific research. Taken together, these asymmetries (in capability and ethical standards) can—and often do—create opportunistic windows that can expedite neuroS/T research and advance outcomes and products to ultimately affect international markets and global balances of power. Key examples of such exercise in capability include recent neuroS/T endeavors in/by China
and Russia (Chen, et al., 2018; Giordano, et al., 2019; Giordano, 2017).

A Novel Case Study in Corporate Commercialization: *Neuralink*[17]

In 2019, Elon Musk announced that his company, *Neuralink*, would advance the clinical translation of a novel BMI that he claims holds ". . . promise for the restoration of sensory and motor function and the treatment of neurological disorders." The BMI involves implantation of microelectrodes in the brain to record neurological activity, which then convey signals to sensors that can be detected by an external device, such as a smartphone. Due to the complex nature of this procedure, *Neuralink* plans to develop a robotic system for implanting electrodes. This system will be monitored and managed by a neurosurgeon who can manually adjust the robotic system as needed during the procedure. Although the company's efforts to develop such a BMI have only been underway for little more than two years, it has already created an innovative, functioning application in an *in vivo* rat model. Musk seeks to begin clinical trials this year for treatments of certain neurological disorders, and he asserts that this technology could and should be available to any individual who wishes to achieve "better access" and "better connections" to "the world, each other, and ourselves."

Presentations by Musk have asserted that a primary goal is to make the procedure ". . . as simple and automated as LASIK." Yet, until the robotics, external devices, and neurosurgeons are available worldwide, there will only be a few places in the world that will be able to offer this intervention. Given current views of scientists in the United States, Europe, Japan, and Australia regarding medical

[17] For more on this, consult DeFranco & Giordano (2020).

interventions intended for “non-therapeutic” (i.e., optimization/enhancement) purposes, it seems unlikely that surgeons would (want to) perform the *Neuralink*/BMI procedure.

If this is the case, questions arise as to where these procedures would be provided and how this technology and these interventions will be funded. As noted, some nations’ cultural views, needs, values, philosophies, ethics, and politics may make them more inclined, if not eager to adopt (and support, nurture, and further) BMIs and other forms of emerging neuroS/T for use in healthcare, various occupations, the general population, and military and intelligence personnel. This then raises the specter of if—and to what extent—such enterprises could be viewed, solicited, and used to influence local and global bioeconomies, and the relative balance(s) of power yielded by position and prominence within these hierarchies.

In the coming years, it is likely that such neuroS/T will become more available, effective, and employed. Using and/or modifying neuroS/T while requiring specific disciplinary expertise (e.g., bioengineering, neurosurgery, computational neuroscience, etc.), will not pose excessive difficulty, given that several nations:

- already have neuroS/T programs that are—and could be—devoted to military and intelligence efforts;
- have relatively seamless integration of governmental, research/academic, and industrial sectors’ “triple helix” that facilitate rapid throughput of S&T R&D for economic and military/intelligence agendas that could be engaged in non-kinetic and/or kinetic operations; and
- have differing cultural values and ethical norms and mores that may enable more rapid research timelines, and broader translation and use in these ways.

Recommendations

In sum, it is not a question of whether neuroS/T will be utilized in military, intelligence, and political operations, but rather when, how, to what extent, and perhaps most importantly, whether or not the US and its allies will be prepared to address, meet, counter, or prevent these risks and threats. In this light (and based upon the information presented in this report), it is and will be increasingly important to address the complex issues generated by the brain sciences’ influence upon global biosecurity and the near-term future scope and conduct of both non-kinetic and kinetic military and intelligence operations (DeFranco et al., 2019).

Thus, if the US and its international allies seek to retain a leading role in the global balance(s) of power, it will be essential to establish and sustain an iterative stake in the funding, guidance, and oversight of brain sciences in national security, intelligence, and defense operations. This is particular important given the recent opinion statement and recommendation(s) of the Task-Force on Dual-Use Neuroscience of the European Union Human Brain Project (EU-HBP), which advocated that any/all R&D projects, outcomes, techniques, and tools conducted under the auspices and support of the HBP not be utilized in/for military and/or intelligence (or other forms of security and defense) initiatives or operations (Evers et al., 2017). While noteworthy for its pacifist stance and advocacy, the unavailability of these state-of-the-art developments to the collaborative US-NATO mission (and the publication/dissemination of these studies and methods in the international scientific literature) essentially create an opportunity for competing nations to usurp and exploit such developments for use in their own military, intelligence, and political programs, projects, and operations.

Therefore, the following steps are recommended:

- recognition that brain science can and will be developed and used for non-kinetic and kinetic WINS engagements;
- acknowledgement that other countries may employ different ethical systems to govern neuroscientific research and development. This will mandate a rigorous, more granular, and dialectical approach to negotiate and resolve issues and domains of ethical dissonance in multinational/international biosecurity discourses;
- ongoing review and evaluation of national intellectual property laws, both in relation to international law(s) and in scrutiny of potential commercial veiling of dual-use enterprises;
- ongoing surveillance of international activities in brain science and their dual- and direct-use in military and intelligence operations;
- identification and quantification of current and near-term risks and threats posed by such enterprise(s);
- assessment of extant capabilities and gaps in US (and its allies') infrastructure and function(s) relevant to maintaining a stance of biosecurity preparedness, readiness, and response;
- proactive bridging or de-limiting of gaps in biosecurity infrastructure and function so as to establish and sustain readily active resources, mechanisms, and policies to mitigate existing and near-term threats;
- dedication of resources for developing and sustaining US (and allied nations') capabilities to prevent escalation of future risk and threat by (1) continued surveillance, (2) organizational and systemic preparedness, and (3) conjoinment of any/all entities necessary to remain apace with and/or ahead of tactical and strategic competitors' and adversaries' capabilities in this space; and
- a US program (or network of programs) to:
    - coordinate governmental, academic, and industrial sectors to study and evaluate current and near-future risks and threats;
    - establish (titular US government and allied) institutes/centers specifically dedicated to these pursuits, so as to obviate burden of participation/responsibility from any/all

academic and other scientific institutions that are operating within/under current guidelines proscribing dual- or direct-use/involvement with military/defense initiatives;

- defend US and allied interests from these threats; and
- develop methods to exploit competitors' gaps and weaknesses in these domains so as to maintain a favorable balance of power (in and across socio-economic, political, and military domains) in global engagements.

Development and coordination of a *whole-of-nation* (versus merely whole-of-government or military) approach to mobilize the organizations, resources, and personnel required to meet global competitors and potential adversaries' synergistic triple helix capabilities for advancing neuroS/T that is viable and valuable in military and intelligence operations.

Acknowledgements

This report was based upon and adapted (with permission) from Dr. Giordano's prior work with François du Cluzel contributing to the NATO Innovation Hub June-November 2020 *Cognitive Warfare* whitepaper. Dr. Giordano's ongoing work is supported by NATO; the Henry Jackson Foundation for Military Medicine; Leadership Initiatives; Brain NeuroBio International; Coburg University Distinguished Visiting Professorship in Biotechnology, Health Promotions, and Ethics; and federal funds 2UL1TR001409-06 from the National Center for Advancing Translational Sciences (NCATS), National Institutes of Health, through the Clinical and Translational Science Awards (CTSA) Program, a trademark of the US Department of Health and Human Services and part of the Roadmap Initiative, "Re-Engineering the Clinical Research Enterprise."

References

Besser, R. (2020, March 5). As coronavirus spreads, the bill for our public health failures is due. *The Washington Post*. https://www.washingtonpost.com/opinions/as-coronavirus-spreads-the-bill-for-our-public-health-failures-is-due/2020/03/05/9da09ed6-5f10-11ea-b29b-9db42f7803a7_story.html

Chen, C., Andriola, J., & Giordano, J. (2018). Biotechnology, commercial veiling, and implications for strategic latency: The exemplar of neuroscience and neurotechnology research and development in China. In Z. S. Davis & M. Nacht (Eds.), *Strategic latency: Red, white and blue: Managing the national and international security consequences of disruptive technology* (pp. 12-32). Lawrence Livermore Press.

DeFranco, J., DiEuliis, D., Bremseth L. R., Snow, J. J., & Giordano, J. (2019). Emerging technologies for disruptive effects in non-kinetic engagements. *The Journal of the Homeland Defense & Security Information Analysis Center, 6*(2), 49-54.

DeFranco, J., DiEuliis, D., & Giordano, J. (2019). Redefining neuroweapons: Emerging capabilities in neuroscience and neurotechnology. *PRISM, 8*(3), 48-63.

DeFranco, J., & Giordano, J. (2020). Mapping the past, present, and future of brain research to navigate the directions, dangers, and discourses of dual-use. *EC Neurology, 12*(1), 1-6.

DeFranco, J., Rhemann, M., & Giordano, J. (2020). The emerging neurobioeconomy: Implications for national security. *Health Security, 18*(4), 66-80. https://doi.org/10.1089/hs.2020.0009

DiEuliis, D., & Giordano, J. (2016). Neurotechnological convergence and "big data": A force-multiplier toward advancing neuroscience. In J. Collmann & S. A. Matei (Eds.), *Ethical reasoning in big data*: *An exploratory analysis* (pp. 71-80). Springer.

DiEuliis, D., Lutes, C. D., & Giordano, J. (2018). Biodata risks and synthetic biology: A critical juncture. *Journal of Bioterrorism and Biodefense, 9*(1), 2-14. DOI: 10.4172/2157-2526.1000159

European Medical Agency & Heads of Medicines Agencies. (2017). *Guideline on good pharmacovigilance practices (GVP): Annex I - Definitions (Rev 4).* https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-annex-i-definitions-rev-4_en.pdf

Evers, K., Farisco, M., Giordano, J., & Salles, A. (2017). *Dual use in neuroscientific and neurotechnological research. A report on background, developments and recommendations for ethical address, assessment and guidance of Human Brain Project activities*. European Union Human Brain Project.

Gerstein, D., & Giordano, J. (2017). Rethinking the biological and toxin weapons convention? *Health Security, 15*(6), 638-641. https://doi.org/10.1089/hs.2017.0082

Giordano, J. (2014, October 28-29). *Intersection of "big data," neuroscience, and national security: Technical issues and derivative concerns* [Presentation]. 8th Annual Department of Defense (Joint Staff) Strategic Multilayer Assessment Conference, Washington, DC. https://nsiteam.com/social/wp-content/uploads/2015/12/A-New-Information-Paradigm-From-Genes-to-Big-Data-and-Instagram-to-Persistent-Surveillance...Implications-for-National-Security.pdf

Giordano, J. (Ed.). (2015). *Neurotechnology in national security and defense: Practical considerations, neuroethical concerns*. CRC Press.

Giordano, J. (2017a). Battlescape brain: Engaging neuroscience in defense operations. *The Journal of the Homeland Defense & Security Information Analysis Center, 3*(4), 13-16.

Giordano, J. (2017b). Neuroscience and technology as weapons on the twenty-first century world stage. In W. Aviles & S. Canna (Eds.), *Influence in an age of increasing connectedness* (pp. 58-66). Department of Defense, Joint Staff J3, Strategic Multilayer Assessment. https://nsiteam.com/social/wp-content/uploads/2017/10/17.08.04-Influence-in-an-Age-of-Rising-Connectedness_Public-Release-R.pdf

Giordano, J. (2017c, May 11). Weaponizing the brain: Neuroscience advancements spark debate.

National Defense Magazine. https://www.nationaldefensemagazine.org/articles/2017/5/11/weaponizing-the-brain-neuroscience-advancements-spark-debate

Giordano, J., Bremseth, L. R., & DeFranco, J. (2019). Dual- and non-kinetic use of Chinese brain science: Current activities and future implications. In N. Petersen (Ed.), *Chinese strategic intentions: A deep dive into China's worldwide activities* (pp. 55-62). Department of Defense, Joint Staff J3, Strategic Multilayer Assessment. https://nsiteam.com/social/wp-content/uploads/2019/10/SMA-Chinese-Strategic-Intentions-White-Paper-FINAL-01-Nov-2.pdf

Giordano, J., & Evers, K. (2018). Dual use in neuroscientific and neurotechnological research: A need for ethical guidance. *Advances in research ethics and integrity: Vol 4. Ethics and integrity in health and life sciences research.* Emerald Publishing Limited, Bingley. https://doi.org/10.1108/S2398-601820180000004009

Giordano, J., & Wurzman, R. (2014). Validity, viability and value of neuro-cognitive science and technology in operational intelligence and deterrence. In H. Cabayan & S. Canna (Eds.), *Multimethod assessment of ISIL* (pp. 87-94). Department of Defense, Joint Staff J3, Strategic Multilayer Assessment. https://nsiteam.com/social/wp-content/uploads/2016/01/Multi-Method-Assessment-of-ISIL.pdf

Jin, H., Hou L-J., & Wang, Z-G. (2018). Military brain science – How to influence future wars. *Chinese Journal of Traumatology, 21*(5), 277-280. https://doi.org/10.1016/j.cjtee.2018.01.006

Tennison, M., Giordano, J., & Moreno, J. (2017). Security threat versus aggregated truths: Ethical issues in the use of neuroscience and neurotechnology for national security. In J. Illes & S. Hossein (Eds.), *Neuroethics: Anticipating the future* (pp. 531-553). Oxford University Press.

Vaseashta, A., Braman, E., & Sussman, P. (Eds.). (2012). *Technological innovations in sensing and detection of chemical, biological, radiological, nuclear threats and ecological terrorism*. Springer Netherlands.

Wurzman, R., & Giordano, J. (2015). NEURINT and neuroweapons: Neurotechnologies in national intelligence and defense. In J. Giordano (Ed.), *Neurotechnology in national security and defense: Practical considerations, neuroethical concerns* (pp. 79-114). CRC Press.