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The use of chemicals as agents of war

Cassandra Granlund

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Øyvind Voie, *Research Manager*
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Summary

Military forces have used chemicals for centuries. This includes the use of chemical weapons, which appeared on battlefields throughout the 20th century, fentanyl as a “knock-out gas” in an anti-terror operation in Russia in 2002, and the use of amphetamine (per 2023) as a stimulant in the U.S. Air Force.

Besides destroying enemy forces and seizing territory, one of the objectives of war is to shape perceptions and beliefs, and gain political and social control over populations. To achieve this, chemicals or pharmaceuticals might be used to enhance the cognitive skills of own forces or degrade that of adversaries. Examples are psychoactive substances, neurotoxic chemicals and incapacitating agents. Such agents can be used adversely to affect cognitive abilities and the decision-making process causing harmful consequences. Thus, their use needs to be assessed from a cognitive warfare perspective.

Cognitive warfare aims to exploit cognition facets to disrupt, undermine, influence, or modify human and technological decisions. NATO Allied Command Transformation (ACT) defines cognitive warfare as activities conducted in synchronization with other instruments of power to affect attitudes and behavior by influencing, protecting, or disrupting individual and group cognition to gain advantage over an adversary. Its impact is across all operational domains. It represents the convergence of a wide range of advanced technologies and human factors and systems, such as artificial intelligence, neuroscience, biotechnology, and human enhancement, which NATO’s adversaries deliberately use in the 21st-century battlespace.

As adversaries can target humans’ ability and vulnerability to make timely and wise decisions and situational awareness adversely, it is crucial to understand the threats of such agents against military personnel and the civilian population/society. This report aims to contribute to the ongoing effort to advance our understanding of adversary cognitive warfare attack vectors by providing an overview of chemicals as agents of war, with a focus on their cognitive effects.

The main findings of this report are:

- The rapidly advancing field of drug development and drug delivery systems should be closely monitored due to the inherent dual-use issue of neuroscience.

- There is a wide range of chemicals that can be used to enhance or degrade cognition. However, there is a key challenge of controlled delivery and uptake for both the development and use of such agents.

- Research-based knowledge is needed to obtain a more in-depth understanding of potential cognitive weapons to counteract their development and the effects of chemicals that can affect cognition. This is critical because NATO’s adversaries do not necessarily operate under the same ethical standards and values as liberal democracies.

Sammendrag

I århundrer har militære styrker brukt kjemiske agens. Bruken inkluderer kjemiske våpen som er brukt på slagmarker gjennom det 20. århundre, fentanyl som en “knock-out gass” i en antiterroroperasjon i Russland i 2002, og bruk av amfetamin (pr. 2023) som et sentralstimulerende middel i det amerikanske luftforsvaret. Et av krigens mål er å ødelegge fiendtlige styrker og erobre territorium. Et annet krigsformål er å forme oppfatninger, og få politisk og sosial kontroll over befolkningen. Flere kjemikalier og legemidler kan brukes for å oppnå dette. De kan anvendes til å forbedre de kognitive ferdighetene til egne styrker eller forringer motstandernes. Eksempler er psykoaktive substanser, nevrotoksisike kjemikalier og inkapasiterende agens. Slike midler kan brukes til negativt å påvirke kognitive evner og beslutningsprosesser, og bruk må vurderes fra et kognitivt krigføringsperspektiv.

Kognitiv krigføring tar sikte på å utnytte ulike fasetter innenfor kognisjon for å forstyrre, undergrave, påvirke eller modifisere menneskelige og teknologiske beslutninger. NATO Allied Command Transformation (ACT) definerer kognitiv krigføring som aktiviteter utført i synkronisering med andre maktmidler for å påvirke holdninger og atferd ved å influere, beskytte eller forstyrre kognisjon på individuelt og gruppenivå for å oppnå en fordel over en motstander. Den kognitive krigføringen kan innvirke på tvers av alle operasjonelle domener. Den representerer konvergensen av et bredt spekter av avanserte teknologier og menneskelige faktorer og systemer. Eksempler på slike er kunstig intelligens, nevrovitenskap, bioteknologi og menneskelig forbedring, som Natos motstandere bevisst bruker i det 21. århundrets kamprom.

Det er avgjørende å forstå fordelene og truslene slike agens utgjør mot både militært personell og sivilbefolkningen. Dette er spesielt viktig fordi en motstander målrettet kan angripe menneskers situasjonsbevissthet, og påvirke ens evne til å ta hurtige og veloverveide avgjørelser. Rapportens formål er å bidra til den pågående innsatsen for å kartlegge motstanders mulige angrepsvektorer innen kognitiv krigføring ved å gi en oversikt over kjemiske agenser som kan påvirke kognisjon.

Hovedfunnene i denne rapporten er:

- På grunn av nevrovitenskapens iboende flerbruksproblematikk bør de raske framskrittene innenfor legemiddelutvikling og i ulike systemer for kontrollert levering av legemidler nøye holdes øye med.

- Det finnes et bredt spekter av kjemiske midler som kan brukes til å forbedre eller forringe kognisjon. Det er imidlertid en sentral utfordring med kontrollert levering og opptak, både for utvikling og bruk av slike midler.

- Det er behov for mer forskningsbasert kunnskap for å få en inngående forståelse av potensielle kognitive våpen for tilegnelse av informasjon om hvordan utviklingen og potensielle negative effekter av kjemiske agens som kan påvirke kognisjon kan motvirkes. Dette er viktig fordi Natos motstandere nødvendigvis ikke opererer under de samme etiske standardene og verdiene som liberale demokratier.

Contents

Preface

This report is a product of ongoing research programs at the Norwegian Defence Research Establishment (FFI) that aims to strengthen the Armed Forces' and civil society's knowledge of and the ability to prevent, protect against and manage intended and unintended incidents involving CBRNE means or weapons.

I want to thank the scientific experts who made this study possible. Special thanks to Dr. Gitanjali Adlakha-Hutcheon, Defence Scientist at the Department of National Defence in Canada, and my FFI colleagues Dr. Else Marie Fykse, Dr. Stig Rune Sellevåg, and Dr. Leif Haldor Bjerkeseth for their valuable and important contributions.

Cognitive warfare has been discussed for several years; however, there has been a rapidly growing interest in the topic in the last few years. The increased focus has led to the establishment of a NATO Allied Command Transformation (ACT) Concept and a NATO Science and Technology Organisation (STO) Collaborative Programme of Work (CPoW).

This report aims to contribute to the ongoing work of understanding adversary cognitive warfare attack vectors by reviewing scientific literature on chemicals as agents of war, with a particulate focus on how chemicals can be used to improve or adversely affect cognition. The report does not focus on biological agents or biotechnology. The report is a preliminary work on the topic and sheds light on potential concerns that merit further investigation.

Kjeller, 18 April 2023
Cassandra Granlund

Abbreviations

ACT	Allied Command Transformation
ADHD	Attention Deficit/Hyperactivity Disorder
AI	Artificial Intelligence
BWC	Biological Weapons Convention
BZ	3-Quinuclidinyl Benzilate
CA	Bromobenzylcyanide
CIA	Central Intelligence Agency
CN	Chloroacetophenone
CNS	Central Nervous System
CPoW	Collaborative Programme of Work
CR	Dibenzoxazepine
CS	Chlorobenzylidenemalononitrile
CW	Chemical Weapons
CWA	Chemical Warfare Agent
CWC	Chemical Weapons Convention
DMT	N, N-dimethyltryptamine
DURC	Dual-Use Research of Concern
GHB	Gamma-hydroxybutyrate
HPA	Human Performance Augmentation
HPE	Human Performance Enhancement
HPO	Human Performance Optimization

JNLWD	Joint Non-Lethal Weapons Directorate
LSD	Lysergic Acid Diethylamide
MCDC	Multinational Capability Development Campaign
NPS	New/novel/emerging Psychoactive Substances
OP	Organophosphate
OPCW	Organisation for the Prohibition of Chemical Weapons
PBA	Pharmaceutical Based Agent
PCP	Phencyclidine
PS	Chloropicrin
RCA	Riot Control Agents
R&D	Research and Development
STO	Science and Technology Organisation
TIC	Toxic Industrial Chemical
UN	United Nations
VX	O-Ethyl S-(2-diisopropylaminoethyl) methylphosphonothioate
WWI	World War I
WWII	World War II

1 Historical use of chemicals as agents of war

1.1 Chemical warfare agents

According to the Convention on the Prohibition of the Development, Production, Stockpiling and Use of Chemical Weapons and on Their Destruction (The Chemical Weapons Convention, CWC), a "toxic chemical" is any chemical which through its chemical action on life processes can cause death, temporary incapacitation or permanent harm to humans or animals (See Chapter 6 for more details). This definition is the foundation for this reports discussion of "chemical agents." Chemical agents are a spectrum of toxic chemicals that range from toxic industrial chemicals (TICs), pesticides, toxins, and bioregulators to "chemical warfare agents" (CWAs), with some terminological overlap. The term "chemical weapons agents" is in this report characterized as the subset of chemical agents that have been or are being created, produced, stockpiled, or used as chemical weapons. CWAs are extremely toxic synthetic chemicals that can be dispersed as a gas, liquid, or aerosol or as agents adsorbed to particles to become a powder (Ganesan et al. 2010). The CWAs have either lethal or incapacitating effects on humans (Aas 2003). Table 1.1 shows a list of different CWAs with their primary symptoms and examples of use.

The industrial revolution and the expansion of industrial chemistry during the 19th century made mass production and deployment of chemical warfare agents possible in warfare. During World War I (WWI), the use of toxic chemicals such as phosgene, sulfur mustard, and lewisite resulted in 1.3 million casualties. Chemical weapons appeared on battlefields throughout the 20th century, including in the Russian civil war in 1919, and in conflicts in North Africa (1920s), Abyssinia (1930s), and Manchuria (1930s and 1940s) (Tucker 2008, Schmaltz 2017). The Germans forever changed chemical warfare by discovering organophosphorus nerve agents before World War II (WWII). Nerve agents are highly toxic and can cause death within a few minutes to hours after exposure, depending on concentration and route of exposure.

The Germans produced and stockpiled large amounts of nerve agents throughout WWII, including tabun, sarin and soman, but for tactical and unknown reasons, they were never used (Tucker 2008). Significant use of chemical weapons since WWII repeatedly occurred in the Syrian civil war between 2012 and 2018 (Schneider and Lütkefend 2019, OPCW 2022) and in the 1980s during the Iran-Iraq war, where Iraqi troops employed sulfur mustard and nerve agents against both Iranian and Kurdish military personnel and civilians. The use of chemical warfare agents on the Kurdish civilian population of Halabja killed 5,000 civilians (Smart 1997).

Generally, chemical warfare agents are easier to protect against, harder to contain, and are no more deadly (and often less so) than high explosives. As agents of terror, though, whether delivered by dysfunctional states against rebel populations or by irregulars against civilians under the protection of their target governments, they are a potent tool (The Economist 2022). Additionally, some chemical warfare agents are relatively easy to produce, which makes them attractive to terrorists as weapons, made particularly evident by the sarin attacks by a Japanese cult in Matsumoto city (1994) and the Tokyo subway system (1995), causing 5,500 injuries and 12 deaths. Fortunately, the delivery method was ineffective and prevented mass causalities. However, the group also succeeded in producing tabun, soman, VX and botulinum toxin (Okumura et al. 1998).

Table 1.1 Chemical warfare agents used in war and conflict. Modified from Gupta (2015) and Pacsial-Ong and Aguilar (2013).

Chemical warfare agent		**Symptoms**	**Examples of use**
Blood agents	Hydrogen cyanide	Dizziness, mental confusion, cardiac and respiratory distress, seizures.	Used by Nazis in concentration camps during WWII (Lee 1997).
	Cyanogen chloride		
Blistering agents (Vesicants)	Sulfur mustards	Tissue blistering, damaging respiratory tract, vomiting.	During WWI and the Iran-Iraq war (Haines and Fox 2014).
	Nitrogen mustard		
	Lewisite		
Choking agents	Phosgene	Attack lung tissue, cause edema.	During WWI and the Syrian civil war (Schneider and Lütkefend 2019).
	Chlorine		
Nerve agents	Tabun	Muscular cramps, cardiac arrhythmias and death due to respiratory paralysis (Ganesan et al. 2010). VX is more potent, stable, and less volatile and water-soluble than previously developed nerve agents (Newmark 2009).	In the 1980s, during the Iran-Iraq war, sarin attacks in Matsumoto city (1994) and the Tokyo subway system (1995). Syrian civil war (Schneider and Lütkefend 2019). Poisoning of the half-brother of North Korea's leader Kim Jong-Un with VX (2017) (Chai et al. 2017). Poisonings in Salisbury in 2018 and of Alexei Navalny in 2020 using Novichok (Brunka et al. 2022).
	Sarin		
	Soman		
	Flouride-containing organophosphate		
	VX		
	Novichok		

1.2 Incapacitating agents

In contrast to "classical" chemical warfare agents' exposure, which often is lethal, incapacitants ideally have only temporary incapacitating effects. According to Blain (2009), an ideal incapacitant is a compound that rapidly produces total incapacitation or disruption of a specific capability in an individual or group; is reversible over time, or by specific treatment, without any residual adverse effects; does not compromise survival or safety, and is predictable. Additionally, it must be capable of deployment and targeted delivery. Table 1.2 summarizes the properties of the below-mentioned agents, and Figure 1.1 illustrates the overlap among them.

Historically, lachrymators were first used as riot control agents (RCAs) in military settings during the early 1900s, in order to incapacitate (Smart 1997). Following World War II and in the coming decades, incapacitating agents were of extreme interest. The U.S. Military and the Central Intelligence Agency (CIA) particularly focused on psychochemical warfare research and overlapping mind control drug research in the context of the Cold War (Strassman 1999). The research focused on developing incapacitating agents using chemicals that could alter or impair the brain's function. Some initially saw these as a panacea to make warfare safe and humane (Department of Defense 1998).

Although several promising compounds were extensively studied, such as the psychotropic agents lysergic acid diethylamide (LSD) and methedrine, and psychotomimetic agents including 3-quinuclidinyl benzilate (BZ), only the latter was ever standardized as a weapon (Aas 2003, Ketchum 2006). Psychotomimetic agents are drugs that mimic the symptoms of psychosis, including delusions and delirium, as opposed to only hallucinations (Fusek et al. 2020). In contrast to previously used chemical warfare agents, BZ was developed without the intention of taking human lives, but rather cause temporary incapacitation (Fusek et al. 2020). However, due to the complex and unpredictable psychological effects, LSD and BZ were considered too unreliable for military use and were ultimately discontinued in usage (Blain 2009).

There are already significant numbers of known harmful chemicals and examples of their weaponization; fentanyl, for example, which is an opioid anesthetic and painkiller (Lindsay et al. 2016, Forman and Timperley 2018) and may impact cognition. The idea of opioid-based chemical weapons dates back to the discovery of fentanyl in 1960. Fentanyl and several fentanyl analogs were the focus of extensive U.S. military research from the 1970s through the 1990s, including inhalation studies on non-human primates to develop novel incapacitating agents "for situations where a quick knock-down agent is needed" (Pearson 2006). The lethality of fentanyl is comparable to that of the organophosphorus nerve agents if used without medical support (Worek et al. 2016).

Opioid agents have not been used in large-scale terrorist attacks. However, the potential of these agents as mass incapacitants that consequently can cause mass casualties was demonstrated in October 2002 when the Russian military Special Forces used a combination of synthesized fentanyl analogs (Kolokol-1) to end a siege where Chechen separatists had taken over 900 hostages in a Moscow theater (Blain 2009, Lee and Kulkarni 2016). An overdose accidentally killed more than 120 hostages during the rescue attempt by the Russian forces (Wax et al. 2003). Kolokol-1's devastating results did not discourage Russian authorities from utilizing synthetic opioids to counter other domestic terrorist groups. In 2005, Russian Special Forces used an unidentified aerosol chemical against militants holding hostages in a local business. The aerosol is believed to contain carfentanil and remifentanil, similar to the Kolokol-1 cocktail used in the Moscow theatre (Lee and Kulkarni 2016, Mörén et al. 2021).

Another category of pharmaceuticals that can cause incapacitation (depending on the specific drug and dosage), including effects such as blurry vision, sedation, hallucinations, memory problems and confusion, is anticholinergic compounds. The medical use of these agents is diverse and ranges from treating seasickness to poisoning caused by organophosphates (Dawson and Buckley 2016). There are many myths regarding the use of one of the most infamous anticholinergic drugs, scopolamine, also known as "Devil's Breath." The alleged side effects of exposure include being able to remove a person's free will or incapacitate people in a "zombie-like" state. Scopolamine is one of five drugs reported in the scientific literature to be most often associated with drug-facilitated sexual assault. In South America, where it is known as burundanga, criminals have been using it to rape, rob and kidnap victims for decades (Negrusz et al. 2005, Saner 2015). Additionally, the U.S. Embassy in Colombia warns visitors to be aware of scopolamine because it is used to incapacitate and rob victims (U.S. Embassy in Colombia 2021).

1.3 Human enhancement

Human enhancement is the process to augment physical form or cognitive, physiological, sensory, or social functions beyond baseline performance. By extension, human augmentation is an amplification of performance above the baseline (NATO 2022c). The Multinational Capability Development Campaign (MCDC) defines human performance augmentation (HPA) as the application of science and technologies to temporarily or permanently improve human performance. HPA can be further divided into human performance optimization (HPO) and human performance enhancement (HPE), where the former allows individuals to reach their biological potential, and the latter allows individuals to exceed it (MCDC 2021).

Humankind has successfully used stimulants to enhance alertness in military operations for a long time; one of the earliest examples is the Inca warriors' use of coca leaves many centuries ago, whereas a more modern example is the use of amphetamine (Royal Society 2012). World War II is considered the most pharmacologically enhanced war due to the mass consumption of amphetamines and their war-facilitating psychoactive effects (Andreas 2020). The U.S. Air Force sanctioned amphetamine use in 1960, and U.S. military aircrew and ground personnel used amphetamines during the Vietnam War and the Gulf War in the 1990s. The Air Force continues to approve the use of amphetamine in specific operational scenarios (Ehlert and Wilson 2021).

Science and technology to maximize human performance is not new and is a recognized and often essential feature of armed forces' operations (Brunyé et al. 2020, Sattler et al. 2022). Moreover, investments to improve a warfighter's physical and cognitive capacity and performance are critical to maintaining a competitive advantage and overcoming threats from their adversaries (NATO 2020). As a result, there is a considerable focus on enhancing the warfighter, with, e.g., the Pentagon spending 400 million dollars yearly (per 2011) on enhancement research (Hanlon 2011).

The human performance optimizations with the widest use and longest history, though often not commonly recognized as such by the public, are, in all likelihood, behavioral strategies (Dresler et al. 2019). An increasing body of evidence shows that everyday activities like sleep and physical exercise improve cognitive functioning (Phillips 2017, McSorley et al. 2019, Sewell et al. 2021). Musical training, dancing, and learning a second language are also well-established cultural practices that have been shown to improve cognition beyond the specifically trained skills (Bialystok et al. 2012, Benz et al. 2016, Predovan et al. 2019).

Regarding human enhancement drugs, some of the most common include high doses of caffeine and synthetic stimulants such as amphetamine, methylphenidate (Ritalin) and modafinil (Dresler et al. 2019). Stimulants are psychoactive drugs that enhance alertness, attention, concentration, and energy while boosting mood, heart rate, and blood pressure (Romach et al. 2014). Stimulants are among the best-understood and most useful drugs for military use, especially in emergencies when sleep is impossible (Caldwell et al. 2009). Other human enhancement drugs include mood and behavior enhancers (e.g., Diazepam and low doses of GHB) (Blain 2009, Evans-Brown et al. 2012), and caffeine and nicotine, culturally accepted drugs in western society (Pesta et al. 2013).

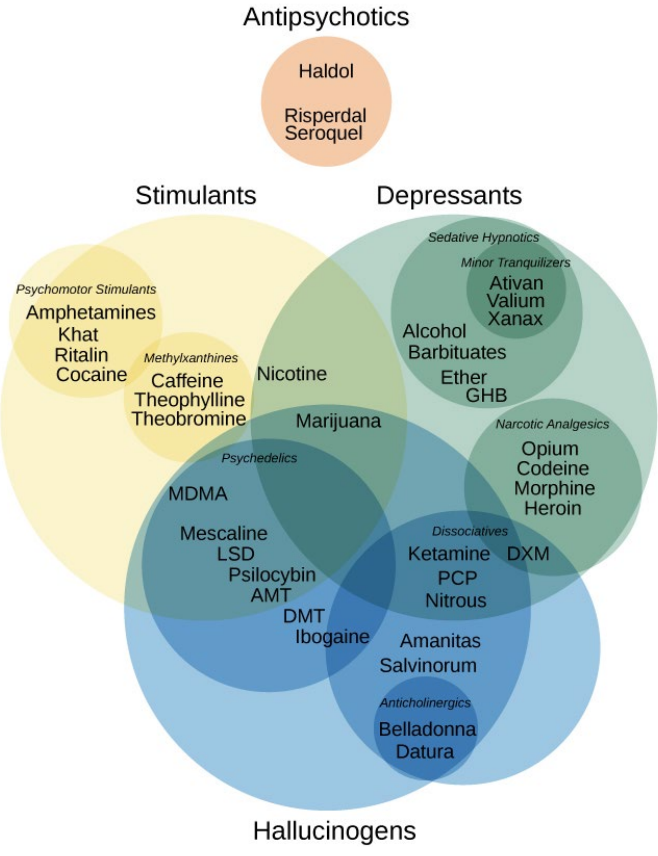

Figure 1.1 The illustration shows different pharmaceutical categories (Table 1.2) in each circle and the overlap between them. It shows that the effect of a given substance can be diverse. There are examples of drugs within each category. Credit: Derrick Snider, Rice University.

Table 1.2 Brief summary of chemical agents that can impair or enhance cognitive functions and/or alter emotional states (Dawson and Buckley 2016, Dresler et al. 2019, Brunyé et al. 2020, Petersen et al. 2020).

Chemical agent		**Effects/side effects**	**Examples of use**
Anticholinergics	Include atropine, scopolamine, tricyclic antidepressants and antipsychotics.	Memory problems, confusion, lessen ability to concentrate, blurry vision, rapid heart rate.	Atropine autoinjector has been in use since 1973 (U.S.) for the treatment of exposures to chemical warfare nerve agents and insecticides (Lofton 2005).
Calmatives/depressants	Include sedative-hypnotic agents (e.g., benzodiazepines, barbiturates), anesthetic agents, skeletal muscle relaxants, opioid analgesics, antipsychotics, antidepressants, and anxiolytics.	Diverse, can include deep sedation, hypnosis, and lethal overdose.	Synthesized fentanyl analogs used in Moscow theater siege in 2002, killing over 120 hostages (Wax et al. 2003).
Hallucinogens/ psychedelics	LSD, psilocybin, peyote, DMT, dissociative agents (PCP, ketamine), NPS, salvia.	Profound changes in auditory and visual perception, the experience of time or space, alterations in moods, thoughts, judgment, memory, and other mental states. Can cause paranoia, psychosis, disorientation, memory loss, seizures, and depression.	Microdosing psychedelics to enhance cognitive performance, mood, energy and creativity (Liokaftos 2021). Extensive LSD testing by the U.S. Army 1955-1967 (Ross 2017).

Human enhancement drugs	Stimulants. High doses of caffeine, nicotine, amphetamine, methylphenidate (Ritalin), atypical stimulants (modafinil), mood and behavior enhancers (e.g., Diazepam and low doses of GHB).	Enhance alertness, attention, concentration, and energy while boosting mood, heart rate, and blood pressure	Mass consumption of amphetamines during World War II (Andreas 2020), used by U.S. military aircrew and ground personnel during the Vietnam War and the Gulf War in the 1990s, and currently used by the U.S. Air Force in specific operational scenarios (Royal Society 2012).
Psychotomimetics	Cannabis, BZ.	Chemical agents that reliably and dose-dependently induce a psychosis or schizophrenia-like illness, often including hallucinations and delusions in normal individuals. Implicit in this term is a mimicking of naturally occurring psychosis.	BZ was tested on human subjects in Utah under the codename "Project Dork" in the early 1960s and later in Hawaii between 1966 and 1967 (Harris and Paxman 1982). BZ was subsequently weaponized until stocks were destroyed in the early 1990s (Misik 2013).
Riot control agents	CN, CS, PS, CA, CR and combinations of various agents.	Irritate eyes, mouth, skin and upper respiratory system.	World War I, Vietnam war, Iran-Iraq war, currently commonly used by law enforcement agencies and military (Hilmas et al. 2009).

2 Chemicals as agents of cognitive warfare

Besides destroying enemy forces and seizing territory, one of the objectives of war is to shape perceptions and beliefs and gain political and social control over populations. The hostility aims toward maintaining psychological and informational control. Terms like information-, political-, and cognitive warfare are often used to describe this phenomenon (Blank 2013, Bernal et al. 2020). The concept of "cognitive warfare" creates a new arena for competition beyond the land, sea, air, cybernetic, and geographical domains opponents have previously incorporated. Cognitive warfare has gained significant traction in the last two years, particularly within NATO's Allied Command Transformation (ACT) and NATO's Science and Technology Organization (STO) (Cowles and Verrall 2023). NATO ACT defines cognitive warfare as activities conducted in synchronization with other instruments of power to affect attitudes and behavior by influencing, protecting, or disrupting individual and group cognition to gain advantage over an adversary (NATO 2022a). In cognitive warfare, the human mind becomes the battlefield (Cluzel 2020, Cao et al. 2021), and has the goal to exploit cognition facets to disrupt, undermine, influence, or modify human and technological decisions (NATO 2022b). Its fundamental essence is acquiring control of civilians, military personnel, organizations, and nations, as well as ideas, psychology, behavior, and thoughts.

The topic cognitive warfare may focus on how information, social engineering, and psychology can be used on the internet and in social media to sow doubt, introduce conflicting narratives, polarize opinions, radicalize groups, and motivate acts that can disrupt or fragment an otherwise cohesive society (Cao et al. 2021, NATO 2023). In addition, several chemical agents can be used to impair or enhance cognition, affect emotion, and behavior, and thereby supplement the ongoing form of cognitive warfare. For example, many pharmaceuticals and incapacitants can enhance or impair nervous system functions, such as motor activity and other capabilities necessary for combat, e.g., perception, judgment, morale, pain tolerance, or physical abilities and stamina (Ketchum and Sidell 1997, U.S. Army et al. 2005, Balali-Moo et al. 2014).

Additionally, computational neuroscience and neuropharmacological research can be used indirectly to simulate, interact with, and optimize brain functions, as well as to detect emotional and motivational states, in order to boost intelligence or counterintelligence operations (Cluzel

2020, Khaleghi et al. 2022, Wurzman and Giordano 2014). Neuroscience- and technology can be utilized to affect (Cluzel 2020, Giordano and DiEuliis 2021):

- Memory, learning, and cognitive speed
- Wake-sleep cycles, fatigue, and alertness
- Impulse control
- Mood, anxiety, and self-perception
- Decision-making
- Trust and empathy
- Movement and performance (e.g., speed, strength, stamina, motor learning)

Modifying these functions in military/warfare circumstances might reduce aggression, promote cognition and emotions of affiliation or passivity, reduce fatigue, increase learning, cause morbidity, impairment, or pain, and "neutralize" potential opponents or incur fatality (Cluzel 2020, NATO 2022b, Zilincik 2022).

Hostile exploitation of chemical technologies, combined with a creeping legitimization of chemical weapons, threatens to introduce such weapons to twenty-first-century conflicts (Ilchmann and Revill 2014, NATO 2022d). Furthermore, incremental and interconnected advances in science and technology expand the possibility of new chemical capabilities. There is an increasing trend to integrate multiple disciplines, including chemistry, biology, information technology, mathematics, and engineering sciences. The integration coupled with the rapid progress in the availability and power of enabling technologies, the widespread research capacity across the globe and to actors outside of a traditional research setting, can give rise to new avenues of attack and the misuse of knowledge (Chai et al. 2022, NATO 2022b, Urbina et al. 2022).

3 Chemicals’ adverse effects on the brain

The human brain, a three-pound organ, is the most complex structure known in the universe (Yuste 2014). Like any complex machine, the brain contains many parts, each of which has subparts, which themselves can be broken down into smaller units, all the way down to the "nuts and bolts" – the neurons. Everything a person thinks and does results from the processes in these 100 billion neurons (Fischbach 1992). The brain is the seat of intelligence, interpreter of the senses, initiator of body movement, and controller of behavior. Being one of the hardest working organs in the body makes it an energy-hungry organ, which gobbles up more than 20% of the body's daily energy intake. Therefore, to maintain a healthy brain and cognition, factors such as a nutritious diet, being psychically active, avoiding smoking, having no diseases, and getting enough sleep are essential (Figure 3.1) (Magistretti and Allaman 2015).

On the other hand, a wide range of factors and compounds can be harmful or toxic to the central nervous system and human cognition, including drugs, stress, diseases and chemical substances. Xenobiotics are chemicals an organism is exposed to that are extrinsic to the normal metabolism of that organism (Spencer and Lein 2014, Scott et al. 2015). The nervous system has unique biochemical and physical properties that may contribute to its susceptibility to xenobiotics (Patterson et al. 2010). For example, many xenobiotic agents, such as drugs, environmental pollutants, pesticides and chemical warfare agents, cause neurotoxic effects (Figure 3.1). In some cases, the effects of toxic compounds are caused by direct interactions between the compound and specific targets within the nervous system, while in other cases, there is not a specific target, but rather a more general damage to the tissue. In yet other cases, effects on other organ systems can indirectly impair neurologic function (Wright et al. 2009). The central nervous system has a limited capacity for repair or regeneration; therefore, even minor damage can cause long-term effects (Freed et al. 1985, Tian et al. 2015, Nagappan et al. 2020).

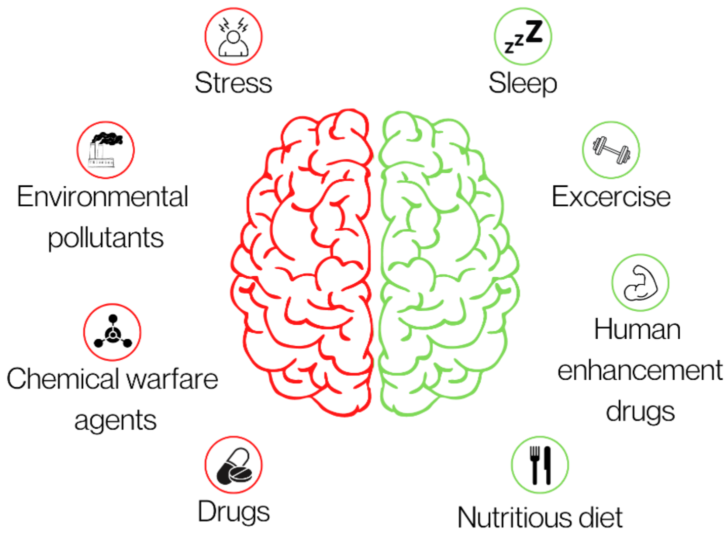

Figure 3.1 Illustration of some factors and compounds that can be harmful to human cognition (in red) or improve cognition (in green). Cassandra Granlund, FFI.

Another complicating issue in the field of neurotoxicology is that drug effects in individual humans arise from interactions of multiple factors, including (but not limited to):

- The drug itself
- Dose and route of exposure
- The demand characteristics of the current situation
- The individual's health, physiology, sex, and prior experience with drugs and performance demands.

Further, some neurotoxic agents are nontoxic at "normal" concentrations and do not cause apparent neurological effects. Most xenobiotic agents are metabolized to inactive compounds, eliminated, or both, in healthy adults, such as military personnel. However, agents may accumulate over time and thus reach toxic levels, which could be due to prolonged exposure or insufficient metabolism and/or elimination. In addition, brief exposure may cause alterations that are not readily detectable in the early stages but may manifest much later (Wallace 2009). Additionally, the possibility of unexpected changes in drug structure, targets, delivery, methods of action, combinations with other drugs, and shifting performance conditions complicates the attempts to predict the effects of novel drugs (National Research Council 2008). Advances in understanding the brain and the nervous system and developments in neuropharmacology, functional neuroimaging, human-machine systems, and related areas will enable improved treatment of neurological impairment, disease, and psychiatric illness (Royal Society 2012). However, it can also give rise to novel cognitive weapons.

4 Trends and advances in the use of chemicals as agents of war

Historically, nerve agents (Table 1.1) and various drugs, pharmacologic stimulants, sedatives, and sensory stimulation (Table 1.2) have been used to kill, incapacitate the enemy, cause sleep deprivation, and distribute emotionally provocative information in psychological operations (DeFranco et al. 2019). The operational significance of chemical weapons encompasses the agents' primary physiological effects, such as incapacitation, debilitation, and lethality. On the other hand, secondary effects of chemical weapons use may include economic damage, such as contamination of land, machinery, or crops, as well as psychological and social impacts of terrorizing. The psychological consequences of wars are especially important since they can have a disproportionately more significant strategic impact than the primary effects of actual use, not least because chemical weapons evoke a distinct kind of terror (Erikson 1994, Krieger and Rogers 2013).

This chapter further addresses how current and novel chemicals, mainly incapacitants, can be used to temporarily or permanently modulate cognition based on a literature review.

4.1 Agents causing cognitive impairment: Human degradation

Many unconventional warfare tactics related to cognition and hybrid warfare could be deployed. For example, an adversary might consider exposing people to neurotoxic compounds, introducing psychoactive chemicals into the food supply, spraying metallic nanoparticles that are ingested and debilitate the brain and CNS, or use ionizing and non-ionizing radiation (Bushnell 2001, Krishnan 2016). In today's society, many substances are highly toxic and widespread, such as organophosphate (OP) based pesticides, fire retardants, and prescription medications (Johnson et al. 2009). The widespread use of OPs is a growing environmental concern because accidental and deliberate exposure to OPs has been linked to adverse health effects for decades. These effects include long-term neurological and psychiatric disorders, such as impairments in attention, memory, and other cognitive domains (Naughton and Terry Jr 2018).

Further examples include an adversary exposing the population of an enemy state to chemicals causing damage to the developing nervous system and intentionally causing adverse effects on the cognition of the coming generation. Developmental neurotoxic compounds include lead, arsenic, polychlorinated biphenyls, ethanol, flame-retardants and methylmercury (Grandjean and Landrigan 2014). The latter is infamously known to cause Minamata disease (Harada 1995). Additionally, researchers have found that toddlers exposed to particulate matter from air pollution score lower on IQ tests (Ni et al. 2022).

Novel chemicals are constantly being discovered, and there are more theoretically possible chemical structures with drug-like properties than atoms in the universe, making the weaponization of new toxic substances a continuous possibility (Lindsay et al. 2016). Furthermore, artificial intelligence with drug-discovery software can be misused to create new and more toxic chemicals and pharmaceuticals (Urbina et al. 2022). A category of substances worth noting in this regard is new/novel/emerging psychoactive substances (NPS), meaning drugs that are not controlled by the United Nations' 1961 Narcotic Drugs/1971 Psychotropic Substances Conventions and may pose a threat to public health (Corkery et al. 2020). These NPS include (Schifano et al. 2015, Schifano et al. 2021):

- Synthetic cannabinoids/cannabimimetics
- New synthetic opioids
- Ketamine-like dissociatives
- Novel stimulants and psychedelics
- Prescription and over-the-counter medicines

NPS might be of interest in warfare due to their constant innovation and unregulated distribution and use. For example, higher doses of synthetic cannabinoids can cause auditory/visual hallucinations, intense feelings of paranoia, and suicidal ideation (Glue et al. 2013, Bonaccorso et al. 2018). New synthetic opioids can cause mood lift, dysphoria, dissociation, and intense sedation (Solimini et al. 2018). Phencyclidine (PCP, "angel dust") can cause acute psychopathological symptoms such as memory impairments, slowness, anxiety, psychosis, and violent behavior (Schifano et al. 2015, Tracy et al. 2017). Designer benzodiazepines have recently emerged and can be several times more potent than Diazepam (Tracy et al. 2017). The side effects of designer benzodiazepines include amnesia, long-lasting (60 h) confusion and disorientation, dizziness, loss of coordination, drowsiness, blurred vision, slurred speech, and ataxia (Baumeister et al. 2015).

4.1.1 Bioregulators

Advances in neuroscience have also increased our understanding of receptor systems on nerve cells that are critically important in receiving chemical transmitter substances released by other nerve cells (Bokan et al. 2002). Bioregulators are natural organic compounds that regulate diverse cellular processes in all organisms. They regulate normal and critical biological processes, such as blood pressure, respiration, mood control, emotions, immune responses and sleep. The main groups of bioregulators are cytokines, eicosanoids, neurotransmitters, hormones, and proteolytic enzymes (Bajgar et al. 2020).

Bioregulators are currently considered to be prospective incapacitating agents, and their research is being performed by scientific teams worldwide (for example, in the United States, Great Britain, France, Russia, China, and Israel), which increases the potential for the use of bioregulators as incapacitating agents (Pitschmann 2014). For example, according to research conducted by the Swedish Defense Research Establishment on the effects of aerosolized peptide Substance P, it may be possible to engineer more stable aerosolized bioregulator molecules that are able to cross the blood-brain barrier (Koch et al. 1999, Wheelis and Dando 2005, Bajgar et al. 2020). If so, bioregulators can induce a state of sleep, conduction, or placidity, with potential applications in law enforcement, counterterrorism, and urban warfare (Tucker 2009, Royal Society 2012). Endorphins and enkephalins are other examples of bioregulators that have potential use as biochemical agents. These are so-called "hormones of happiness", which are opioid polypeptides excreted in the course of physical stress that can block pain or induce feelings of peace of mind (Kagan 2001, Pitschmann 2014).

4.2 Agents causing cognitive improvement: Human enhancement

Investigating pharmacological agents intended for incapacitation may also reveal how manipulation of similar mechanisms can be employed to improve rather than degrade performance. For example, many military tasks, particularly in operational theatres, require personnel to remain alert and attentive over extended periods in anticipation of an emergency or a surprise attack. The military is often at the cutting edge of research, contributing significant resources to research and development (R&D). Various research programs attempt to either maintain peak performance in the face of environmental and operational stressors or amplify performance beyond existing capacities (Brunyé et al. 2020, Sattler et al. 2022).

In addition to drugs that stimulate neurotransmission, drugs with novel mechanisms that modulate the action of neuroreceptors are promising. Compounds such as ampakines have been created as cognitive enhancers that, for example, can in the future be used to: treat ADHD symptoms, such as inattention and impulsivity; alleviate exhaustion due to sleep disorder; and improve memory and cognitive performance (Urban and Gao 2014, Marois and Lafond 2022). Military-funded initiatives have investigated ampakines for memory and alertness improvement, with promising results in non-human primates. The study showed that ampakines proved effective in alleviating impairment of performance due to sleep deprivation, in addition to enhancing cognitive performance under normal alert conditions (Porrino et al. 2005, Hampson et al. 2009).

Hypocretin (orexin) is yet another promising performance-sustaining intervention, having a fundamental role in sleep-deprived brains, and also the subject of French military investigations of sleeping sickness (Dauvilliers et al. 2008, Dauvilliers 2021). However, the human mind is not a monolithic entity but consists of various cognitive functions. Therefore, it should come as no surprise that no single cognitive enhancer can augment every cognitive function. Instead, most cognitive enhancers have specific profiles regarding their efficacy for different cognitive domains (Dresler et al. 2019).

A better understanding of human physical, psychological, and social capabilities and capacities is necessary to develop and implement human enhancement measures. Research-based knowledge is needed to understand the dynamics of the human biome and the impact of nutrition, hydration, rest, exercise, and other external factors on human physiology and cognition to determine how to manipulate them for performance enhancement (Shu et al. 2015). Furthermore, the superordinate aim of neuroenhancement in the military is usually not the welfare of the enhanced individual but rather the successful execution of missions and the accomplishment of military objectives (Annas and Annas 2008).

4.3 The dual-use problem

The advances in neuroscience significantly benefit society on the one side and offer potential applications for military and law enforcement on the other. The Royal Society's Brain Waves project (Royal Society 2012) identified various ways neuroscience and neuropharmacology might be used for weaponization, performance enhancement or degradation. In the report, the Royal Society defined the dual-use problem as "intentional misuse," referring primarily to the cooptation of civilian technology for military purposes. Significantly, the report highlights several examples of ongoing, sustained, and specific interest in the research and development of incapacitating and advanced riot control agents, such as behavioral modulation, vomiting agents, knock-out agents, and psychoactive agents. To keep oversight of developments in neuroscience, the United States government has introduced the term Dual-Use Research of Concern (DURC). DURC is a classification for security-sensitive research in the life sciences with the goal of identifying science that can be expected to provide informational or technical resources for the development of threats to public health, individual safety, or national security (Ienca et al. 2018).

Tracking market drivers can forecast some aspects of how applied cognitive neuroscience technology might threaten national security. According to the National Research Council (2008), three market drivers are creating a demand for developing and delivering cognitive neuroscience technology goods and services (National Research Council 2008):

1) Health: Where the customers seek help addressing mental illness, brain disease and injury.
2) Enhancement: To gain a performance advantage or prevent decline.
3) Degradation: Where customers seeking advantage by degrading, temporarily or permanently, the cognitive abilities of others, thereby driving the development of cognitive degradation technologies.

Dual-use dilemmas are inherent to neuroscience. The problem of dual-use within the field is exacerbated by the fact that national security and military applications are not the only way to repurpose civilian neurotechnologies; non-state actors, malevolent individuals or groups are likely to misuse neuroscience and become a substantial risk in the near future (Ienca et al. 2018). Therefore, there is a need for increased monitoring and careful risk assessment in the context of dual-use neurotechnology to mitigate the risks of a disproportionate weaponization of neuroscience (Ienca and Andorno 2017, Ienca et al. 2018).

5 Weaponization of chemicals agents

In February 2022, Russia invaded Ukraine, causing the worst humanitarian crisis in Europe since the end of World War II. This invasion has amplified the concerns posed by Russia's demonstrated capability to produce chemical weapons, its large, diverse and expanding nuclear capabilities, as well as its continued assault on international non-proliferation tools and regimes. For instance, Russia has attempted to shield the Syrian government from accountability for the use of chemical weapons and deliberately attacked the legitimacy and authority of the Organisation for the Prohibition of Chemical Weapons (OPCW) and its attribution and investigative mechanisms (NATO 2022d). Therefore, unlike other recent conflicts in Libya, Afghanistan, and Yemen, the threat of chemical (including pharmaceutical-based) and radiological weapons use by state actors is higher than ever (Chai et al. 2022, NATO 2022d).

Any country with a chemical industry has the capability, if not the desire, to manufacture toxic chemicals. The majority of the technologies are old and described in the open literature (Department of Defense 1998). New means of warfare, combined with an increased understanding of, for example, the neural correlates of behavior and processes of sensation, cognition, and locomotion, allows for beneficial uses such as medical interventions and new avenues to influence these processes. Furthermore, advancements in drug administration provide novel ways of employing some agents, opening up new application spaces. Generally, two key factors influence the effective delivery of an agent – dissemination, which is the transport of the agent from the attacker to the immediate vicinity of the targeted person or persons, and uptake, which is the subsequent movement of the agent to its active site within the target (Royal Society 2012).

There are several possible routes for administering an agent, including direct injection, ingestion, cutaneous or other topical application, and inhalation (Royal Society 2012). Regarding the latter, the pulmonary route has attracted great interest today among formulation scientists, as it has evolved into an important targeted drug delivery platform for the delivery of therapeutic proteins and peptides (Chellappan et al. 2022). An important factor in the effectiveness of an agent is tailored dissemination to the specific type of agent, as it determines its efficiency. Regarding incapacitating agents, the inhalational route is of particular interest. Aerosolization of an incapacitating agent could meet various perceived operational requirements, including large-scale open-air dissemination for battlefield use, local area dispersal via a ventilation system for counterterrorism or hostage rescue purposes, as in the case of the Moscow theatre siege, and individual targeting for riot control purposes. For example, during the ongoing urban warfare conducted in Ukraine, opioid agents can be pumped into enclosed spaces to cause significant casualties among opposing warfighters or civilians trapped in apartment blocks, hospitals, subways, or bomb shelter complexes (Schiermeier 2002, Chai et al. 2022).

In theory, chemical agents, including pharmacological substances, can be used in covert attacks directed against military and political leadership to assassinate, degrade their ability to make sound decisions or manipulate them psychologically – and with the possibility of recruiting these military and political leaders surreptitiously (Quinn 2022). Likewise, advances in neuroscience may pave the way for new means of controlling populations and crowds, such as psychochemicals or directed-energy weaponry, to capacitate or modify behavior temporarily. There is also potential for states to regulate the people to comply with their policies and thus not riot (Krishnan 2016). Previously, the Joint Non-Lethal Weapons Directorate (JNLWD) has considered delivering some microencapsulated psychoactive drugs by shotgun, airburst munitions, or drone (Davison 2009). LSD and BZ have been of intense interest to the U.S. military, and they stockpiled BZ-containing cluster bombs and ammunition during the 1960s. However, BZ was declared obsolete in the 1970s, and no other psychochemical incapacitant has taken its place. Additionally, it is hypothesized that various calmatives also may be suitable as biochemical incapacitants. Suggested delivery mechanisms for calmatives (e.g., barbiturates and benzodiazepines) include application to drinking water, topical administration to the skin, an aerosol spray inhalation route, or a drug-filled rubber bullet (Lakoski et al. 2000). Even though calmatives and other pharmaceutical agents have the potential to induce desirable military effects, numerous practical challenges limit their usage.

The controlled delivery of incapacitating chemical agents remains a key challenge for those who seek to develop such weapons. There are several crucial differences between drug delivery in a clinical and a weapons context (Royal Society 2012). Such challenges include delivering the appropriate concentration in the right places (dose-response), having unpredictable effects, and a given drug's pharmaceutical window. For instance, the therapeutic index, the ratio of the lethal dose to the effective dose of a drug, should theoretically allow estimating the safety margin. However, the outcome of the Moscow theater operation suggests otherwise. When considered a complete weapon system in an operational context, there are further challenges to developing a safe incapacitating chemical agent. There will always be uncontrollable variables such as the diverse body masses, health and age of the target population, in addition to the possibility of secondary injury and the requirement for medical aftercare (Royal Society 2012). The inability to provide uniform dosing to individuals when administered on a large scale would result in various clinical effects among mass casualties (Lee and Kulkarni 2016).

Microencapsulation is one technique developed that can possibly enhance chemical agents' stability, penetration and release into an organism. The aim is to cover a CWA microdroplet with a biologically degradable polymer envelope, a technique used in manufacturing pharmaceutical products for targeted drug delivery. The dissemination can be carried out by producing an aerosol cloud that penetrates the respiratory tract before the envelope is dissolved and the CWA is released. Microencapsulation technology can also easily be used to deliver incapacitants; thus, it is intensively studied (Davison 2007, Pitschmann 2014).

Another critical challenge is that the effective dissemination of an agent is not necessarily compatible with effective uptake. A remaining obstacle that prevents delivery of certain chemicals to the brain is the blood-brain barrier. This barrier restricts the passage of many molecules and microorganisms from the bloodstream into neural tissue, protecting the brain from harm and many common infections. However, advances in nanotechnology-based drug delivery systems demonstrate the potential to deliver peptides to the brain (Alshawwa et al. 2022, Ayub and Wettig 2022, Royal Society 2012).

Concerns have been raised regarding whether breakthroughs in drug delivery, notably with nanomedicines and the development of nanoparticles that can target specific types of cells, may enable the weaponization of substances previously dismissed as chemical warfare agents and incapacitating agents (Royal Society 2012, Caster et al. 2017). The concept is that developing nanoparticles that target specific cell types could lead to the weaponization of toxic chemicals. However, assessing this concern through monitoring progress in nanomedicines presents challenges. For practical reasons, the nanoparticles used in medicines are limited due to the need to minimize drug toxicity and side effects. Additionally, nanoparticle development as treatment is intended for medical use. Thus, particle delivery occurs under controlled conditions, in controlled doses, and under the supervision of a medical doctor. These requirements differ from those that could be desirable for dispersing nanoparticles over a large region as a weapon. Furthermore, it is estimated that 50% of pre-clinical research is not reproducible; implying that developing targeted drug delivery is difficult even in accredited facilities. Therefore, nanomedicine is unlikely to pose a threat to the CWC currently (Park 2019, Germain et al. 2020, Alshawwa et al. 2022).

However, due to its many advantages, there is a significant scientific focus on developing nanocarriers as drug delivery systems (Alshawwa et al. 2022, Ayub and Wettig 2022, Banthia et al. 2022). While the application of this research in the development of incapacitating chemical agents remains unclear, it is a rapidly advancing field and should be closely monitored. Notably, there should be a focus on advances in pulmonary drug delivery systems using nanocarriers (Royal Society 2012, Germain et al. 2020, Chellappan et al. 2022) due to the prospect of weaponizing aerosols.

6 Regulation of the use of chemicals as weapons

Many of the chemical agents addressed in this paper are subject to stringent regulations. According to United Nations Security Council resolution 1540 (2004), UN member states are required to establish domestic controls to prevent the proliferation of nuclear, chemical, or biological weapons and their means of delivery. Thus, UN member states must exercise export control to hinder such proliferation. Furthermore, each State Party to the CWC must adopt the necessary measures to implement its obligations under the convention, including establishing a national authority that must declare activities with scheduled chemicals, including transfers outside its territory, to OPCW.

According to the Single Convention on Narcotic Drugs (1961), as amended by the 1972 protocol, and the Convention of Psychotropic Substances (1971), a Party to the conventions shall apply a range of measures of control to scheduled drugs. The 1925 Geneva Protocol prohibits "the use in war of asphyxiating, poisonous, or other gases and of all analogous liquids, materials or devices" and "bacteriological methods of warfare." The treaty prohibited the employment of chemical and biological agents and weapons in warfare, intending to prevent a repetition of the atrocities committed by the belligerents during WWI. However, the Geneva Protocol of 1925, like other agreements before it, was not a disarmament treaty; instead, it was an arms control agreement. Therefore, it banned the use of chemical and biological agents and weapons in war, but did not prohibit their development, production, research or possession.

Some states ratified the protocol subject to the fact that it shall cease to be binding for them concerning the use of chemical agents if an enemy state or any of its allies does not respect the prohibitions contained in the protocol (USA) or ratified subject to that the protocol is only binding for states that have ratified or acceded to the protocol (The Soviet Union). For that reason, the Biological Weapons Convention (BWC) of 1972 and the CWC of 1993 later supplemented the protocol (Ilchmann and Revill 2014, OPCW 2020, United Nations 2022).

The CWC defines for the purposes of the convention "chemical weapons" (OPCW 2020):

1. “Chemical Weapons” means the following, together or separately:

> *a) Toxic chemicals and their precursors, except where intended for purposes not prohibited under this Convention, as long as the types and quantities are consistent with such purposes;*
>
> *b) Munitions and devices, specifically designed to cause death or other harm through the toxic properties of those toxic chemicals specified in subparagraph (1), which would be released as a result of the employment of such munitions and devices;*

c) Any equipment specifically designed for use directly in connection with the employment of munitions and devices specified in subparagraph (b).

2. "Toxic chemical" means:

Any chemical which through its chemical action on life processes can cause death, temporary incapacitation or permanent harm to humans or animals. This includes all such chemicals, regardless of their origin or of their method of production, and regardless of whether they are produced in facilities, in munitions or elsewhere.

7. "Riot Control Agent" means:

Any chemical not listed in a Schedule, which can produce sensory irritation or disabling physical effects rapidly in humans and which disappear within a short time following termination or exposure.

9. "Purposes Not Prohibited Under this Convention" means:

(a) Industrial, agricultural, research, medical, pharmaceutical or other peaceful purposes;

(b) Protective purposes, namely those purposes directly related to protection against toxic chemicals and to protection against chemical weapons;

(c) Military purposes not connected with the use of chemical weapons and not dependent on the use of the toxic properties of chemicals as a method of warfare,

(d) Law enforcement including domestic riot control purposes.

The CWC bans the development, production, acquisition, stockpiling, transfer, and use of chemical weapons (as defined by the convention) and requires all possessor states to destroy their stockpiles. The OPCW serves as the implementing body of the CWC and inspects and monitors State Parties' facilities and activities relevant to the convention to ensure compliance (OPCW 2020).

Thus, except when intended for purposes not prohibited under the CWC and as long as the types and quantities are consistent with such purposes, the convention explicitly prohibits production, acquisition, stockpiling, transfer, and use of toxic chemicals – including chemicals not listed on a schedule in the CWC Annex on Chemicals. Therefore, it comprehensively covers all hostile uses of agents, existing and future ones, which rely on toxicity to cause harm.

Two of the purposes not prohibited are, firstly, chemicals used for industrial, agricultural, research, medical, pharmaceutical or other peaceful purposes. Thus, many chemicals that may be used as cognitive weapons, such as fentanyl, are pharmaceuticals. Secondly, employment of chemicals by law enforcement, notably domestic riot control agents. In general, the use of RCA as a weapon in warfare is prohibited by the CWC, but their manufacture, stockpiling and use as domestic riot control agents are allowed, as long as the types and quantities are consistent with such purpose. According to Article 1 of the Convention, paragraph 5, "Each State Party concur not to use riot control agents as a method of warfare."

Regarding the more general exemptions for law enforcement and pharmaceutical purposes as purposes not prohibited, there is serious concern that development, manufacturing, stockpiling and use by law enforcement of pharmaceuticals can be used as cover for developing pharmaceutical-based agents (PBAs) or more specifically central nervous system-acting chemicals (hereinafter CNS-acting chemicals) as new types of chemical agents. As a barrier in preventing the re-emergence of chemical weapons, including new types, the Conference of the States Parties (to the CWC) decided in 2021 that aerosolised use of CNS-acting chemicals is understood to be inconsistent with law enforcement purposes as a "purpose not prohibited" under the convention. CNS-acting chemicals differ from RCA and do not meet the definition of RCA, as they act primarily on the central nervous system, and their effects are not usually confined to sensory irritation of a temporary nature. Such chemicals can have a very low safety margin when delivered as an aerosol, based on factors including uneven dissemination, variability in human response, and a need for rapid onset of action. Their aerosolized use in law enforcement is thus inconsistent with the convention.

Biological and chemical weapons control has traditionally been viewed as a balancing act between the desire to 'completely eliminate' the possibility of such weapons being used and the need to promote, or at the very least not obstruct, socially beneficial applications of chemical and biological sciences and technologies (Ilchmann and Revill 2014).

7 Avenues for future research

The chemical weapon threat is multifaceted, encompassing military-grade agents, novel incapacitating agents, and TICs. Since development, production and stockpiling of toxic chemicals for industrial, agricultural, research, medical, pharmaceutical or other peaceful purposes are not prohibited by the CWC (except when types and quantities are not consistent with such purposes or the purpose is for the development of chemical weapons), there exists room for misuse of chemicals. New chemical hazards providing diverse threats can be developed while hidden in a legitimate chemical production facility, e.g., PBA. In a world of hybrid war, it is all more possible. There are already a considerable number of known harmful chemicals and examples of their weaponization (Lindsay et al. 2016). For example, fentanyls and its derivatives, or calmatives, could be used to cause harm or used as a biochemical incapacitant. However, to assess how chemicals, such as pharmaceuticals, might be used in cognitive warfare, requires attention to both the existing and new. It also requires a holistic view that considers science and technology's practical capabilities and limitations (Forman and Timperley 2018).

The Center for the Study of Weapons of Mass Destruction has concluded that within the year 2030, chemical agents will be more accessible to state and non-state actors due to lower barriers to acquiring current and emerging relevant technologies. Further, chemical agents (not including CWAs) will be more capable, particularly in terms of their ability to defeat current or currently emerging defensive countermeasures by being able to, e.g., circumvent import/export control and watch lists (Caves Jr and Carus 2014). New technologies may also allow for improving current non-lethal techniques, which need a higher degree of specificity, safety and reversibility to avoid producing a lasting impairment to a subject (Caves Jr and Carus 2014, Dando 2015).

In contrast to the chemical warfare agents used on the battlefield during WWI, in the age of hybrid warfare, numerous chemicals may be used as weapons in altering cognition, thereby; as a result, altering behavior at the individual and potentially even societal level. A significant challenge for adversaries who seek to weaponize pharmaceuticals is achieving effective delivery and uptake of the agent. Therefore, pharmaceutical developments and advances in drug delivery systems should be closely monitored, especially technologies that allow drugs to cross the blood-brain barrier, improve delivery precision, bypass immune system defenses, evade metabolism, or prolong effects at cellular or downstream targets. Furthermore, advances in drug delivery technologies will increase the likelihood that certain peptides or other brain proteins may be used as drugs in the future. Therefore, developing antidotes or protective agents against several classes of pharmaceuticals that an enemy force could use will be crucial.

Similarly, the majority of human enhancement opportunities originate from advances in medical research technologies to treat injury and disease. Repurposing medical technologies for human enhancement is inevitable because some actors aim to be the first to employ any potential competitive advantage (Friedl 2009). For example, the U.S. Department of Defence has engaged in cognitive enhancement R&D for over a century, exploring novel pharmaceutical, dietary, neuroscientific, instructional, technological, and sleep-related enhancement strategies (Brunyé et al. 2020). Because at the heart of all human performance is the warfighter's brain, with critical roles in how stressors are perceived, how this information is translated and affects physiology, and how behaviors of the individual, in turn, affect brain physiology (Lieberman et al. 2006, McEwen et al. 2015). However, although NATO's special operation forces operators are required to perform a broad range of physically and mentally challenging specialized training and missions, mental performance programming is less common (NATO 2021).

Notably, there is a shifting focus on cyberwarriors and themes of "cognitive dominance", meaning intellectual advantage over a situation or adversary (U.S. Army Combined Arms Center 2014, NATO 2023). Moreover, advances in nanotechnology and computational methods leading to new drug delivery systems with precisely defined parameters regulating release timing, location, and secretion rates can enable further enhancement of warfighters' cognition. As a result, warfighters could be pharmacologically enhanced by giving prophylaxes or antidotes for neurotoxic chemicals and other combat threats with high precision (Saxena et al. 2006). However, while the risks associated with some performance-enhancing drugs are generally well understood, their nonmedical use in healthy individuals may present significant health risks, especially in previously untested doses and combinations (Friedl 2009). Additionally, most research on cognitive enhancement focuses on countering a loss of cognitive function from a medical perspective, e.g., dementia. Therefore, military R&D on human performance enhancement must foster a thorough understanding of the risks and the possibilities for tactical advantages.

8 Conclusion

Chemical agents used in war are not new. However, new attack vectors are emerging in cognitive warfare due to the integration and convergence of multiple technological advancements and the expanding accessibility of information and technology. Cognitive warfare elevates well-known methods used in warfare to a new level by aiming to change and mold how people think, act, and make decisions. Due to its invasive, intrusive, and covert character, cognitive warfare has evolved, posing a number of challenges to national security and defense. Its goal is to exploit facets of cognition to disrupt, undermine, influence, or modify human decisions.

Based on open published scientific literature, this report shows that it is possible to achieve the goal of adversarial cognitive warfare by using chemical agents as attack vectors. The adversary doing cognitive warfare operates under different ethical boundaries than liberal democracies, which results in significant asymmetries. Therefore, to acquire and preserve national and NATO's situational awareness and cognitive superiority, it is essential to increase our understanding of how adversaries can engage in novel ways to target human cognition through chemical agents, and thereby gain insight regarding the development and validation of countermeasures and defensive strategies.

The main findings in this report are:

- The rapidly advancing field of drug development and drug delivery systems should be closely monitored due to the inherent dual-use issue of neuroscience.

- There is a wide range of chemicals that can be used to enhance or degrade cognition. However, there is a key challenge of controlled delivery and uptake for both the development and use of such agents.

- Research-based knowledge is needed to obtain a more in-depth understanding of potential cognitive weapons to counteract their development and the effects of chemicals that can affect cognition. This is critical because NATO's adversaries do not necessarily operate under the same ethical standards and values as liberal democracies.

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The Norwegian Defence Research Establishment (FFI) was founded 11th of April 1946. It is organised as an administrative agency subordinate to the Ministry of Defence.

FFI's mission

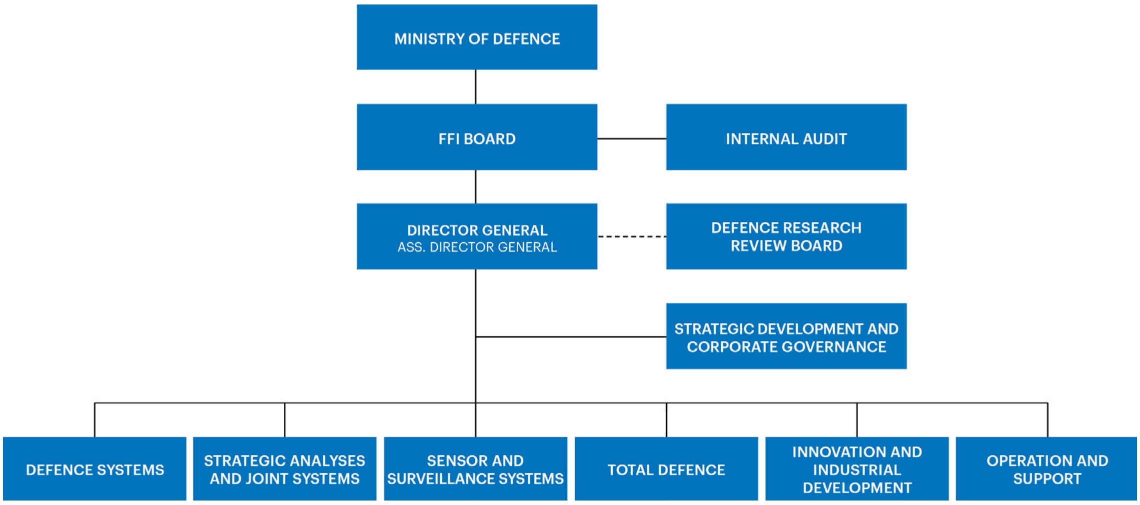
FFI is the prime institution responsible for defence related research in Norway. Its principal mission is to carry out research and development to meet the requirements of the Armed Forces. FFI has the role of chief adviser to the political and military leadership. In particular, the institute shall focus on aspects of the development in science and technology that can influence our security policy or defence planning.

FFI's vision

FFI turns knowledge and ideas into an efficient defence.

FFI's characteristics

Creative, daring, broad-minded and responsible.



Forsvarets forskningsinstitutt (FFI)
Postboks 25
2027 Kjeller

Besøksadresse:
Kjeller: Instituttveien 20, Kjeller
Horten: Nedre vei 16, Karljohansvern, Horten

Telefon: 91 50 30 03
E-post: post@ffi.no
ffi.no

Norwegian Defence Research Establishment (FFI)
PO box 25
NO-2027 Kjeller
NORWAY

Visitor address:
Kjeller: Instituttveien 20, Kjeller
Horten: Nedre vei 16, Karljohansvern, Horten

Telephone: +47 91 50 30 03
E-mail: post@ffi.no
ffi.no/en